

# Serum Sodium Level and Its Correlation with Curb-65 Score in Community Acquired Pneumonia – A Study from Bangalore, India

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## ABSTRACT

### BACKGROUND

Community acquired pneumonia (CAP) refers to pneumonia contracted by a person with little or no contact with health care system. Severity scores like CURB 65 severity score are useful in estimating the outcome. Hyponatremia is defined as serum sodium level < 135 mEq/L. 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). Hence this study is an effort to explore how hyponatremia is associated with severity and outcomes, in hospitalized patients with pneumonia. The purpose of this study was to assess the proportion of hyponatremia in patients with community acquired pneumonia and compare hyponatremia with CURB-65 as an initial screening tool for assessment of severity of CAP.

### METHODS

This is a hospital-based cross-sectional study. 75 community acquired pneumonia patients admitted as inpatients are included in this study. Information is collected and detailed history is taken using pre-formed proforma at the time of admission. Serum sodium levels were measured, after initial assessment of patients. The lab values of serum sodium levels were analysed with the clinical profile and outcome in these study groups.

### RESULTS

In our study, it was observed that as the sodium levels are decreasing, the CURB 65 score increases. Study subjects who had sodium levels < 125 mg/dl, presented with CURB 65 score as 4 (30 %). Inversely, the study subjects with high sodium levels (> 135 mg/dl) had CURB 65 scores as 1 (75 %). The association between sodium levels and CURB 65 score was significant in patients who got discharged but not in patients who expired.

### CONCLUSIONS

Present study of serum sodium levels as biomarkers in CAP showed that hyponatremia carried poor prognosis which correlated with high CURB 65 score.

### KEYWORDS

Sodium, Community Acquired Pneumonia, SIADH, CURB 65, Hyponatremia, COPD

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*DOI: 10.18410/jebmh/2021/497*

*How to Cite This Article:*

*Rajanna AH, Rajoli S, Gurav NA. Serum sodium level and its correlation with Curb-65 score in community acquired pneumonia – a study from Bangalore, India. J Evid Based Med Healthc 2021;8(30):2702-2707. DOI: 10.18410/jebmh/2021/497*

*Submission 22-03-2021,  
Peer Review 02-04-2021,  
Acceptance 09-06-2021,  
Published 26-07-2021.*

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## BACKGROUND

Community acquired pneumonia is 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 lungs. It refers to pneumonia contracted by a person with little or no contact with health care system. Groups with highest risk of morbidity and mortality with CAP include infants, elderly and inhale corticosteroids (ICS). Predisposed by chronic obstructive pulmonary disease (COPD), smoking, diabetes and structural lung disease etc. The risk factors for early deterioration in community acquired pneumonia are hypoalbuminemia, neutropenia, thrombocytopenia, hyponatremia, hypoglycaemia, multilobar infiltrates, severe hypoxemia (SPO<sub>2</sub> < 90), mental confusion and severe tachypnea.<sup>1</sup>

Severity scores like CURB 65 severity score<sup>1</sup> are useful in estimating the outcome. Chest X ray is a useful tool in diagnosis of pneumonia with its correlation with clinical findings and laboratory values. Tests include sputum smear Gram staining, acid-fast bacilli (AFB), sputum and blood culture. > 50 % cases, specific aetiology is not identified.<sup>2</sup> Identified pathogens in community acquired pneumonia are streptococcus pneumoniae (most common), *Haemophilus influenza*, *Staphylococcus aureus*, gram negative bacilli, Legionella species, *Mycoplasma pneumoniae*, Chlamydia, viruses, aspiration. Hyponatremia, which is defined as a plasma Na<sup>+</sup> concentration < 135 mEq is a very common disorder, occurring in up to 22 % of hospitalized patients is the most common electrolyte imbalance seen in clinical practice.<sup>3</sup> It frequently accompanies pulmonary diseases, both infectious and neoplastic.<sup>4</sup> 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).

Various other pulmonary disorders have been associated with SIADH especially tuberculosis, advanced chronic obstructive lung disease, bronchiectasis. Hypoxia stimulated secretion of vasopressin in animals, but in humans, hypercarbia was more associated with abnormal water retention. Elevated vasopressin levels may be limited to the initial days of hospitalization, when respiratory failure is most marked. Therefore, with SIADH in nontumor pulmonary disease, pulmonary disease is obvious with severe dyspnoea or extensive radiographically evident infiltrates and the inappropriate antidiuresis is usually limited to the period of respiratory failure. Mechanical ventilation can cause inappropriate secretion of vasopressin and can worsen SIADH caused by other factors. The mechanism is thought to be decreased venous return.<sup>5</sup>

Hypoxia stimulated secretion of vasopressin in animals, but in human's hypercarbia was more associated with abnormal water retention.<sup>6</sup> Elevated vasopressin levels may be limited to the initial days of hospitalization, when respiratory failure is most marked. Therefore, with SIADH in nontumor pulmonary disease, pulmonary disease is obvious with severe dyspnoea or extensive radiographically evident infiltrates and the inappropriate antidiuresis is usually limited to the period of respiratory failure. Mechanical ventilation

can cause inappropriate secretion of vasopressin and can worsen SIADH caused by other factors. The mechanism is thought to be decreased venous return.

The presence of hyponatremia is associated with not only prolongation of hospitalization, but also an increase in hospital mortality, the incidence of which has been found to be 7 %.<sup>4</sup> Hence study of serum phosphate levels in community acquired pneumonia is of clinical significance.

## Objectives

1. To assess the proportion of hyponatremia in patients with community acquired pneumonia (CAP).
2. To compare hyponatremia with CURB-65 as an initial screening tool for assessment of severity of CAP.

## METHODS

A cross-sectional study, total of 75 patients from those attending medicine out-patient department (OPD) and getting admitted in medicine ward, Victoria & Bowring hospital, attached to Bangalore Medical College and Research Institute, from November 1<sup>st</sup> 2016 to August 30<sup>th</sup> 2018, satisfying the inclusion and exclusion criteria were selected.

## Inclusion Criteria

1. Patients willing to give written informed consent
2. Infiltrate on chest X ray taken at the time of admission
3. Presence of one or more major finding (cough with mucopurulent or haemoptysis, axillary temperature > 37.5-degree Celsius)
4. Presence of at least one minor finding (pleuritic chest pain, dyspnoea, decreased level of consciousness, WBC > 12000 cells/cum)

## Exclusion Criteria

1. Hospital acquired pneumonia.
2. Patients with pseudohyponatremia.
3. Patients with HIV positive status.
4. Patients with co-existing malignancies.
5. Patients taking drugs causing SIADH.
6. Patients with pulmonary tuberculosis.
7. Patients with other diagnosed causes of hyponatremia on admission.

All clinically diagnosed pneumonia patients requiring hospitalization based on CURB 65 scores were admitted and chest X ray proven cases were taken into this study. Before taking into the study, all patients had signed the informed consent. Routine haematological investigations along with serum sodium, chest X- ray were carried out. Patients were clinically assessed on day 1 and day 3 and their pulse, blood pressure, respiratory rate, temperature, sensorium level, signs of dehydration were noted.

The lab values of serial serum sodium levels, total counts and vital signs were analysed with the clinical profile and outcome in these study groups. The data was compiled & appropriate statistical tests were applied.

### Sample Size

Based on Mohammad E. Naffaa et al.  $p$  = proportion of patients who had hyponatremia (82 %) according to Mohammad E. Naffa et al.  $q$  = (100- $p$ ) and  $d$  = precision

$$n = \frac{(4pq)}{d^2}$$

$$n = \frac{(4 * 82 * 18)}{8.7^2} = 75$$

$n = 75$  (round off)

### Method of Statistical Analysis

The data was entered in Microsoft Excel sheet and was analysed using statistical package for social sciences (SPSS) version 22 software. The categorical data was represented in the form of frequency and percentage. Chi square test/Fisher's exact test was used to test the significance for qualitative data. Continuous data was represented as mean and standard deviation.  $P$  value < 0.05 was considered as significant.

## RESULTS

### Age and Sex Distribution of Patients

In the present study, majority of the study subjects belonged to the age group < 45 (33.3 %), followed by 24 % in the age group 65 – 74 years and males (53.3 %) outnumber females (46,7 %).

### Comorbidities and Risk Factors

Out of the total study subjects, 42.6 % of patients had no significant co morbidity. 29.3 % of patients were diabetic, 16 % patients were hypertensive, 14.6 % had both diabetes and hypertension, 14.6 % had COPD, 10.6 % patients had retroviral disease, 10.6 % patients had other co morbidities like old pulmonary tuberculosis, malignancy, interstitial lung disease and ischemic heart disease etc. 46.6 % of patients were chronic smokers, which goes with the well-known fact that smoking is an important risk factor for community acquired pneumonia.

### Clinical Parameters of Patients

Evaluation of vital data at the time of admission and on day 3 was recorded. The mean pulse rate of the study subjects on day 1 and day 3 was  $102.96 \pm 15.087$  and  $99.85 \pm 15.895$  respectively (Figure 1). The mean difference between the two pulse rate readings was  $3.107 \pm 15.470$ . The mean difference between the pulse rates with respect to time was not significant ( $P = 0.086$ ).

The systolic blood pressure of the study subjects on day 1 and day 3 was  $118.13 \pm 33.216$  and  $116.08 \pm 22.473$

respectively. The mean difference between the two systolic blood pressure readings was  $2.053 \pm 19.430$ . The mean difference between the systolic blood pressures with respect to time was not significant ( $P = 0.363$ ).

The diastolic blood pressure of the study subjects on day 1 and day 3 was  $76.59 \pm 16.723$  and  $77.28 \pm 10.073$  respectively. The mean difference between the two diastolic blood pressure readings was  $-0.693 \pm 13.741$ . The mean difference between the diastolic blood pressures with respect to time was not significant ( $P = 0.663$ ).

The mean respiratory rate of the study subjects on day 1 and day 3 was  $32.49 \pm 4.944$  and  $30.15 \pm 5.056$  respectively. The mean difference between the two respiratory rate readings was  $2.347 \pm 3.108$  (Figure 2). The mean difference between the respiratory rates with respect to time was significant ( $P = 0.001$ ).

Majority of the study subjects had haemoglobin in the range of 10.01 – 11.99 gm/dl (24 %), followed by 46.7 % with haemoglobin greater than 12 gm/dl (Table 1).

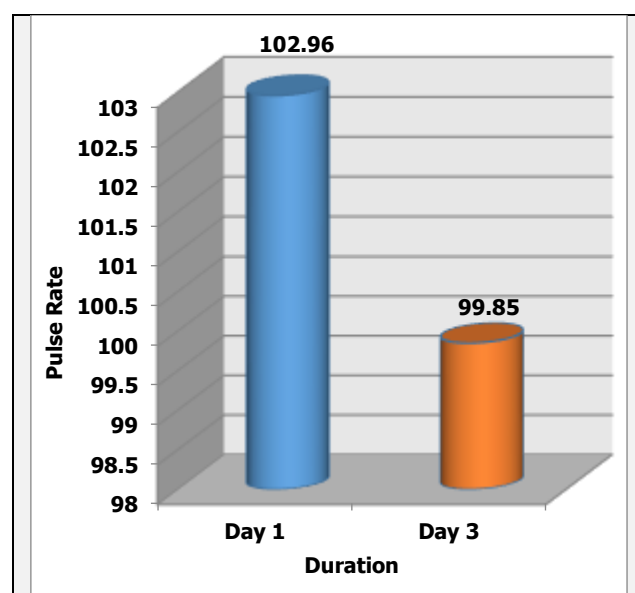


Figure 1. Mean Distribution of the Pulse Rate at Day 1 and Day 3

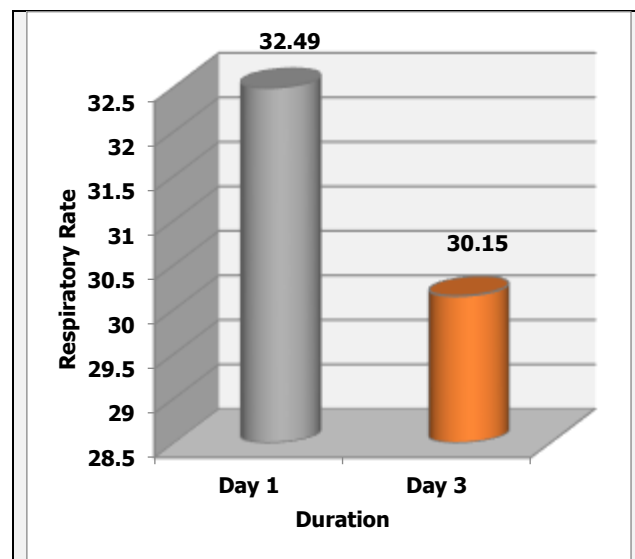


Figure 2. Mean Distribution of the Respiratory Rate at Day 1 and Day 3

Haemoglobin	Frequency	Percent
<9	11	14.7
9-10	11	14.7
10.01-11.99	18	24.0
> 12	35	46.7
<b>Total</b>	<b>75</b>	<b>100.0</b>

**Table 1. Haemoglobin (g/dl) Values in Study Patients**

TLC	CURB 65					Total	P Value
	0	1	2	3	4		
< 4000	0	0	0	2	0	2	0.186
	0.0 %	0.0 %	0.0 %	9.1 %	0.0 %	2.7 %	
4000 – 11000	4	7	5	7	3	26	
	50.0 %	50.0 %	45.5 %	31.8 %	15.0 %	34.7 %	
>	4	7	6	13	17	47	0.186
	50.0 %	50.0 %	54.5 %	59.1 %	85.0 %	62.7 %	
<b>Total</b>	<b>8</b>	<b>14</b>	<b>11</b>	<b>22</b>	<b>20</b>	<b>75</b>	
	100.0 %	100.0 %	100.0 %	100.0 %	100.0 %	100.0 %	

**Table 2. Total Counts Distribution in Different Study Points of Patients Studied**

The above table is presenting the association between TLC and CURB 65 score. It can be seen that the CURB 65 scores were high in the study subjects who had TLC > 11,000 (> 50 %) (Table 2). There was no statistical significance found between TLC and CURB 65 score (P – 0.186).

Urea (mg/dl)	Frequency	Percent
10 - 38	38	50.7
38.01 - 50	23	30.7
> 50	14	18.7
<b>Total</b>	<b>75</b>	<b>100.0</b>

**Table 3. Urea (mg/l) Distribution among Patients Studied on Admission**

Majority of the study subjects had urea levels in the range of 10 - 38 mg/dl (50.7 %), followed by 38.01 – 50 mg/dl (30.7 %) and > 50 mg/dl (18.7 %) (Table 3).

S. Albumin	CURB65					Total	P Value*
	0	1	2	3	4		
1.04 - 2.4	1	2	1	7	10	21	0.003
	12.5 %	14.3 %	9.1 %	31.8 %	50.0 %	28.0 %	
2.5 - 3.5	2	4	4	13	8	31	
	25.0 %	28.6 %	36.4 %	59.1 %	40.0 %	41.3 %	
3.6 - 6.8	5	8	6	2	2	23	0.003
	62.5 %	57.1 %	54.5 %	9.1 %	10.0 %	30.7 %	
<b>Total</b>	<b>8</b>	<b>14</b>	<b>11</b>	<b>22</b>	<b>20</b>	<b>75</b>	
	100.0 %	100.0 %	100.0 %	100.0 %	100.0 %	100.0 %	

**Table 4. Correlation between CURB 65, Albumin Levels and Outcome**

\*Chi square test

CXR	CURB65					Total	P value
	0	1	2	3	4		
Single lobe involvement	6	13	10	14	8	51	0.007*
	75.0 %	92.9 %	90.9 %	63.6 %	40.0 %	68.0 %	
>1lobe involvement	2	1	1	8	12	24	
	25.0 %	7.1 %	9.1 %	36.4 %	60.0 %	32.0 %	
<b>Total</b>	<b>8</b>	<b>14</b>	<b>11</b>	<b>22</b>	<b>20</b>	<b>75</b>	
	100.0 %	100.0 %	100.0 %	100.0 %	100.0 %	100.0 %	

**Table 5. Cross-Tabulation of Chest X Ray Features and CURB 65 Score**

\*chi-square test

The table shows the association between S. albumin and CURB 65 scores. 50 % of the study subjects had S. albumin in the range of 1.04 – 2.4 and CURB 65 score of 4. Among the study subjects with S. albumin in the range of 2.5-3.5 mg/dl, 59.1 % had CURB 65 score of 3, followed by 40 % (CURB 65 – 4) and 36.4 % (CURB 65 – 3). Those who had

normal albumin levels (3.6-6.8) had less CURB 65 scores. Chi square test results showed that the association between S. albumin and CURB 65 scores are statistically significant (P – 0.003) (Table 4).

CXR single lobe involvement was seen in high number (68 %). More than one lobe involvement was seen in 32 % of the study subjects. The CURB 65 scores were high in number in single lobe involvement except with CURB 65 score of 4 where the study subjects had more than one lobe involvement (60 %). The association between CURB 65 scores and chest X ray findings was significant (P – 0.007) (Table 5).

Outcome	Na +	CURB 65					Total	P Value
		0	1	2	3	4		
Discharged	< 125	0	0	1	1	5	7	0.000
		0.0 %	0.0 %	9.1 %	5.6 %	41.7 %	11.1 %	
	125 – 129	1	0	0	9	3	13	
		12.5 %	0.0 %	0.0 %	50.0 %	25.0 %	20.6 %	
	130 – 134	1	4	3	6	3	17	
		12.5 %	28.6 %	27.3 %	33.3 %	25.0 %	27.0 %	
	>135	6	10	7	2	1	26	
		75.0 %	71.4 %	63.6 %	11.1 %	8.3 %	41.3 %	
Death	<b>Total</b>	<b>8</b>	<b>14</b>	<b>11</b>	<b>18</b>	<b>12</b>	<b>63</b>	0.771
		100.0 %	100.0 %	100.0 %	100.0 %	100.0 %	100.0 %	
	< 125	0	0	0	0	1	1	
		0.0 %	0.0 %	0.0 %	0.0 %	12.5 %	8.3 %	
	125 – 129	0	0	0	2	2	4	
		0.0 %	0.0 %	0.0 %	50.0 %	25.0 %	33.3 %	
	130 – 134	0	0	0	1	2	3	
		0.0 %	0.0 %	0.0 %	25.0 %	25.0 %	25.0 %	
Total	>135	0	0	0	1	3	4	0.000
		0.0 %	0.0 %	0.0 %	25.0 %	37.5 %	33.3 %	
	<b>Total</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>4</b>	<b>8</b>	<b>12</b>	
		0.0 %	0.0 %	0.0 %	100.0 %	100.0 %	100.0 %	
	< 125	0	0	1	1	6	8	
		0.0 %	0.0 %	9.1 %	4.5 %	30.0 %	10.7 %	
	125 – 129	1	0	0	11	5	17	
		12.5 %	0.0 %	0.0 %	50.0 %	25.0 %	22.7 %	
Total	130 – 134	1	4	3	7	5	20	0.000
		12.5 %	28.6 %	27.3 %	31.8 %	25.0 %	26.7 %	
	>135	6	10	7	3	4	30	
		75.0 %	71.4 %	63.6 %	13.6 %	20.0 %	40.0 %	
	<b>Total</b>	<b>8</b>	<b>14</b>	<b>11</b>	<b>22</b>	<b>20</b>	<b>75</b>	
		100.0 %	100.0 %	100.0 %	100.0 %	100.0 %	100.0 %	

**Table 6. Sodium (mEq/l) Distribution among Patients Studied on Admission**

The table present the association between Sodium, outcome of the study subjects and CURB 65 score. It can be observed that as the sodium levels are decreasing, the CURB 65 score increases. Study subjects who had sodium levels < 125 mg/dl, presented with CURB 65 score as 4 (30 %). Inversely, the study subjects with high sodium levels (> 135 mg/dl) had CURB 65 scores as 1 (75 %) (Table 4). The association between sodium levels among discharged study subjects and CURB 65 scores was significant (P < 0.001) but the association between sodium levels among study subjects who died and CURB 65 scores was not significant (P – 1.000) (Table 6).

## DISCUSSION

CAP is the second most common cause of death from infectious diseases in India and the leading cause of childhood mortality. The 2014 World health organization (WHO) Global burden of disease study shows global burden

of lower respiratory tract infections (LRTIs), were 429.2 million episodes of illness which included CAP. It shows 94.5 million disability adjusted life years (DALYs) in adults aged over 59 years, with an annual mortality of 1.6 million.<sup>7</sup>

Our study included age groups above 18 years. Majority of the study subjects belonged to the age group < 45 years (33.3 %), followed by the age group 65 – 74 years (24 %). Least number of subjects were in age group > 75 years. Males (53.3 %) outnumbered females (46.7 %) in the present study. Out of the total study subjects, 42.6 % of patients had no significant co morbidity. 29.3 % of patients were diabetic, 16 % patients were hypertensive, 14.6 % had both diabetes and hypertension, 14.6 % had COPD, 10.6 % patients had retroviral disease, 10.6 % patients had other co morbidities like old pulmonary tuberculosis, malignancy, interstitial lung disease and ischemic heart disease etc. 46.6 % of patients were chronic smokers, which goes with the well-known fact that smoking is an important risk factor for community acquired pneumonia and most of these patients were having history of smoking for 5-10 year. The CURB 65 score was less in patients who had no past history (75 %). The highest score of CURB 65 was seen in patients who had past history of retroviral diseases (RVD) (30 %), followed by COPD with other risk factors (20 %). The association between past history and CURB 65 along with the outcome was not significant ( $P > 0.005$ ).

Majority of the study subjects had haemoglobin in the range of 10.01 – 11.99 gm/dl (24 %), followed by 46.7 % with haemoglobin greater than 12 gm/dl. It was observed that the CURB 65 scores were high in the study subjects who had TLC > 11,000. (> 50 %) There was no statistical significance found between TLC and CURB65 score ( $P = 0.186$ ). Urea levels in majority of the study subjects were in the range of 10 - 38 mg/dl (50.7 %), followed by 38.01 – 50 mg/dl (30.7 %) and > 50 mg/dl (18.7 %). In a study on adult patients with pneumonia at Papua New Guinea showed elevation of blood urea levels in 55 % of bacteraemic and 26 % of non bacteraemic pneumonia. This observation was more so in patients with extensive consolidation and the cause was attributed to both pre renal and renal mechanisms causing elevated blood urea levels.

Single lobe involvement was seen in high number (68 %). More than one lobe involvement was seen in 32 % of the study subjects. The CURB 65 scores were high in number in single lobe involvement except with CURB 65 score of 4 where the study subjects had more than one involvement (60 %). The association between CURB 65 scores and chest X ray findings was significant ( $P = 0.007$ ). In a study done by Mustafa el-Ebiary et al. on community acquired pneumonia patients showed that the extent of Chest X ray infiltration was one of many significant prognostic indicators in CAP.<sup>8</sup>

### Sodium Analysis

Analysis of Sodium in pneumonia was done. The normal range taken for adults was 135-145 mEq/L and all patients with sodium < 135 were considered to have hyponatremia. On admission 26.7 % of patients had serum Sodium levels

between 130 to 134, 22.7 % had levels between 125 - 129, and 10.7 % of them had levels less than 125 mEq/L

### Sodium Level and CURB 65 Scores

It can be observed that as the sodium levels are decreasing, the CURB 65 score increases. Study subjects who had sodium levels < 125 mg/dl, presented with CURB 65 score as 4 (30 %). Inversely, the study subjects with high sodium levels (> 135 mg/dl) had CURB 65 scores as 1 (75 %) (Table 4). The association between sodium levels among discharged study subjects and CURB 65 scores was significant ( $P < 0.001$ ) but the association between sodium levels among study subjects who died, and CURB 65 scores was not significant ( $P = 1.000$ ).

A study done by Marya D Zilberberg et al 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 %).<sup>9</sup> A study conducted by Jayaraj Patil et al. in 2015 showed that the incidence of hyponatremia in pneumonia is 26 %. (n = 300). In this study out of the severely affected pneumonic patients, nearly 95 % of them (18 out of 19) suffered from hyponatraemic imbalance.<sup>10</sup>

## CONCLUSIONS

Present study of serum sodium levels as biomarkers in CAP showed that hyponatremia carried poor prognosis which correlated with high CURB 65 score. Normal sodium levels in CAP patients had low CURB65 score and carried better prognosis. Patients who had diabetes, COPD, retroviral disease, smoking etc. had significant risk of developing CAP according to the study.

### Limitation

Sample size was small, and it was a single centre study.

Data sharing statement provided by the authors is available with the full text of this article at jebmh.com.

Financial or other competing interests: None.

Disclosure forms provided by the authors are available with the full text of this article at jebmh.com.

The authors take this opportunity to thank Department of Medicine for their whole hearted support for this study.

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