

Original Article

Serum phosphorus levels as a predictor and severity marker for mechanical ventilation in adults versus elderly patients – A cross-sectional study

Anand P Ambali¹, Priyanka Tomar², Shivanand L K³Departments of ¹Geriatrics, ²Medicine, ³Anesthesia, Bijapur Lingayat District Education Deemed to be University, Vijayapura, Karnataka, India

ABSTRACT

Objectives: Mechanical ventilation (MV) is a supportive therapy for patients with acute respiratory failure. Studies have shown direct relationship between serum phosphorus on admission and risk of respiratory failure requiring MV. This study aims to determine admission serum phosphorus level's ability to predict severity in 64 mechanically ventilated patients among two groups: Group A was designated to adults (<60 years of age) and Group B to elderly (60 years or older) admitted to the critical care unit (CCU). Study Design: It is a cross-sectional study.

Material and Methods: Data were collected from 64 adults admitted to CCU. The Sequential Organ Failure Assessment (SOFA) score and serum Phosphorus level on admission were assessed. Patients with Diabetic Ketoacidosis, Head Trauma, Renal Failure, Hyper or Hypoparathyroidism, Leukaemia, and Lymphoma were excluded.

Results: The study had 32 subjects in each group. The commonest indication for mechanical ventilation was Poisoning (31.25%) in Group A and Cerebrovascular Accident (34.37%) in Group B. The common complication among the study group was ventilator-associated pneumonia (14.06%). Out of 64 patients requiring mechanical ventilation, nine patients had hypophosphatemia, and eighteen had hyperphosphatemia. In the case of hypophosphatemia, 100% and in hyperphosphatemia, 55.5% mortality was observed.

Conclusion: Altered serum phosphorus levels on admission can be a potential indicator for requiring MV and mortality. Both hypophosphatemia and hyperphosphatemia are potential risk factors for the development of respiratory failure. Also, age-related variation in phosphorus levels has not shown any association with the outcome.

Keywords: Mechanical ventilation, Mortality, Serum phosphorus, SOFA score, Adults, Elderly

INTRODUCTION

The concept of artificial respiration was introduced by Vesalius in the sixteenth century and by the twentieth century it became a widely accepted modality for the management of acute respiratory failure.¹ Although mechanical ventilation is vital as supportive therapy in acutely ill patients, prolonged use of it can result in life-threatening complications like ventilator-associated pneumonia (VAP), barotrauma, sepsis, acute respiratory distress syndrome (ARDS), pulmonary edema, and embolism.^{1,2}

Phosphorus was first discovered by Hennig Brandt in 1669 in Hamburg by condensation of the putrefied urine vapor.³ It is one of the most important elements found mostly inside

cells and is naturally contained in food. It is a crucial part of ribonucleic acid (RNA), deoxyribonucleic acid (DNA), bones, and teeth. Phosphorus, as phospholipids, is an important part of cell membranes and adenosine triphosphate (ATP), which is required for cellular activity in the body.⁴ Many elements in the body exist in phosphorylated forms. Also, it is necessary for the storage and translation of genetic information in nucleotides, intracellular signaling via the phosphorylation or dephosphorylation of important enzymes, energy transfer, and acid-base buffering.⁵

Serum phosphate levels in adults typically range from 2.5 to 4.5 mg/dL.⁴ Hypophosphatemia is characterized as serum phosphate levels below 2.5 mg/dL, and hyperphosphatemia is defined as levels above 4.5 mg/dL.⁶

*Corresponding author: Dr Anand P Ambali, Department of Geriatrics, Bijapur Lingayat District Education Deemed to be University, Shri B M Patil Medical College Hospital and Research Centre, Vijayapura 586103 Karnataka India. anand.ambali@bldedu.ac.in

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The mortality in a critical care setup is directly related to the rate of organ failure and its severity. The Sequential Organ Failure Assessment (SOFA) score is a helpful tool for predicting the prognosis of the patient in the Intensive Care Unit (ICU).⁷

Mohammad Tinawi *et al.*⁶ reported that abnormal phosphate levels are linked to a higher 180-day mortality rate. Hence, immediate action should be taken to stabilize the patient's phosphate profile and correct the phosphate values in case of any alterations.

Thongprayoon *et al.*⁸ conducted the study on 37,728 hospitalized patients and concluded that there is an association between serum phosphate level on admission and the risk of respiratory failure requiring mechanical ventilation. A similar study was carried out by Miller *et al.*⁹ who deduced that hyperphosphatemia can be a predicting factor for poor outcome in mechanically ventilated patients with severe sepsis or septic shock.

The literature proving the association of serum phosphorus with mechanical ventilation comparing the age-related changes in blood phosphorus with the outcome in mechanically ventilated patients is sparse. This study assessed the serum phosphorus level as a severity and prognostic marker in patients on mechanical ventilation among adults and the elderly.

MATERIAL AND METHODS

A cross-sectional study was conducted with the approval from the ethical committee obtained on 11th January 2021 (IEC/No. 9 /2021). The study was conducted for 18 months on all patients aged 18 years and above, irrespective of sex, admitted to the critical care unit of Bijapur Lingayat District Education Deemed to be University, Shri B. M. Patil Medical College, Hospital and Research Center and subsequently requiring mechanical ventilation, were recruited in the study. The consent for enrolling the case was obtained from a close relative of the patient. Patients with Diabetic ketoacidosis (DKA), malnutrition, hyperparathyroidism or hypoparathyroidism, leukemia and lymphomas, acute/chronic renal failure, and conditions requiring elective mechanical ventilation (e.g., neuromuscular syndrome) were excluded from the study.

The patients requiring ventilator support were divided into two groups based on their age. Group A was assigned to the adults (age 18–59 years) whilst the elderly (60 years or older) were assigned to Group B.

The Sequential Organ Failure Assessment (SOFA) scoring, which objectively described organ (dys)function in critically ill patients, was done on admission. Each organ system is assigned a point value from 0 (normal) to 4 (high degree

of dysfunction/failure) in SOFA scoring. The relevant investigations, along with serum phosphorus, were assessed on the day of admission and the patient was followed for the need for ventilator support.

All the recruited patients were followed for their outcome and conclusions correlating the admission phosphorus levels with the results were drawn. The data were obtained in a Microsoft Excel sheet, and statistical analysis was done using a statistical package for the social sciences (Version 20). Categorical variables were compared using the Chi-square test. The p-value of <0.05 was considered statistically significant. All statistical tests performed were two-tailed.

RESULTS

A total of 64 critically ill patients who required mechanical ventilation over a period of 18 months were included in the study. The patients were divided into groups based on their ages. Thirty-two patients were in Group A (adults) and the other 32 were in Group B (elderly) [Table 1]. In Group A, most patients (18.74%) belonged to the age group 30–39 years. While in Group B, the majority (28.12%) of patients were in the 60–69 years age group. The study had male predominance. The oldest subject in the study was a 90-year-old male.

Patients in the study had one or more pre-existing comorbidities. In Group A, among patients requiring mechanical ventilation, 9.37% had diabetes mellitus and epilepsy each, 6.25% had rheumatoid arthritis and depression each, 3.12% had hypertension and bronchial asthma each, 6.25% had coexisting diabetes and hypertension while remaining 56.25% had no comorbidities [Table 2].

On the contrary, of patients in Group B, 9.37% patients had hypertension, 6.25% had bronchial asthma, 3.12% had Parkinson's disease, diabetes, and old cerebrovascular accidents each while 25% of patients had multiple coexisting comorbidities like diabetes, hypertension, ischemic heart disease, chronic obstructive pulmonary disease, and the remaining 50% were devoid of any comorbidities [Table 2].

The majority of Group A patients requiring mechanical ventilation in our study were diagnosed as poisoning in

Table 1: Age and sex distribution.

Group	Male	Female
Young (18–59 years) (Group A) (n = 32)	24	08
Elderly (60 years or above) (Group B) (n = 32)	24	08
Total	48 (75%)	16 (25%)

Table 2: Diagnosis, comorbidities, and Complications.

	Group A	Group B
Diagnosis		
Poisoning	10 (31.25%)	3 (9.37%)
Cerebrovascular accident	6 (18.75%)	11 (34.37%)
Seizure disorder	5 (15.62%)	-
Infections	4 (12.50%)	-
Musculoskeletal injuries	2 (6.25%)	-
Alcoholic liver disease	2 (6.25%)	1 (3.12%)
Carcinoma	2 (6.25%)	-
Autoimmune disease	1 (3.12%)	-
Ischemic heart disease	-	8 (25.00%)
Septic shock	-	4 (12.50%)
Carbon dioxide narcosis	-	2 (6.25%)
Megaloblastic anemia	-	1 (3.12%)
Bronchial asthma	-	1 (3.12%)
COPD	-	1 (3.12%)
Comorbidities		
Diabetes mellitus	15.62%	21.87%
Hypertension	9.37%	28.12%
CAD	3.12%	9.37%
Bronchial asthma	3.12%	6.25%
Epilepsy	9.37%	-
Rheumatoid arthritis	6.25%	-
Depression	6.25%	6.25%
COPD	-	3.12%
Parkinson's disease	-	3.12%
None	56.25%	50%
Complications		
Ventilator-associated pneumonia (VAP)	9.37%	18.75%
Pleural effusion	6.25%	-
Pulmonary edema	6.25%	-
No complications	78.12%	81.25%

CAD: Coronary artery disease, COPD: Chronic obstructive pulmonary disease.

31.25% of cases, cerebrovascular accident in 15.62%, seizure disorder in 15.62%, sepsis in 15.62%, musculoskeletal disease in 6.25%, alcoholic liver disease in 6.25%, carcinomas in 6.25%, and autoimmune disease in 3.12%. The most common diagnosis among Group B was cerebrovascular accident in 34.37% followed by ischemic heart disease in 25%, septic shock in 12.50%, poisoning in 9.37%, carbon dioxide narcosis in 6.25%, alcoholic liver disease in 3.12%, megaloblastic anemia in 3.12%, bronchial asthma in 3.12%, and chronic obstructive pulmonary disease in 3.12% [Table 2].

The serum phosphorus levels were categorized as normal (2.5–4.5 mg/dL), hypophosphatemia (<2.5 mg/dL), and hyperphosphatemia (>4.5 mg/dL). Normal serum phosphorus levels were seen in 20 patients in Group A and 17 in Group B. Of nine hypophosphatemic patients, six belonged to Group A and three to Group B. Among 18 patients with increased serum phosphorus levels on admission, six were in

Group A and 12 in Group B. The levels were compared to the two groups and no association (p -value = 0.198) was found between the age groups and admission serum phosphorus. Regarding the duration of ventilation, 22 patients were on a ventilator for 1 day, while one elderly with left capsule ganglionic ischemic stroke stayed on a ventilator for 17 days.

The SOFA score was applied and it showed that 14 patients presented with a SOFA score of 8. Of these 14, eight were young and six were elderly. Out of these eight young, five died and three recovered while among six elderly, one died and the other five recovered. Among the 64 patients in our study, two elderly patients had the highest SOFA score of 13 on admission. There was no significant association between the SOFA score on admission and the outcome of our study.

In Group A, 78.12% and in Group B 81.25% of subjects had no complications following mechanical ventilation while 9.37% in Group A subjects and 18.75% in Group B developed ventilator-associated pneumonia (VAP). Patients in Group A have developed additional complications like pulmonary edema (6.25%) and pleural effusion (6.25%) secondary to mechanical ventilator. Whereas in Group B, no other complications were seen [Table 2].

Blood phosphorus levels at admission were also compared with the outcomes of the patients. In Group A, 12 patients had abnormal serum phosphorus on presentation, of which 50% had hypophosphatemia, and the other 50% had hyperphosphatemia. Among the patients with low blood phosphorus levels, 100% mortality was noticed, whereas in the patients with hyperphosphatemia, mortality was seen in 50% of them.

In Group B, 15 patients presented with deranged phosphorus levels, of which 20% had hypophosphatemia with 100% mortality, while among 80% hyperphosphatemic patients, mortality was 58.3%. It was noticed in our study that there was a significant relation between serum phosphorus levels on admission and the outcome of the patient (p -value <0.05) [Table 3].

DISCUSSION

Our study assessed the severity and prognostic value of the serum phosphorus level in mechanically ventilated patients on admission among adults (<60 years) and elderly (60 years or older).

Critically ill patients who develop acute respiratory failure are managed by supportive therapy like mechanical ventilation, but prolonged mechanical ventilation is itself associated with deleterious effects. Hence, the key to survival in such cases is early weaning from the ventilator support.^{10,11} Removal of the endotracheal tube and withdrawal of ventilator support are both steps in the process of weaning from invasive ventilation.

Table 3: Association of serum phosphorus levels with the outcome of the patient.

Serum phosphorus		Outcome		Total (n = 64)	Chi-square value	p-Value
		Recovered	Died			
<2.5	Count	0	9	9	16.617	<0.05
	%	0.00%	100%	14.06%		
2.5–4.5	Count	27	10	37		
	%	72.97%	27.02%	57.81%		
>4.5	Count	8	10	18		
	%	44.44%	55.55%	28.12%		

It can only be started once the underlying issue or respiratory failure has been addressed.¹² Boles *et al.*¹³ have mentioned in their study that one of the crucial causes of respiratory failure is hypophosphatemia and other metabolic derangements. In a similar study, Dooley *et al.*¹⁴ have stated that the inability to wean from a mechanical ventilator may be caused by insufficient 2,3 diphosphoglycerate (2,3-DPG) synthesis, which shifts the hemoglobin dissociation curve to the left and reduces oxygen supply to the tissues. Also, phosphorylated intermediates like ATP are not produced adequately in hypophosphatemic states which hampers diaphragmatic contractility. Gravelyn and colleagues¹⁵ studied 23 patients and concluded that respiratory muscle weakness is common among the patients with hypophosphatemia which can be improved with phosphate repletion. Furthermore, a number of studies^{16–22} have demonstrated that, in the absence of any underlying lung pathology, a correlation exists between respiratory muscle weakness and altered serum phosphorus levels. Miller *et al.*⁹ have concluded that time-weighted hyperphosphatemia is directly associated with increased mortality.

Hypo- and hyperphosphatemia is difficult to diagnose as it presents with nonspecific symptoms. Therefore, it is crucial to get the baseline serum phosphorus levels for all patients admitted to a critical care unit.

The study has male dominance (75%) which was similar to Miller *et al.*⁹ Identical to Alsumrain *et al.*²³ most of the individuals in our study belonged to the age group of 60 to 69 years. Also, the common comorbidities in the study were diabetes mellitus and hypertension which resembled our analysis. Unlike other studies,^{4,9,23} the common diagnosis in our subjects was poisoning and cerebrovascular accidents. Compared to Moitra *et al.*,²⁴ only 12.5% of patients spent a day in the ICU. In contrast, most of the patients (14.06%) in our study have been hospitalized for 8 days while a maximum length of hospital stay of 55 days was recorded. Nine patients in Group A and 13 in Group B were mechanically ventilated for a single day.

Sequential Organ Failure Assessment (SOFA) score was used as the tool to predict the mortality of admitted critically ill patients. It was found that most of the patients had a score of

8 on admission which was in contrast to the low on admission SOFA score (median SOFA score of 3.38+/-0.39 and 2.89+/-0.31) documented by Talakoub *et al.*⁴

The most common complication among the patients on ventilators was ventilator-associated pneumonia (VAP) seen in 14.06%, among these 18.75% were elderly while 9.37% belonged to the young adult group which was similar to Vincent *et al.*²⁵

A significant association (p-value <0.05) between serum phosphorus at admission and outcome was established as all the patients who had presented with low blood phosphorus needed mechanical ventilation and subsequently died.

There was no relation found between serum phosphorus levels and age group during the study.

Limitations

The study has a limited number of subjects involved; the hypothesis can further be evaluated by a cohort-type study involving a larger group. Though our study did not recognize the levels of serum phosphorus and the need for ventilator support on admission with statistical significance, we recommend serial measurements of serum phosphorus levels in critically ill patients for accurate prediction of ventilator support needs.

CONCLUSION

Patients admitted in critical care units are at risk of respiratory failure or sudden cardiac death. The assessment of serum phosphorus levels at the time of admission in critical care setup helps us to identify the group of patients who are at risk for respiratory failure and may require artificial ventilation. Both hypophosphatemia and hyperphosphatemia are potential risk factors for the development of respiratory failure.

Ethical approval

This cross-sectional study was conducted with the approval from the ethical committee obtained on 11th January 2021 (IEC/No. 9/2021).

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Nil.

Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of Artificial Intelligence (AI)-Assisted Technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

REFERENCES

- Slutsky AS. History of mechanical ventilation. From vesalius to ventilator-induced lung injury. *Am J Respir Crit Care Med* 2015;191:1106–15.
- Boles JM, Bion J, Connors A, Herridge M, Marsh B, Melot C, *et al.* Weaning from mechanical ventilation. *Eur Respir J* 2007;29:1033–56.
- Sharples A, Jarvie H, Flaten D, Kleinman P. Celebrating the 350th anniversary of phosphorus discovery: A conundrum of deficiency and excess. *J Environ Qual* 2018;47:774–7.
- Talakoub R, Bahrami M, Honarmand A, Abbasi S, Gerami H. The predicting ability of serum phosphorus to assess the duration of mechanical ventilation in critically ill patients. *Adv Biomed Res* 2017;6:51.
- Amanzadeh J, Reilly Jr RF. Hypophosphatemia: An evidence-based approach to its clinical consequences and management. *Nat Clin Pract Nephrol* 2006;2:136–48.
- Tinawi M. Disorders of phosphate metabolism: Hypophosphatemia and hyperphosphatemia. *Arch Clin Biomed Res* 2021;5:538–55.
- Hewett J, Rodgers GW, Chase JG, Le Compte AJ, Pretty CG, Shaw GM. Assessment of SOFA score as a diagnostic indicator in intensive care medicine. *IFAC Proceed Vol* 2012;45:467–72.
- Thongprayoon C, Cheungpasitporn W, Chewcharat A, Mao MA, Thirunavukkarasu S, Kashani KB. Admission serum phosphate levels and the risk of respiratory failure. *Int J Clin Pract* 2020;74:e13461.
- Miller CJ, Doepker BA, Springer AN, Exline MC, Phillips G, Murphy CV. Impact of serum phosphate in mechanically ventilated patients with severe sepsis and septic shock. *J Intensive Care Med* 2020;35:485–93.
- Eskandar N, Apostolakis MJ. Weaning from mechanical ventilation. *Crit Care Clin* 2007;23:263–74.
- Lermite J, Garfield MJ. British Journal of Anaesthesia. Continuing Education in Anaesthesia. Critical Care and Pain, 2005;5:113–17.
- Alía I, Esteban A. Weaning from mechanical ventilation. *Crit Care* 2000;4:72.
- Boles JM, Bion J, Connors A, Herridge M, Marsh B, Melot C, *et al.* Weaning from mechanical ventilation. *Eur Respir J* 2007;29:1033–56.
- Dooley J, Fegley A. Laboratory monitoring of mechanical ventilation. *Crit Care Clin* 2007;23:135–48.
- Gravelyn TR, Brophy N, Siegert C, Peters-Golden M. Hypophosphatemia-associated respiratory muscle weakness in a general inpatient population. *Am J Med* 1988;84:870–6.
- Patel U, Sriram K. Acute respiratory failure due to refeeding syndrome and hypophosphatemia induced by hypocaloric enteral nutrition. *Nutrition* 2009;25:364–7.
- Agusti AG, Torres AN, Estopa RA, Agustividal A. Hypophosphatemia as a cause of failed weaning: The importance of metabolic factors. *Crit Care Med* 1984;12:142–3.
- Varsano SH, Shapiro ME, Taragan RO, Bruderman I. Hypophosphatemia as a reversible cause of refractory ventilatory failure. *Crit Care Med* 1983;11:908–9.
- Oud L. Transient hypoxic respiratory failure in a patient with severe hypophosphatemia. *Med Sci Monit* 2009;15:CS49–53.
- Liu PY, Jeng CY. Severe hypophosphatemia in a patient with diabetic ketoacidosis and acute respiratory failure. *JCMA* 2004;67:355–9.
- Hasselstrøm L, Wimberley PD, Nielsen VG. Hypophosphatemia and acute respiratory failure in a diabetic patient. *J Intensive Care Med* 1986;12:429–31.
- Brown EL, Jenkins BG. A case of respiratory failure complicated by acute hypophosphatemia. *Anaesthesia* 1980;35:42–5.
- Alsumrain MH, Jawad SA, Imran NB, Riar S, DeBari VA, Adelman M. Association of hypophosphatemia with failure-to-wean from mechanical ventilation. *Ann Clin Lab Sci* 2010;40:144–8.
- Moitra VK, Guerra C, Linde-Zwirble WT, Wunsch H. Relationship between ICU length of stay and long-term mortality for elderly ICU survivors. *Crit Care Med* 2016;44:655.
- Vincent JL, Bihari DJ, Suter PM, Bruining HA, White J, Nicolas-Chanoine MH, *et al.* The prevalence of nosocomial infection in intensive care units in Europe: Results of the European Prevalence of Infection in Intensive Care (EPIC) study. *JAMA* 1995;274:639–44.

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