# ORIGINAL ARTICLE

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# A study of serum phosphate levels and its correlation with curb-65 score in community acquired pneumonia



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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. Phosphorus is an essential molecule in ATP, playing a central role in energy production. A normal range is 2.5 to 4.5 mg/dl. Phosphate disturbance are noted in patients with pneumonia. Hypophosphatemia, plays a role in impairing chemotaxis, phagocytosis and bactericidal activity of macrophages. Hyperphosphatemia in pneumonia result in hypocalcaemia and pulmonary calcification. Hence study of serum phosphate levels in community acquired pneumonia is of clinical significance. Aims and Objective: The was aimed to estimate the levels of serum phosphate in patients with community acquired pneumonia and to correlate serum phosphate levels with CURB 65 severity score. Materials and Methods: Seventy-five CAP patients admitted as inpatients are included in this study. Chest X ray is obtained in all suspected cases. Serum phosphate levels are determined through blood investigation on Day 1 and Day 3. Results: Serum phosphate levels on Day 1 and Day 3 were significantly associated with CURB65 score. Both high and low phosphate levels were associated with high CURB 65 score. The association between phosphate levels and CURB 65 score was significant in patients who got discharged but not in patients who expired. Conclusions: Present study of serum phosphate levels as biomarkers in CAP showed that both hypophosphatemia and hyperphosphatemia carried poor prognosis which correlated with high CURB65 score.



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Hyperphosphatemia; COPD

Key words: Community acquired pneumonia; CURB65; Hypophosphatemia;

# **INTRODUCTION**

Community acquired pneumonia 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 ICS. Predisposed by COPD, smoking, diabetes and structural lung disease etc. The risk factors for early deterioration in community acquired pneumonia are hypoalbuminemia, neutropenia, thrombocytopenia, hyponatremia, hypoglycemia, multilobar infiltrates, severe hypoxemia (SPO2 <90), mental confusion, 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, AFB, Sputum and blood culture. >50% cases, specific etiology 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.

Phosphorus is an essential molecule in ATP, playing a central role in energy production. A normal range is

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generally 2.5 to 4.5 mg/dl. Phosphate disturbance are noted in patients with pneumonia. Hypophosphatemia, which plays a role in impairing chemotaxis, phagocytosis and bactericidal activity of macrophages. Fisher et al found that hypophosphatemia is associated with longer hospital stay.<sup>3</sup>

Hyperphosphatemia in pneumonia is less widely studied and may result in hypocalcemia and pulmonary calcification. Saldias et al showed that hyperphosphatemia as a poor prognostic indicator in pneumonia.<sup>4</sup> Di Marco et al have reported that high phosphorus levels can impair endothelial cell function at several levels including induction of sustained stiffening, increased apoptosis, impaired angiogenesis, impaired cell migration, downregulation of extracellular annexin II expression and shedding of endothelial microparticles.<sup>5</sup> Hence study of serum phosphate levels in community acquired pneumonia is of clinical significance

#### Aims and Objective

The was aimed to estimate the levels of serum phosphate in patients with community acquired pneumonia and to correlate serum phosphate levels with CURB65 severity score.

# MATERIALS AND METHODS

A total of 75 patients from those attending medicine OPD and getting admitted in medicine ward, Victoria &Bowring hospital, attached to Bangalore medical college and research institute, during the period of November 1st 2016 to august 30<sup>th</sup> 2018 will be taken for study, satisfying the inclusion and exclusion criteria.

#### **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 hemoptic sputum, axillary temperature >37.5 degree celsius)
- Presence of at least one minor finding (pleuritic chest pain, dyspnea, decreased level of consciousness, WBC > 12000 cells/cum)

#### **Exclusion criteria**

- 1. Age <18 yrs
- 2. Transferred from another hospital
- 3. Prior hospitalization within a duration of 30 days
- 4. Hospital acquired pneumonia
- 5. Patients with deranged RFT or any other conditions causing change in phosphate, calcium levels

All clinically diagnosed pneumonia patients requiring hospitalization based on CURB 65 scores were admitted

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and chest X ray proven cases were taken into this study. Before taking into the study, all patients had signed the informed consent.

Routine hematological investigations along with serum calcium and phosphate levels on day 1 and day 3, 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 phosphate levels, total counts and vital signs were analyzed with the clinical profile and outcome in these study groups. The data was compiled & appropriate statistical tests were applied.

Sample size: 
$$n = \frac{(4pq)}{d^2}$$
  
 $n = \frac{(4*72*28) = 70.43}{10.7^2}$ 

n=75 (round off)

#### **Statistical analysis**

The data was entered in Microsoft excel sheet and was analysed using 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%) outnumbered females (46. 7%).

#### Co morbidities and risk factors

Out of the total study subjects, 42.6 % of patients had no significant co morbidity. Twenty-nine point three percent 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 + 15.087 and 99.85+ 15.895 respectively. The mean difference between the two pulse rate readings was 3.107 + 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 + 33.216 and 116.08 + 22.473 respectively. The mean difference between the two systolic blood pressure readings was 2.053 + 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+16.723 and 77.28+10.073 respectively. The mean difference between the two diastolic blood pressure readings was -0.693+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+4.944 and 30.15+5.056 respectively. The mean difference between the two respiratory rate readings was 2.347 + 3.108. The mean difference between the respiratory rates with respect to time was significant (p - 0.001).

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

Table 2 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 65score (p - 0.186).

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).

#### Phosphate Day 1 with CURB 65

The mean phosphate value on day 1 was high in patients who had CURB 65 score of 1 (3.79 + 0.43), followed by CURB 65 score of 0, 2, 3 and 4 (3.59 + 0.76), (3.45 + 0.56), (3.32 + 1.27) and (2.70 + 1.05). The t test results showed that there was significant difference between the CURB65 scores and phosphate levels (p - 0.02) (Figure 1).

#### Phosphate Day 3 v/s CURB 65

The mean PO4 value on day 3 was high in patients who had CURB 65 score of 1 (3.79 + 0.36), followed by CURB 65

score of 0, 3, 2 and 4 (3.78 + 0.66), (3.34 + 1.27), (3.18 + 0.61) and (2.61 + 0.75) (Table 2). The t test results showed that there was significant difference between the CURB65 scores and phosphate levels (p - 0.002).

#### Phosphate – Average v/s CURB 65

The mean of Phosphate value was high in patients who had CURB 65 score of 1 (3.93 + 0.27), followed by CURB 65 score of 0, 3, 2 and 4 (3.88 + 0.64), (3.23 + 1.23), (3.18 + 0.60) and (2.60 + 0.82) (Figure 3). The t test results showed that there was significant difference between the CURB65 scores and phosphate levels (p - 0.001).

The graphs present the association between phosphate levels, outcome of the study subjects and CURB 65 score. It can be observed that as the phosphate levels are increasing or decreasing, the CURB 65 score increases. Study subjects who had phosphate levels < 2.5 mg/dl, presented with CURB 65 Score as 4 (45%). Similarly, the study subjects with high phosphate levels (> 5 mg/dl) had CURB 65 scores as 3 (22.7%). The association between phosphate

study patients					
Hemoglobin	Frequency	Percent			
<9	11	14.7			
9-10	11	14.7			
10.01-11.99	18	24.0			
> 12	35	46.7			
Total	75	100.0			

Table 1: Hemoglobin (g/dl) values in patients

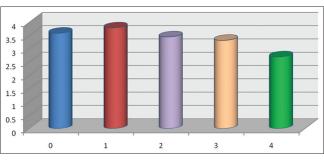


Figure 1: Phosphate Day 1 with CURB 65

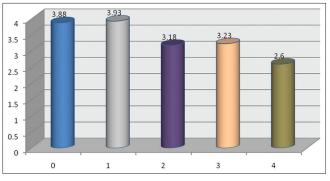


Figure 2: Phosphate Day 3 v/s CURB 65

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Table 2: Total counts distribution in different study points of patients studied								
TLC			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%		
>11000	4	7	6	13	17	47		
	50.0%	50.0%	54.5%	59.1%	85.0%	62.7%		
Total	8	14	11	22	20	75		
	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%		

Table 3: Urea (mg/l)	distribution	patients	studied
on admission			

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

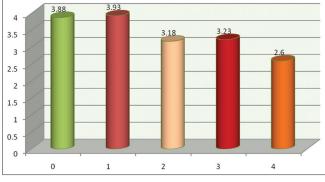
levels among discharged study subjects and CURB 65 scores was significant ( p < 0.001) but The association between phosphate levels among study subjects who died and CURB 65 scores was not significant ( p - 0.087)(Table 4).

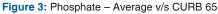
The table shows the association between S. albumin and CURB 65 scores. 50% of the study subjects had S. albumin in the range of 1.04 - 2.4 and CURB 65 score of 4. Among the study subjects with S. albumin in the range of 2.5-3.5 mg/dl, 59.1% had CURB 65 score of 3, followed by 40 % (CURB 65 - 4) and 36.4% (CURB 65 - 3)(Table 5). 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).

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 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 Global Burden of Disease Study shows global burden of 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>4</sup>Hypophosphatemia plays a role in impairing chemotaxis, phagocytosis and bactericidal activity of macrophages, Vivian Barak MD et al studied hypophosphatemia in sepsis and infection. The study showed that 80% of patients had hypophosphatemia associated with high levels of TNF alpha, IL6. The study demonstrated relationship between high levels of inflammatory cytokines and their receptors and serum phosphate levels especially in patients with positive blood culture.<sup>6</sup>

Our study included age groups above 18yrs. 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 having history of smoking for 5-10 year.

Outcome	phosphate	CURB 65						
		0	1	2	3 4		Total	
Discharged	< 2.5	0	0	1	6	4	11	0.001
-		0.0%	0.0%	9.1%	33.3%	33.3%	17.5%	
	2.5 – 3.5	3	4	7	9	8	31	
		37.5%	28.6%	63.6%	50.0%	66.7%	49.2%	
	3.51 - 5	5	10	3	1	0	19	
		62.5%	71.4%	27.3%	5.6%	0.0%	30.2%	
	>5	0	0	0	2	0	2	
		0.0%	0.0%	0.0%	11.1%	0.0%	3.2%	
	Total	8	14	11	18	12	63	
		100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	
Death	< 2.5	0	0	0	1	5	6	0.087
		0.0%	0.0%	0.0%	25.0%	62.5%	50.0%	
	2.5 – 3.5	0	0	0	0	2	2	
		0.0%	0.0%	0.0%	0.0%	25.0%	16.7%	
	3.51 - 5	0	0	0	0	0	0	
		0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	
	>5	0	0	0	3	1	4	
		0.0%	0.0%	0.0%	75.0%	12.5%	33.3%	
	Total	0	0	0	4	8	12	
		0.0%	0.0%	0.0%	100.0%	100.0%	100.0%	
Total	< 2.5	0	0	1	7	9	17	0.000
		0.0%	0.0%	9.1%	31.8%	45.0%	22.7%	
	2.5 – 3.5	3	4	7	9	10	33	
		37.5%	28.6%	63.6%	40.9%	50.0%	44.0%	
	3.51 - 5	5	10	3	1	0	19	
		62.5%	71.4%	27.3%	4.5%	0.0%	25.3%	
	>5	0	0	0	5	1	6	
	-	0.0%	0.0%	0.0%	22.7%	5.0%	8.0%	
	Total	8	14	11	22	20	75	
		100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	

# Table 5: Correlation between CURB65, Albumin levels and outcome

S.Albumin			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	
	62.5%	57.1%	54.5%	9.1%	10.0%	30.7%	
Total	8	14	11	22	20	75	
	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	

\*Chi square test

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

\*chi-square test

Majority of the study subjects had hemoglobin greater than 12 gm/dl (46.7%), followed by 10.01 - 11.99 gm/dl (24%).

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 CURB 65 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 bacteraemia and 26% of non-bacteraemia 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.<sup>7</sup>

#### Phosphate levels and CURB 65 scores

The mean phosphate value on day 1 was high in patients who had CURB 65 score of 1 (3.79 + 0.43), followed by CURB 65 score of 0, 2, 3 and 4 (3.59 + 0.76), (3.45 + 0.56), (3.32 + 1.27) and (2.70 + 1.05). The t test results showed that there was significant difference between the CURB 65 scores and phosphate levels (p - 0.02).

The mean phosphate value on day 3 was high in patients who had CURB 65 score of 1 (3.79 + 0.36), followed by CURB 65 score of 0, 3, 2 and 4 (3.78 + 0.66), (3.34 + 1.27), (3.18 + 0.61) and (2.61 + 0.75). The t test results showed that there was significant difference between the CURB 65 scores and phosphate levels (p - 0.002).

The mean of phosphate value of Day1 and Day 3 was high in patients who had CURB 65 score of 1 (3.93 + 0.27), followed by CURB 65 score of 0, 3, 2 and 4 (3.88 + 0.64), (3.23 + 1.23), (3.18 + 0.60) and (2.60 + 0.82). The t test results showed that there was significant difference between the CURB 65 scores and phosphate levels (p - 0.001).

Mohammad E. Naffaa et al studied 3876 patients in Rambam Health Care Campus with community acquired pneumonia. Severe hyperphostemia is associated with increased mortality. Higher CURB65 is associated with hyperphosphatemia and hypophosphatemia with significant p value of <0.0001.<sup>8</sup>

# Correlation between CURB65, Phosphate levels and outcome

On comparing the association between phosphate levels, outcome of the study subjects and CURB 65 score, it was observed that as the phosphate levels are increasing or decreasing, the CURB 65 score increases. Study subjects who had phosphate levels < 2.5 mg/dl, presented with CURB 65 Score as 4 (45%). Similarly, the study subjects with high phosphate levels (> 5 mg/dl) had CURB 65 scores as 3 (22.7%). The association between phosphate levels among discharged study subjects and CURB 65 scores was significant (p < 0.001) but the association

between phosphate levels among study subjects who died and CURB 65 scores was not significant (p - 0.087).

Ramkumar T. Sankaran MD et al studied 302 patients admitted to Long Jewish Medical Centre. Serum phosphates levels on admission and 4 days before onset of pneumonia were done. Hypophosphatemic patients had longer hospital stay and mortality compared to normophosphatemic patients. The study also concluded that pneumonia was associated with hypocalcemia, hypophosphatemia and hypoalbuminemia.<sup>9</sup>

C Feldman, J.M. Kallenbach et al conducted retrospective study of 73 patients of CAP. The study compared various clinical features with initial lab investigations. A lower total WBC count, high creatinine and high phosphate levels had poor prognosis. In these patients the mortality rate remained high despite advanced antibiotic usage and ICU care.<sup>10</sup>

**Comparison chest X ray features and CURB 65 score** 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>11</sup> In a study by R Riquelme et al. showed poor prognosis in CAP in patients who were bedridden, high temperature and respiratory rate at admission and three or more lobes (multilobar) involvement on chest Xray.<sup>12</sup>

#### Comparison between ICU admissions and outcome

Among the study subjects, 73% were discharged who had no ICU admission, whereas 91.7% of the study subjects died who had ICU admission. The association between ICU admission and outcome was significant (p - 0.000).

### CONCLUSION

Present study of serum phosphate levels as biomarkers in CAP showed that both hypophosphatemia and hyperphosphatemia carried poor prognosis which correlated with high CURB65 score. Normal phosphate 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 single centre study

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#### Author's contribution:

**NAG** - Concept and design of the study; prepared first draft of manuscript; **AHR** - Interpreted the results; reviewed the literature and manuscript preparation and revision of the manuscript; **SBH** - Statistically analysed and interpreted, preparation of manuscript; **RKR** - Concept, coordination, review of literature and manuscript preparation.

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