Original Article

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Association of Serum Phosphate Levels with Disease Severity and Clinical Outcomes in Patients with Community Acquired Pneumonia: A Hospital-based Prospective Observational Study

Internal Medicine Section

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ABSTRACT

Introduction: Community Acquired Pneumonia (CAP) remains a major cause of morbidity and mortality worldwide. Early identification of patients at risk of severe disease is essential for timely intervention. This prospective observational study evaluated the prognostic significance of serum phosphate levels in hospitalised CAP patients.

Aim: To evaluate the association between serum phosphate levels, CURB-65 (Confusion, Urea, Respiratory rate, Blood pressure, and Age 65 or older) score, Intensive Care Unit (ICU) admission, and mortality in hospitalised patients with CAP.

Materials and Methods: This hospital-based prospective observational study was conducted between May 2022 and October 2022 at Government Royapettah Hospital and Government Kilpauk Medical College Hospital, Chennai, Tamil Nadu, India after Institutional Ethics Committee approval. A total of 79 patients diagnosed with CAP were enrolled. Serum phosphate levels were measured at admission and on day 3 of hospitalisation. Disease severity was assessed using the CURB-65 score, and early ICU admission was defined as transfer within 48 hours. Data were analysed using Student's t-test, Chi-square test, Analysis of Variance (ANOVA), and Kendall's Tau correlation, with p-value <0.05 considered statistically significant.

Results: Serum phosphate levels demonstrated a significant inverse correlation with CURB-65 scores at admission (τ=-0.273, p-value=0.001) and on day 3 (τ=-0.456, p-value <0.0001). Lower serum phosphate levels were significantly associated with higher CURB-65 scores, increased ICU admission rates, and poorer clinical outcomes (p-value <0.0001).

Conclusion: These findings suggest that serum phosphate, an inexpensive and routinely available laboratory parameter, is associated with disease severity in patients with CAP and may serve for identifying high-risk patients and guiding clinical management in CAP.

Keywords: Hospitalisation, Intensive care units, Prognosis, Serum phosphate

INTRODUCTION

CAP remains a grave infectious disease with high mortality rates, especially among patients with co-morbidities or underlying pathogens. Despite advances in hospitalisation, ICU care, and antibiotic therapy, the disease burden remains substantial [1]. CAP occurs in individuals with minimal healthcare exposure, and high-risk groups include infants, the elderly and immunocompromised patients, with elderly individuals showing increased hospitalisation rates [2]. Mortality further increases in patients having co-morbidities such as diabetes and chronic lung disease, as well as adverse clinical factors including electrolyte imbalance, cytopenias, hypoxemia, and altered mental status [3,4]. Diagnosis is based on chest radiography and laboratory parameters, while sputum Gram staining, Acid Fast Bacilli (AFB) testing, and blood cultures help to gauge the aetiology [5].

Phosphate plays a pivotal role in cellular energy metabolism via its involvement in ATP synthesis, and abnormalities in the level of serum phosphate have been observed in subjects with pneumonia, potentially contributing to poor outcomes and increased mortality rates [6]. Previous studies indicate that both hyperphosphatemia and hypophosphatemia are linked to higher CURB-65 scores and greater complications [7]. The CURB-65 score is a well-established and reliable tool for evaluating disease severity in hospitalised patients with pneumonia [8]. Therefore, early identification of altered levels of serum phosphate may help predict severity, and overall outcomes of the disease. This study aims to evaluate the association and significance of serum phosphate levels in hospitalised patients with CAP and to establish their correlation with disease severity, mortality, and the necessity for early ICU admission.

MATERIALS AND METHODS

This prospective observational study was conducted over a period of six months, from May 2022 to October 2022, at Government Royapettah Hospital, Chennai, and Government Kilpauk Medical College Hospital, Chennai, Tamil Nadu, India. Following the approval from the institutional ethics committee (IEC Protocol No.718/2022), a total of 79 patients diagnosed with CAP were enrolled for the study. Written informed consent was obtained from all participants before their enrolment in the study. The study procedures were explained to each participant, and confidentiality of patient information was maintained throughout the study.

Sample size: The sample size was estimated with reference to the study conducted by Gurav NA et al., which evaluated the association between serum phosphate levels and CURB-65 score in patients with CAP. Considering the comparable study design and feasibility, a minimum sample size of 75 participants was adopted, and 79 patients were ultimately included [5].

Inclusion criteria: Patients admitted to either hospital with a clinical and radiological diagnosis of CAP were included in the study.

Exclusion criteria: Patients with a previous history of hospitalisation within the preceding 30 days, those diagnosed with hospital-acquired pneumonia, were excluded from the study. Chronic Kidney Disease (CKD) was excluded to minimise its confounding effect on the serum phosphate levels, while other co-morbidities such as diabetes and sepsis were documented and analysed as baseline clinical variables.

CAP Assessment

The study included 79 patients with clinical features indicative of CAP, defined as pneumonia that has been acquired in a patient by the community, with no prior history of hospitalisation (14 days period) to onset of symptoms or hospitalised less than four days before symptom onset [9]. Diagnosis was based on clinical features of lower respiratory tract infection with new radiographic evidence of pneumonia. A detailed history, including symptoms, duration, co-morbidities, prior hospitalisation, and CKD, was obtained. All subjects underwent physical examination, vital assessment, routine laboratory investigations, chest X-ray, and specialised tests including sputum analysis and serum phosphate estimation.

CURB 65 Score Evaluation

All study participants with CAP were assessed using the CURB-65 scoring system. The five parameters of CURB-65 included: 1) confusion (C); 2) blood urea level >7 mmol/L (U); 3) respiratory rate >30/min (R); 4) systolic blood pressure <90 mmHg or diastolic blood pressure <60 mmHg (B); 5) and age >65 years [10]. Scores of 0-1 indicate low risk, score 2 indicates moderate risk requiring hospitalisation, and scores ≥3 indicate severe pneumonia requiring close monitoring and possible intensive care management. Radiological findings such as infiltrates, consolidation, pleural effusion, multilobar involvement, and lobar predominance were also documented. Serum phosphate and serum calcium levels were estimated on the day of admission and repeated on the third day of hospitalisation. Serum phosphate levels were interpreted with regard to the standard clinical reference range of 2.5-4.5 mg/dL, and any or all deviations from this range were deemed as disturbances of phosphate homeostasis [11,12]. Serum phosphate estimation was repeated on day 3 as serial phosphate assessment during early hospitalisation better reflects disease progression and treatment response than a single baseline value.

Mortality Assessment

In-hospital mortality was recorded for those patients who expired during the hospital stay. One-month mortality was assessed through follow-up visits and telephonic communication. The requisite for early ICU admission and recovery status were also documented.

STATISTICAL ANALYSIS

Data collected were entered into Microsoft Excel and analysed using Statistical Package for the Social Sciences (SPSS) software version 22.0 IBM Corp., Armonk, NY, USA. Continuous variables were expressed as mean±standard deviation, and compared using the independent samples Student's t-test One-way Analysis of Variance (ANOVA). Categorical variables were analysed using the Chi-square test or Fisher's exact test as appropriate. Correlation between CURB-65 score and serum phosphate levels was assessed using Kendall's Tau correlation coefficient. A p-value of <0.05 was considered to be statistically significant.

RESULTS

A total of 79 patients with CAP were included in the analysis. Most patients were elderly, with the highest number of subjects belonging to the age group of 61-70 years. This was followed by those above 71 years of age, thereby indicating a clear predominance of CAP among older adult patients [Table/Fig-1]. A male predominance was observed in the study population. Among the co-morbid conditions, diabetes mellitus and hypertension were the most frequently observed, followed by chronic obstructive pulmonary disease, thus highlighting the contribution of underlying systemic condition to disease susceptibility. In terms of social risk factors, smoking was more frequently noted than alcohol consumption. A fraction of patients reported having confusion, and a similar proportion of subjects required ventilatory assistance. ICU admission was only necessary for few numbers of cases. The total mortality rate was low, where only a small number of patients succumbed to the severity of the disease. Among the three patients who died, two patients expired on the third day of hospitalisation and one on the seventh day of hospitalisation. All three patients required ICU admission and had CURB-65 scores of 4. This suggested favourable outcomes in most cases regardless of the presence of risk factors and other co-morbidities.

Characteristic	Category	n (%)
Age group (years)	<30	5 (6.3)
	31-40	10 (12.7)
	41-50	14 (17.7)
	51-60	12 (15.2)
	61-70	24 (30.4)
	>71	14 (17.7)
Gender	Male	50 (63.3)
	Female	29 (36.7)
Co-morbidities	Diabetes mellitus	16 (20.3)
	Hypertension	16 (20.3)
	COPD	11 (13.9)
Social habits	Smoking	17 (21.5)
	Alcohol consumption	6 (7.6)
Clinical findings	Confusion	12 (15.2)
	Need for mechanical ventilation	12 (15.2)
	Need for inotropic support	9 (11.4)
	Empyema	3 (3.8)
	ICU admission	14 (17.7)
	Mortality	3 (3.8)

[Table/Fig-1]: Baseline demographic and clinical characteristics of patients with community-acquired pneumonia (CAP) (N=79).

Serum Phosphate Levels of ICU and Non-ICU Patients

Serum phosphate levels were notably lower in subjects requiring ICU admission in contrast to those managed in the general ward [Table/Fig-2]. At the time of hospitalisation, the mean serum phosphate levels of ICU patients were 2.79±0.65 mg/dL, while non-ICU patients possessed a mean level of 3.47±0.56 mg/dL. This was suggestive of an extremely significant difference (p-value <0.0001). On day 3, ICU patients had lower phosphate levels (2.96±0.67 mg/dL) than non-ICU patients (3.54±0.62 mg/dL), a significant variation (p-value =0.002). These data show a significant correlation between reduced serum phosphate levels and higher disease severity, thereby underscoring the potential relevance of hypophosphatemia as an early indicator of the necessity for intensive care in subjects with CAP.

Parameter	ICU admission (n=14)	Non-ICU admission (n=65)	t-value	p-value
Serum phosphate on admission (mg/dL)	2.79±0.65	3.47±0.56	-3.63	<0.0001*
Serum phosphate on Day 3 (mg/dL)	2.96±0.67	3.54±0.62	-2.98	0.002*

[Table/Fig-2]: Comparison of serum phosphate levels between ICU and non-ICU patients.
*p<0.05 indicates statistical significance; Data expressed as mean±standard deviation. The p-values calculated using independent Student's t-test

Association of Serum Phosphate Levels and Mortality Rate

Patients who died had decreased levels of serum phosphate during the time of admission (2.60±0.26 mg/dL) as opposed to survivors (3.38±0.62 mg/dL), which was statistically significant (p-value=0.036) [Table/Fig-3]. On day 3, expired patients had lower phosphate levels (2.80±0.61 mg/dL) in contrast to survivors (3.46±0.66 mg/dL), although the difference was not statistically noteworthy (p-value=0.090). These data show a substantial link between hypophosphatemia at the time of admission and higher mortality among subjects with CAP. This implied that lower levels of serum phosphate could serve as an early prognostic predictor of poor outcomes.

Parameter	Survived (n=76)	Expired (n=3)	t-value	p-value
Serum phosphate on admission (mg/dL)	3.38±0.62	2.60±0.26	2.97	0.036*
Serum phosphate on day 3 (mg/dL)	3.46±0.66	2.80±0.61	1.69	0.090

[Table/Fig-3]: Comparison of serum phosphate levels and mortality.
*p<0.05 indicates statistical significance; Data expressed as mean±standard deviation. The p-values calculated using independent Student's t-test

Distribution of CURB-65 Score and its correlation with Serum Phosphate levels and Mortality

Subjects were distributed across all severity categories of CURB-65, with the majority falling within the lower scores and fewer in the higher severity groups [Table/Fig-4]. The CURB-65 score was found to have an inverse connection with levels of serum phosphate during admission. As severity rose, phosphate levels decreased and reached 2.41±0.56 mg/dL in individuals with a score of 4. Notably, all expired patients belonged to the highest severity category (scoring 4) with low mean levels of phosphate (2.60±0.26 mg/dL). The association between increasing CURB-65 score, decreasing serum phosphate levels, and mortality was highly statistically significant (p-value <0.0001). These findings signify that elevated CURB-65 scores combined with hypophosphatemia are positively associated with poor outcomes and may enhance early risk stratification in subjects with CAP.

CURB-65 score	Total patients (n)	Survived patients (n=76)	Expired patients (n=3)	p-value
		Serum phosphate (mg/dL) Mean±SD	Serum phosphate (mg/dL) Mean±SD	
Score 0	20	3.43±0.56	-	<0.0001
Score 1	21	3.65±0.46	-	
Score 2	15	3.37±0.66	-	
Score 3	12	3.33±0.48	-	
Score 4	11	2.41±0.56	2.60±0.26	

[Table/Fig-4]: Distribution of CURB-65 score and correlation with mortality and serum phosphate on admission.
Data are expressed as mean±standard deviation. The p-value was calculated using One-way ANOVA: F(4,74)=12.35. *p<0.05 indicates statistical significance

CURB-65 Score and Serial Serum Phosphate Levels

An inverse relationship was noticeable between CURB-65 score and serum phosphate levels both at admission and on day 3 of hospitalisation [Table/Fig-5]. Patients with the highest severity score (score 4) demonstrated the lowest mean phosphate levels at admission (2.41±0.56 mg/dL), with a similar declining pattern evident on day 3 (2.64±0.43 mg/dL). Kendall's Tau analysis revealed a statistically significant negative correlation at admission (τ=-0.273, p-value=0.001), which strengthened further by day 3 (τ=-0.456, p-value <0.0001). The results presented indicate a conclusive inverse link between the severity of pneumonia with quantity of serum phosphate. This strengthened inverse association on Day 3 suggests that prolonged hypophosphatemia may indicate ongoing or escalating disease severity.

CURB-65 score	n	Serum phosphate on admission (mg/dL) Mean±SD	Serum phosphate on day 3 (mg/dL) Mean±SD
Score 0	20	3.43±0.56	3.80±0.52
Score 1	21	3.65±0.46	3.79±0.62
Score 2	15	3.37±0.66	3.33±0.48
Score 3	12	3.33±0.48	3.10±0.54
Score 4	11	2.41±0.56	2.64±0.43
Kendall's Tau correlation coefficient		-0.273	-0.456
p-value		0.001	<0.0001

[Table/Fig-5]: Correlation between CURB-65 score and serial serum phosphate levels.
Correlation between CURB-65 score and serum phosphate levels was assessed using Kendall's Tau correlation coefficient. *p<0.05 indicates statistical significance

Correlation of Day 3 Serum Phosphate Levels with CURB-65 Score and Mortality

Serum phosphate levels declined on day 3 as CURB-65 severity scores increased amongst survivors, reaching 2.57±0.36 mg/dL in subjects with a score of 4 [Table/Fig-6]. Those subjects with lower CURB-65 scores, on the other hand, had significantly greater phosphate levels. All expired patients belonged to the highest severity group (score 4) and had consistently lower mean phosphate levels by day 3 (2.80±0.61 mg/dL). A significant correlation (p-value <0.0001) was established between an elevated CURB-65 score, decreased serum phosphate levels on day 3, and mortality, thereby indicating an affiliation between prolonged hypophosphatemia and negative clinical outcomes.

CURB-65 score	Survived patients (n=76)	Expired patients (n=3)	p-value
	Serum phosphate day 3 (mg/dL) Mean±SD	Serum Phosphate Day 3 (mg/dL) Mean±SD	
Score 0	3.80±0.52	-	<0.0001
Score 1	3.79±0.62	-	
Score 2	3.33±0.48	-	
Score 3	3.10±0.54	-	
Score 4	2.57±0.36	2.80±0.61	

[Table/Fig-6]: Association of Day 3 serum phosphate levels with CURB-65 score and mortality.
*p<0.05 indicates statistical significance; Data expressed as mean±standard deviation; One-way ANOVA: F(4,71)=11.21, p<0.0001

These data imply that the level of serum phosphate at day 3 is not only a sign of disease severity, but also an active indication of clinical improvement. Patients with greater CURB-65 scores who have continuously low phosphate levels appear to have a worse prognosis, whereas stable or improving phosphate levels may indicate better clinical recovery in patients. As a result, serial serum phosphate monitoring may improve risk classification and assist in recognising patients who require additional monitoring or care escalation.

DISCUSSION

The present study demonstrated a significant association between serum phosphate levels and disease severity in patients with CAP. Lower phosphate levels were associated with higher CURB-65 scores, greater need for ICU admission, and poorer clinical outcomes, supporting the potential role of serum phosphate as an adjunctive prognostic indicator in CAP. Hypophosphatemia has been increasingly recognised as a marker of severe systemic illness. Previous studies have suggested that low phosphate levels may result from intracellular redistribution, increased metabolic demand, impaired nutritional status, or inflammatory responses associated with severe infection. These mechanisms may explain the observed association between hypophosphatemia and greater CAP severity in the present study.

CAP was predominantly observed among elderly patients, particularly those aged 61-70 years, which is consistent with previous reports demonstrating a higher incidence of CAP among older adults due to age-related decline in immune function and the presence of multiple co-morbidities. Gurav NA et al., similarly reported lower serum phosphate levels among patients with higher CURB-65 scores, supporting the association between hypophosphatemia and increasing disease severity [5]. Furthermore, Naffaa M et al., demonstrated that serum phosphate abnormalities were independently associated with adverse outcomes and increased mortality in CAP patients. The stronger inverse correlation observed on day 3 in the present study compared to admission findings suggests that serial phosphate monitoring may provide additional prognostic information during hospitalisation [13]. Smoking and alcohol consumption, both established risk factors for CAP due to impaired mucociliary clearance and immune dysfunction, were noted in a subset of patients [7,14].

The observed association between hypophosphatemia and ICU admission suggests that serum phosphate may reflect disease severity and physiological stress in CAP. Similar observations have been reported in critically-ill patients, where phosphate depletion has been associated with respiratory muscle dysfunction, impaired oxygen delivery, and immune dysregulation, all of which may contribute to worsening clinical status and increased need for intensive care support. Hypophosphatemia may adversely affect multiple physiological processes relevant to pneumonia. Phosphate is essential for ATP synthesis, cellular metabolism, diaphragmatic contractility, and leucocyte function. Reduced phosphate levels may therefore impair respiratory muscle performance, compromise host immune responses, and contribute to disease progression in patients with CAP.

A significant inverse correlation was observed between CURB-65 score and serum phosphate levels. Kendall's tau analysis demonstrated a statistically relevant negative association at admission (τ=-0.273, p-value=0.001), which became stronger by day 3 (τ=-0.456, p-value <0.0001), indicating that declining or persistently low phosphate levels are linked with increasing disease severity. These findings suggest that serial phosphate measurements may provide additional dynamic prognostic value beyond initial clinical assessment. Comparable results were reported by Naffaa M et al., in a large cohort of 3,876 patients, where severe hypophosphatemia was significantly associated with higher CURB-65 scores and adverse outcomes (p-value <0.0001) [13]. Similarly, Gurav NA et al., demonstrated a significant association between CURB-65 scores and serum phosphate levels measured at admission and on day 3 (p-value <0.0001), supporting the role of serial phosphate monitoring in severity stratification [5]. Feldman C et al., in a retrospective analysis of CAP patients, also identified abnormal phosphate levels along with other biochemical derangements as predictors of poor prognosis, [15], further emphasising the clinical relevance of phosphate imbalance in CAP.

Although mortality was observed predominantly among patients with severe CURB-65 scores and lower phosphate levels, only three deaths occurred during the study period. Therefore, conclusions regarding mortality prediction should be interpreted cautiously. Consequently, the observed association between serum phosphate levels and mortality should be considered exploratory and requires confirmation in studies with larger sample sizes and greater numbers of mortality events. Bauer TT et al., reported that CURB-65 significantly predicted 30-day mortality and could be effectively applied in both inpatient and outpatient settings [16]. Additionally, Liu JL et al., in a large cohort of 1,164 hospitalised CAP patients, demonstrated that CURB-65 reliably predicted mortality and severity when compared with PSI, SMART-COP, and A-DROP scoring systems [17]. The addition of independent risk factors to the CURB-65 concept improves its clinical utility as well as ease of use.

Importantly, integrating serum phosphate levels alongside the CURB-65 score likely improves prognosis accuracy. The strong correlation (p-value <0.0001) among phosphate levels, severity grading, and death implies that biochemical markers can enhance clinical scoring systems for better risk identification. Serial monitoring, particularly on day three, provides useful dynamic information about illness progression. Serum phosphate estimation is inexpensive, widely available, and routinely performed in most hospital laboratories. The present findings suggest that serum phosphate may serve as a useful adjunctive laboratory marker alongside CURB-65 scoring for identifying patients at increased risk of severe disease and ICU admission. Early recognition of hypophosphatemia may facilitate closer monitoring and timely escalation of care in hospitalised CAP patients.

Limitation(s)

The present study had certain limitations that needed to be acknowledged. The sample size was comparatively small and derived from only two centres, which may limit the generalisability of the findings. Serial phosphate monitoring beyond day 3 was not performed, and several potential confounding factors that may influence serum phosphate levels, including serum vitamin D levels, parathyroid hormone levels, serum albumin, acid-base status, nutritional status, and the use of phosphate-altering medications, were not evaluated. Future large-scale, multicentre studies with longer follow-up periods are warranted to validate these findings. Further research should also explore the mechanistic basis of phosphate imbalance in CAP and assess whether early correction of hypophosphatemia can improve clinical outcomes.

CONCLUSION(S)

Lower serum phosphate levels were significantly associated with increasing CAP severity and ICU admission. Although an association with mortality was observed, the small number of deaths limits definitive conclusions regarding mortality prediction. Serum phosphate levels may represent a simple indicator for risk assessment in hospitalised CAP patients; however, larger multicentre studies are required to validate clinically useful cut-off values and establish its role in prognostic models.

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