Volume 06, Issue 04 (July-August 2023), PP 103-113 www.ijmsdr.org
ISSN: 2581-902X

International Journal of Medical Science and Dental Research

The Effect of Serum Phosphorus Levels on Prognosis And Clinical Outcome in Patients 85 Years and older İn Intensive Care Unit

İrem AKIN ŞEN[1]

[1]*Division of Intensive Care, Department of Internal Medicine, Mersin University, Mersin, Turkey*

ABSTRACT: Background: Phosphate metabolism is often not properly regulated in the course of acute diseases. There are very few publications investigating the relationship between serum phosphorus levels and clinical outcome, cost-effective and mortality in elderly patients.

Aims: The aim of this study was to investigate the relationship between serum phosphorus level and disease course, cost to the healthcare system and clinical outcome in patients aged 85 years and older hospitalized in the intensive care unit.

Study Design: This research is a cross-sectional study.

Methods: Between January 1, 2015 and December 31, 2022, patients aged 85 years and older with no known malignancy or renal disease who were followed up in our clinic were included in the study. The first group (group 1) was hypophosphatemia (< 2.5 mg/dl), group 2 was normophosphatemia (2.5 mg/dl to 4.5 mg/dl) and group 3 was hyperphosphatemia (> 4.5 mg/dl).

Results: Of the patients, 157 (41.5%) were male and 221 (58.5%) were female. According to rehospitalization rates, 6 patients (7%) in group 1, 15 patients (7.3%) in group 2 and 2 patients (2.3%) in group 3 were rehospitalized. According to the clinical outcomes in the first 30-day period, 44 patients (51.2%) in group 1, 103 patients (50%) in group 2 and 68 patients (79.1%) in group 3 died. According to the clinical outcome at the end of intensive care unit stay, 54 (62.8%) of patients in group 1, 117 (56.8%) of patients in group 2 and 70 (81.4%) of patients in group 3 died. There was no difference between the groups according to the cost per patient per day.

Conclusion: Both hypophosphatemia and hyperphosphatemia contribute to mortality as a consequence of impaired energy metabolism. Restoration of normal serum phosphorus levels may have favorable effects on clinical outcome, especially in critically ill elderly patients.

Keywords: *Geriatry, Phosphorus, Mortality, Prognosis, Intensive Care Unit*

I. INTRODUCTION:

The elderly population in Turkey increased by 49% in the last decade and reached 7 million 953 thousand people in 2020. The proportion of the elderly population in the total population increased to 9.5% in 2020. According to forecasts, the proportion of the elderly population in society will gradually increase, reaching 16.3% in 2040 and 22.6% in 2060. Patients over the age of 85 constitute 8% of the entire elderly population. Therefore, it is important that the problems of elderly patients are well defined, prognosis and treatment.

Phosphorus is one of the main building blocks of the cell membrane and is an important anion for cellular events. It also participates in many physiological processes in the human body and is regulated by many organs, including the kidneys, bones and digestive system. (1) However, phosphate metabolism in the body is often not properly regulated in the course of acute diseases.

Many reports have been published on the relationship between serum phosphorus level and life expectancy. Hypophosphatemia in intensive care unit patients causes respiratory failure requiring mechanical ventilation, myocardial dysfunction, impaired response to vasopressor agents, ventricular arrhythmias, paresthesia, tremor, coma, hemolytic anemia and rhabdomyolysis.(2,3)

However, there are very few publications investigating the relationship between serum phosphorus levels and clinical outcome, treatment cost and mortality in elderly patients. The aim of this study was to investigate the relationship between serum phosphorus levels and disease course, cost to the healthcare system and clinical outcome in patients aged 85 years and older hospitalized in the intensive care unit (ICU).

II. MATERİAL AND METHODS

The necessary permissions were obtained from Mersin University Clinical Research Ethics Committee before the study (July/06/2022- 12-457). Written informed consent was obtained from all patients. Every stage of the study was conducted in accordance with the Declaration of Helsinki.

Between January 01, 2015 and December 31, 2022, patients aged 85 years and older with no known malignancy or renal disease who were followed up in our clinic were included in the study. Patients with known malignancy, receiving phosphorus supplements for any reason or undergoing dialysis were excluded.

All patients were divided into 3 groups according to serum phosphorus levels at the time of admission to the intensive care unit. The first group (group 1) was hypophosphatemia (< 2.5 mg/dl), group 2 was normophosphatemia (2.5 mg/dl to 4.5 mg/dl) and group 3 was hyperphosphatemia (> 4.5 mg/dl).

Age, gender and comorbidities of all patients were recorded. Serum biochemical parameters and complete blood count results were noted. Length of stay in intensive care unit was measured and clinical outcome was analyzed.

Compliance of continuous variables with normal distribution was evaluated by Shapiro-Wilk test. Continuous variables conforming to normal distribution are shown as mean ± standard deviation. Continuous variables that do not conform to normal distribution are shown as median (First quarter (Q1) - Third quarter (Q3)). Student's t test was used to compare the means of two independent groups of continuous variables that conform to the normal distribution, while one-way ANOVA test was used to compare the means of more than two independent groups. For continuous variables that do not conform to normal distribution, the Mann Whitney U test was used to compare the medians of two independent groups and the Kruskal-Wallis test was used to compare the medians of more than two groups. Categorical variables are shown with numbers and percentages. The relationships between categorical variables were investigated by Chi-Square analysis. Statistical analysis of the study data was performed with SPSS 29.0.0 package program. Statistical significance level $p < 0.05$ was accepted for all comparisons.

III. RESULTS:

A total of 378 patients were included in this study. Of the patients, 157 (41.5%) were male and 221 (58.5%) were female. The mean age of the patients was 88.8 ± 4.7 years. Comorbidities were found in 347 patients (91.8%). The mean serum phosphorus level was 3.83 ± 1.94 mg/dl in men and 3.58 ± 1.77 mg/dl in women. The differences observed between the groups were not statistically significant (all, $p>0.05$) (Table 1).

When the distribution of laboratory parameters of the patients is analyzed, the median serum glucose level was 121.5 (101 - 185.7) mg/dl. The median serum creatine level was 1.4 (0.8 - 2.6) mg/dl and the mean serum magnesium level was 2.04 ± 0.5 mg/dl. When the distribution of the parameters indicating inflammatory status was analyzed, the mean serum albumin level was 2.73 ± 0.59 g/dl. The median serum C-reactive protein (CRP) level was 71.5 (24 - 137.6) mg/L and the median serum procalcitonin level was 1.71 (0.65 - 7.98) ng/ml. (Table 2)

In the data of complete blood count, the mean red blood cell distribution width (RDW) was 17.9 ± 4.83%, mean platelet volume (MPV) was 11.2 ± 1.77 fL and neutrophil-to-lymphocyte ratio (NLR) was 8 (5-14.1). (Table 3)

The arterial blood gas and coagulation parameters of the patients are shown in Table 3. The mean serum pH level was 7.36 ± 0.11 and the mean O_2 saturation was 80.8 ± 14.22%. The mean serum fibrinogen level was 352.6 ± 144.5 mg/dl and the median INR level was 1.3 (1.13 - 1.72). According to the data on respiratory support parameters of the participants, 334 patients (88.4%) were followed up on room air. Oxygen support was provided by nasal mask in 34 patients (9%) and invasive mechanical ventilation was needed in 10 patients (11.6%) (Table 4).

The resubmit rates and clinical outcomes of the patients are summarized in Table 5. According to the resubmit rates, 6 patients (7%) in group 1, 15 patients (7.3%) in group 2 and 2 patients (2.3%) in group 3 were resubmitted. According to the clinical outcomes in the first 30-day period, 44 patients (51.2%) in group 1, 103 patients (50%) in group 2 and 68 patients (79.1%) in group 3 died. According to the clinical outcome at the end of stay in intensive care unit, 54 (62.8%) of patients in group 1, 117 (56.8%) of patients in group 2 and 70 (81.4%) of patients in group 3 died. The median length of stay in intensive care unit was 6 (3 - 12) days, while the median total length of stay in hospital was 6 (3 - 12) days. There was no difference between the groups according to the cost per patient per day ($p>0.05$).

IV. DISCUSSION:

The fluid-electrolyte balance of elderly patients, especially those hospitalized in the intensive care unit, is very fragile and prone to imbalance. In this study, we evaluated the prognostic value of serum phosphorus levels and its effect on clinical outcome in patients aged 85 years and older hospitalized in the intensive care unit.

The results of this study showed that both hypophosphatemia and hyperphosphatemia were significantly associated with an increased mortality rate in this patient group, both in the first 30 days and throughout the entire study period.

In a retrospective cohort study of 197 patients with severe sepsis or septic shock on mechanical ventilation, patients with hyperphosphatemia had a higher mortality rate in the first 28 days after admission. However, no change was found in the first 28-day mortality in patients with hypophosphatemia. (4)

A study by Kuo et al. reported that hyperphosphatemia in burn patients predicted a higher mortality rate, which was independent of total burn surface area and Acute Physiology and Chronic Health Evaluation II (APACHE II) score (5).

Tazmini et al. conducted a study between serum electrolyte levels and mortality rates in all patients admitted to the emergency department. In multivariate analysis, in-hospital mortality rate with hyperphosphatemia (OR: 3.80 (2.86 - 5.06), $p<0.001$), first 30-day mortality rate (OR: 1.29 (1.13 - 1.48), $p<0.001$) and 1-year mortality rate (HR: 1.37 (1.13 - 1.67), $p=0.001$) were higher than in patients with normophosphatemia (6).

In a retrospective study by Naffaa et al. involving 3894 patients with community-acquired pneumonia, the mortality rate was higher in patient subgroups with serum phosphorus levels less than 1.5 mg/dl (OR: 2.9 (1.8-4.9), $p=0.001$) and more than 4.5 mg/dl (OR: 3.4 (2.7-4.2), $p=0.001$) in the first 24 hours compared to patients with normal serum phosphorus levels. (7)

In a post-hoc analysis study by Jung et al., hyperphosphatemia was found to indicate poor prognosis in 210 septic acute kidney injury patients on continuous renal replacement therapy, while hypophosphatemia was not associated with increased mortality. (8)

In a study by Shor et al., hypophosphatemic patients were divided into two groups according to serum phosphorus levels as severe (serum phosphorus < 1.0 mg/dl) and non-severe (serum phosphorus > 1.0 mg/dl) hypophosphatemia, and it was shown that the risk of death increased approximately eightfold in the severe hypophosphatemia group. (9)

Possible reasons for the association between hyperphosphatemia and increased risk of death in elderly patients hospitalized in the intensive care unit can be explained by considering the following points. First, aging is a process of accelerated cell destruction. Intracellular phosphorus passes from dead cells into blood vessels, destroying vascular endothelial cells and causing vascular inflammation. (10-12) Second, high phosphate concentration leads to an increase in cell mitochondrial membrane potential and reactive oxygen production, further accelerating cell death. (13) Third, both elderly and hyperphosphatemic patients are at higher risk of

developing serious complications such as cardiovascular disease, acute kidney injury (AKI) and end-stage renal disease (14,15).

In our study, we found that hypophosphatemia was associated with an increased need for invasive mechanical ventilation. Phosphorus is the source of ATP (adenosine triphosphate), which is essential for neurological functions and muscle contraction. Disruption of phosphate supply can lead to multiple organ system dysfunctions, including respiratory failure.

In a study reported by Miller et al., the duration of ventilation in the hypophosphatemia group was 3.0 [1.7-5.9] days, while it was 4.8 [2.3-10.5] days in the normophosphatemia group. (4) Similar to this result, the need for more intensive and prolonged mechanical ventilation may occur in patients in the hypophosphatemia group, as found in our study.

Previous evidence has revealed that episodes of hypophosphatemia during ICU stay are associated with higher mortality in the ICU population. After removing confounding factors, Broman et al. found that compared with the normophosphatemic patient group, hypophosphatemic patients had a higher risk of death (HR: 1,2 (1,0-1,5), p=0,009). (16)

On the other hand, data from two studies on this subject also found that hypophosphatemia was associated with longer length of stay in hospital. (17,18) We conducted our study in a general ICU. Hypophosphatemia at ICU admission has not been shown to be associated with ICU and hospital length of stay, but we found that hypophosphatemia was associated with higher mortality compared to normophosphatemic patients.

The advantage of this study is that it included a large number of elderly patients (85 years and older) and is one of the first studies on patients in this age group hospitalized in intensive care. In addition, it allows adjustment for important confounding factors (age, gender, comorbidities and other serum electrolyte imbalances (Na, Ca, Mg)) that may affect mortality rates and allows subgroup analysis. However, the study also has some limitations. First, all laboratory data are initial values at the time of ICU admission and dynamic analysis of long-term follow-up data may help to confirm the findings. Second, serum phosphorus levels are influenced by several factors, including dietary content, fasting time and hormone levels, but not all relevant data of patients were available in our study. Thirdly, since the patients were not subdivided according to the indications for ICU admission and primary diagnoses and the study data were obtained from a database, detailed and accurate data on the specific treatment of certain diseases such as cardiopulmonary arrest and septic shock could not be obtained.

In conclusion, both hypophosphatemia and hyperphosphatemia contribute to mortality as a result of impaired energy metabolism. Normalization of serum phosphorus levels may have favorable effects on clinical outcome, especially in critically ill elderly patients.

ACKNOWLEDGMENTS

We thank all healthcare professionals working in the intensive care unit.

REFERENCES

[1] Kalantar-Zadeh K, Kuwae N, Regidor DL, Kovesdy CP, Kilpatrick RD, Shinaberger CS, McAllister CJ, Budoff MJ, Salusky IB, Kopple JD. Survival predictability of time-varying indicators of bone disease in maintenance hemodialysis patients. Kidney Int. 2006 Aug;70(4):771-80.

[2] Moon H, Chin HJ, Na KY, Joo KW, Kim YS, Kim S, Han SS. Hyperphosphatemia and risks of acute kidney injury, end-stage renal disease, and mortality in hospitalized patients. BMC Nephrol. 2019 Sep 18;20(1):362.

[3] Park KS, Lee Y, Park GM, Park JH, Kim YG, Yang DH, Kang JW, Lim TH, Kim HK, Choe J, Lee SW, Kim YH. Association between serum phosphorus and subclinical coronary atherosclerosis in asymptomatic Korean individuals without kidney dysfunction. Am J Clin Nutr. 2020 Jul 1;112(1):66-73.

[4] 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 May;35(5):485-493.

[5] Kuo G, Lee CC, Yang SY, Hsiao YC, Chuang SS, Chang SW, Tu KH, Fan PC, Tian YC, Chen YC, Chang CH. Hyperphosphatemia is associated with high mortality in severe burns. PLoS One. 2018 Jan 9;13(1):e0190978.
[6] Tazmini K, Nymo SH, Louch WE, Ranhoff AH, Øie E. Electrolyte imbalances in an unselected population in an emergency department: A retrospective cohort study. PLoS One. 2019 Apr 25;14(4):e0215673.
[7] Naffaa ME, Mustafa M, Azzam M, Nasser R, Andria N, Azzam ZS, Braun E. Serum inorganic phosphorus levels predict 30-day mortality in patients with community acquired pneumonia. BMC Infect Dis. 2015 Aug 13;15:332.
[8] Jung SY, Kim H, Park S, Jhee JH, Yun HR, Kim H, Kee YK, Yoon CY, Oh HJ, Chang TI, Park JT, Yoo TH, Kang SW, Lee H, Kim DK, Han SH. Electrolyte and mineral disturbances in septic acute kidney injury patients undergoing continuous renal replacement therapy. Medicine (Baltimore). 2016 Sep;95(36):e4542.
[9] Shor R, Halabe A, Rishver S, Tilis Y, Matas Z, Fux A, Boaz M, Weinstein J. Severe hypophosphatemia in sepsis as a mortality predictor. Ann Clin Lab Sci. 2006 Winter;36(1):67-72.
[10] Lau WL, Pai A, Moe SM, Giachelli CM. Direct effects of phosphate on vascular cell function. Adv Chronic Kidney Dis. 2011 Mar;18(2):105-12.
[11] Wang S, Wu M, Qin L, Song Y, Peng A. DAXX mediates high phosphate-induced endothelial cell apoptosis in vitro through activating ERK signaling. PeerJ. 2020 Jun 19;8:e9203.
[12] Di Marco GS, König M, Stock C, Wiesinger A, Hillebrand U, Reiermann S, Reuter S, Amler S, Köhler G, Buck F, Fobker M, Kümpers P, Oberleithner H, Hausberg M, Lang D, Pavenstädt H, Brand M. High phosphate directly affects endothelial function by downregulating annexin II. Kidney Int. 2013 Feb;83(2):213-22.
[13] Papa S, Skulachev VP. Reactive oxygen species, mitochondria, apoptosis and aging. Mol Cell Biochem. 1997 Sep;174(1-2):305-19.
[14] Liu YL, Lin KH, Tamilselvi S, Chen WK, Shen CY, Chen RJ, Day CH, Wu HC, Viswanadha VP, Huang CY. Elevated Phosphate Levels Trigger Autophagy-Mediated Cellular Apoptosis in H9c2 Cardiomyoblasts. Cardiorenal Med. 2017 Dec;8(1):31-40.
[15] Moon H, Chin HJ, Na KY, Joo KW, Kim YS, Kim S, Han SS. Hyperphosphatemia and risks of acute kidney injury, end-stage renal disease, and mortality in hospitalized patients. BMC Nephrol. 2019 Sep 18;20(1):362.
[16] Broman M, Wilsson AMJ, Hansson F, Klarin B. Analysis of Hypo- and Hyperphosphatemia in an Intensive Care Unit Cohort. Anesth Analg. 2017 Jun;124(6):1897-1905.
[17] Suzuki S, Egi M, Schneider AG, Bellomo R, Hart GK, Hegarty C. Hypophosphatemia in critically ill patients. J Crit Care. 2013 Aug;28(4):536.e9-19.
[18] Haider DG, Lindner G, Wolzt M, Ahmad SS, Sauter T, Leichtle AB, Fiedler GM, Fuhrmann V, Exadaktylos AK. Hyperphosphatemia Is an Independent Risk Factor for Mortality in Critically Ill Patients: Results from a Cross-Sectional Study. PLoS One. 2015 Aug 7;10(8):e0133426.

TABLE LEGENDS

Table 1. Demographic data of the patients and serum phosphorus levels according to gender

	Overall	Hypophosphatemia	Normophosphatemia	Hyperphosphatemia	p	T1-2	T1-3	T2-3
N	378	86	206	86				
Age (years)	88,8 ± 4,7	88,1 ± 7,4	89 ± 3,4	88,9 ± 3,9	0,304	0,326	0,434	0,979
Male	157 (%41,5)	32 (%37,2)	88 (%42,7)	37 (%43)	0,651			
Female	221 (%58,5)	54 (%62,8)	118 (%57,3)	49 (%57)				
Comorbidity - No	31 (%8,2)	7 (%8,1)	19 (%9,2)	5 (%5,8)	0,626			
Comorbidity - Yes	347 (%91,8)	79 (%91,9)	187 (%90,8)	81 (%94,2)				
Male	3,83 ± 1,94	2,07 ± 0,34	3,34 ± 0,62	6,53 ± 2,12				
Female	3,58 ± 1,77	2,03 ± 0,35	3,19 ± 0,56	6,21 ± 1,83				

Table 2. Data on serum biochemical parameters of the patients

	Overall	Hypophosphatemia	Normophosphatemia	Hyperphosphatemia	p	T1-2	T1-3	T2-3
N	378	86	206	86				
Glucose	121,5 (101 - 185,7)	121 (98 - 193,5)	120 (101 - 178)	142 (98,8 - 189)	0,454	0,854	0,806	0,477
Urea	140 (98,8 - 189)	73 (42,7 - 116,4)	77 (50,5 - 130,2)	168 (123 - 217)	< 0,001	0,370	< 0,001	< 0,001
Creatine	1,4 (0,8 - 2,6)	1,09 (0,7 - 1,1)	1,2 (0,75 - 1,9)	3,1 (2,2 - 4,4)	< 0,001	0,497	< 0,001	< 0,001
Sodium (Na)	139,6 ± 11,9	141,9 ± 9,3	139 ± 12,9	138,6 ± 11,7	0,121	0,188	0,108	0,959
Potassium (K)	4,35 ± 0,87	3,94 ± 0,76	4,37 ± 0,87	4,74 ± 0,79	< 0,001	0,006	< 0,001	0,003
Calcium (Ca)	8,2 ± 0,88	8,2 ± 1,1	8,2 ± 0,7	8,2 ± 1,04	0,938	0,972	0,997	0,951
Magnesium (Mg)	2,04 ± 0,5	2,04 ± 0,5	1,96 ± 0,5	2,23 ± 0,5	< 0,001	0,488	0,007	0,001
AST	28 (18 - 54,6)	26 (18,7 - 45,3)	27 (18 - 44)	35,5 (19 - 90,4)	0,099	0,958	0,089	0,161
ALT	16 (10 - 33)	15 (10 - 29)	14 (9 - 29,8)	21,5 (11 - 67)	< 0,001	0,985	0,003	0,002
LDH	249 (190 - 371)	235 (178 - 345)	226 (190 - 326)	320 (202 - 454)	0,095	0,973	0,092	0,148
Total Protein	5,49 ± 1,24	5,16 ± 0,95	5,58 ± 1,45	5,65 ± 0,93	0,024	0,058	0,022	0,925
Albumine	2,73 ± 0,59	2,59 ± 0,64	2,77 ± 0,56	2,77 ± 0,59	0,062	0,083	0,083	0,999

Total Bilirubin	0,74 (0,5 - 1,32)	0,78 (0,53 - 1,57)	0,75 (0,5 - 1,2)	0,7 (0,48 - 1,58)	0,265	0,616	0,178	0,677
Direkt Bilirubin	0,28 (0,14 - 0,59)	0,27 (0,16 - 0,61)	0,28 (0,15 - 0,49)	0,29 (0,11 - 0,79)	0,653	0,879	0,573	0,860
CRP	71,5 (24 - 137,6)	58 (19,8 - 146,3)	64,2 (22,9 - 130,7)	90,9 (31,9 - 168)	0,025	0,038	0,043	0,999
Procalcitonin	1,71 (0,65 - 7,98)	0,56 (0,1 - 3,22)	1,64 (0,73 - 5,81)	8,4 (1,12 - 33,9)	0,193	0,948	0,172	0,288
Parathormone	139,5 (69,8 - 355)	165 (113 - 190,2)	98,2 (67,7 - 191,1)	222 (63,6 - 449,3)	0,192	0,999	0,315	0,339
Vitamin D	12 (9 - 20,3)	17,3 (5,7 - 19,5)	11,6 (8 - 20,3)	14,9 (7,9 - 21,6)	0,893	0,984	0,970	0,915
Troponin	60 (20 - 206)	52 (18 - 201)	51 (19 - 201)	102 (30 - 366)	0,658	0,687	0,829	0,968

Table 3. Data on complete blood count parameters of the patients

	Overall	Hypophosphatemia	Normophosphatemia	Hyperphosphatemia	p	T1-2	T1-3	T2-3
N	378	86	206	86				
Hemoglobin	10,41 ± 2,11	10,5 ± 2,49	10,29 ± 1,91	10,55 ± 2,14	0,531	0,685	0,999	0,661
WBC	10,6 (7,6 - 15,6)	10,25 (7,33 - 14)	10,39 (7,34 - 15,2)	13 (8,51 - 17,1)	0,055	0,394	0,020	0,345

PLT	196 (133,4 - 259,3)	177 (135,9 - 255,4)	212 (140 - 263,2)	174 (122,4 - 254,3)	0,161	0,195	0,728	0,596
RDW	17,9 ± 4,83	17,6 ± 3,12	18,26 ± 5,88	17,34 ± 3,09	0,261	0,553	0,933	0,346
MPV	11,2 ± 1,77	11,4 ± 2,49	11 ± 1,45	11,45 ± 1,57	0,077	0,233	0,987	0,176
NLR	8 (5 - 14,1)	8,17 (5 - 14,5)	7 (4,4 - 11,9)	12 (7 - 22,2)	< 0,001	0,991	< 0,001	< 0,001

Table 4. Data on arterial blood gas and coagulation parameters of the patients

	Overall	Hypophosphatemia	Normophosphatemia	Hyperphosphatemia	p	T1-2	T1-3	T2-3
N	378	86	206	86				
Fibrinogen	352,6 ± 144,5	337,2 ± 102,7	389,9 ± 162,9	296,1 ± 147	0,254	0,631	0,755	0,243
INR	1,3 (1,13 - 1,72)	1,24 (1,12 - 1,76)	1,25 (1,1 - 1,48)	1,48 (1,3 - 2,3)	<0,001	0,900	<0,001	<0,001

aPTT	24,4 ± 10,05	21,6 ± 8,6	25,3 ± 10,7	38,8 ± 4,7	0,018	0,066	0,017	0,863
pH	7,36 ± 0,11	7,38 ± 0,11	7,37 ± 0,1	7,31 ± 0,1	<0,001	0,709	<0,001	0,001
PaO2	61 (43 - 82,4)	58 (43,3 - 82,9)	63 (43 - 82,4)	62 (45 - 82,9)	0,836	0,992	0,896	0,837
PaCO2	40,2 ± 12,7	40,7 ± 11,4	41 ± 13,6	37,9 ± 11,4	0,172	0,983	0,261	0,190
HCO3	22,1 ± 6,3	23,7 ± 6	23 ± 6,5	18,5 ± 4,74	<0,001	0,717	<0,001	<0,001
Base excess	5,28 ± 5,3	4,44 ± 5,51	4,75 ± 5,23	7,36 ± 4,78	<0,001	0,909	<0,001	0,001
O2 saturation	80,8 ± 14,22	80,7 ± 14,4	81,76 ± 14,7	78,7 ± 14,3	0,535	0,927	0,766	0,536

Table 5. Resubmit rates and clinical outcomes of patients

		Overall	Hypophosphatemia	Normophosphatemia	Hyperphosphatemia	p	T1-2	T1-3	T2-3
	N	378	86	206	86				
	LOS - ICU	6 (3 - 12)	5,5 (3 - 10)	6 (4 - 12)	6 (3 - 12)	0,258	0,487	0,981	0,378
	LOS - Hospital	6 (3 - 12)	7 (3 - 12)	6 (4 - 13)	6 (3 - 12)	0,402	0,723	0,906	0,459
First 30 days	Exitus	215 (%56,9)	44 (%51,2)	103 (%50)	68 (%79,1)	< 0,001			
	Alive	163 (%43,1)	42 (%48,8)	103 (%50)	18 (%20,9)				
Clinical Outcome	Exitus	241 (%63,8)	54 (%62,8)	117 (%56,8)	70 (%81,4)	< 0,001			
	Alive	137 (%36,2)	32 (%37,2)	89 (%43,2)	16 (%18,6)				
Resubmit	Yes	23 (%6,1)	6 (%7)	15 (%7,3)	2 (%2,3)	0,251			
	No	355 (%93,9)	80 (%93)	191 (%92,7)	84 (%97,7)				