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ORIGINAL ARTICLE
ORİJİNAL ARAŞTIRMA

Plasma Phosphorus and Mortality from Emergency Department to Intensive Care; A Retrospective Analysis

Plazma Fosforu ve Mortalite, Acil Servisten Yoğun Bakıma; Retrospektif Analiz

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ABSTRACT

Aim: Effective management of unstable patients in the emergency department during the golden hours significantly reduces mortality and morbidity. The world population is getting older and emergency room crowding is increasing. The aim of the study was to analyze the demographic characteristics, initial laboratory values and results of the patients through a retrospective analysis of non-traumatic patients who were admitted to the intensive care unit from the emergency department.

Material and Method: In the study, 1067 patients were included. Blood glucose, phosphorus, platelet, MPW, PDW values and demographic data were taken during the first examinations upon admission to the emergency department. Diagnoses were divided into six groups: pulmonary, internal diseases, cardiac, neurological, poisonings and infections. Outcomes were analyzed.

Results: The mean age of 1067 patients who met the criteria in the study was 69.16±15.61 years and 51.2% were male. Considering the reasons for hospitalization from the emergency service to the Intensive Care; the most frequent hospitalizations were pulmonary with 31.0% (n=337), neurological with 22.1% (n=240) and cardiac with 20.9%. Cut-off point for blood phosphorus levels ≥ 4.15 mg/dL, sensitivity 47.0% specificity 73.0% area under the ROC curve±standard error (AUC±SE)=0.62±in patients hospitalized from the Emergency Department to the Intensive Care Unit and nonsurvivor 0.020 ($p < 0.001$).

Conclusion: Although the study has limitations, it was assumed that the phosphorus level pathologies of critically ill patients at the time of their first admission to the emergency department would negatively affect mortality. To clarify this issue, a large retrospective observational study is needed to determine whether patients with episodes of hypo-hyperphosphatemia have increased morbidity or mortality compared to patients with normal phosphate values. It can be predicted that phosphorus may be an important parameter in mortality scoring in emergency departments in the future.

Keywords: Emergency department, intensive care unit, hyperphosphatemia, mortality

ÖZ

Amaç: Acil serviste stabil olmayan hastaların altın saatlerdeki etkili yönetimi, mortalite ve morbiditeyi önemli oranda azaltmaktadır. Dünya nüfüsu gittikçe yaşlanmakta ve acil servis kalabalıklığı gittikçe artmaktadır. Çalışmada acil servisden yoğun bakıma yatırılan travmatik olmayan hastaların retrospektif analizi ile hastaların demografik özellikleri, ilk laboratuvar değerleri ve sonuçları analiz etmek hedeflendi.

Gereç ve Yöntem: Çalışmaya 1067 hasta dahil edildi. Acil servise başvurudaki ilk tetkiklerinde kan glukozu, fosfor, trombosit, MPW, PDW değerleri ve demografik verileri alındı. Sonlanımları analiz edildi. Tanılar; pulmoner, iç hastalıklar, kardiyak, nörolojik, zehirlenmeler ve enfeksiyonlar olarak altı grupta toplandı.

Bulgular: Çalışmada kriterlere uyan toplam 1067 hastanın yaş ortalaması 69,16±15,61 idi ve %51,2'si erkekti. Acil Servisten yoğun bakıma yatış nedenlerine bakıldığında; yatışların en sık %31,0 (n=337) ile pulmoner, %22,1 (n=240) ile nörolojik ve %20 ,9 ile kardiyak nedenlerden kaynaklandığı tespit edildi. Acil servisten yoğun bakım ünitesine yatırılan ve ölen hastalarda kan fosfor düzeyleri için cut-off noktası ≥ 4,15 mg/dL, sensitivite %47,0 spesifisite %73,0 ROC eğrisi altındaki alan±standart hata (AUC±SE)=0.62±0.020 olarak saptandı ($p < 0.001$).

Sonuç: Çalışmanın sınırlılıkları olsa da, kritik hastaların acil servise ilk başvuru anındaki fosfor düzeyi patolojilerinin mortaliteyi olumsuz etkileyeceği varsayılmıştır. Bu konuyu açıklığa kavuşturmak için, hipo-hiperfosfatemi atakları olan hastaların, fosfat değerleri normal olan hastalarla karşılaştırıldığında artmış morbidite veya mortaliteye sahip olup olmadığını belirlemek için geniş bir retrospektif gözlemsel çalışmaya ihtiyaç vardır. Gelecekte acil servislerde prognoz skorlamalarında fosforun önemli bir parametre olabileceği öngörülebilir.

Anahtar Kelimeler: Acil servis, Yoğun bakım, hiperfosfatemi, mortalite

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INTRODUCTION

Effective management of unstable patients in the Emergency Department (ED) during the golden hours significantly reduces mortality and morbidity. Various scoring systems are used to predict mortality and morbidity of intensive care patients. For the ED, it is thought that the search for similar laboratory parameters to predict mortality and morbidity will affect the patient care plan and quality and will be a guide in Emergency Departments (EDs). The world population is getting older and emergency room crowding is increasing. The Emergency Department is a unique area in the hospital where patients with a wide spectrum of diagnoses, including those in critical condition, are initially treated (1,2).

During acute illnesses, plasma phosphate levels are often impaired regardless of the presence of kidney damage (3,4). Homeostasis of phosphorus is complex and phosphate ion may accumulate due to homeostasis-related changes such as decreased renal clearance, increased consumption in catabolic patients, renal clearance or acidosis (5,6).

Acute hypophosphatemia, with a reported prevalence of 30-50%, is frequently encountered in intensive care units (ICUs). Although the treatment of hypophosphatemia in critically patients is known and practiced, it has not yet been clearly included in the guidelines (7).

Phosphate; It is phosphorus with added oxygen and is 100 times more abundant in the cell than in plasma. Phosphate and phosphorus are used interchangeably in articles. In adults, 85% of phosphate is found in teeth and bones. 14% of the remaining phosphate is in soft tissue and 1% is in extracellular fluid. Phosphorus takes part in intracellular signaling (protein phosphorylation), oxygen transport in the blood (2,3 diphospho glycerate), energy metabolism, bones, cell membrane and nucleic acid structure. In urine, phosphorus plays a role in buffering hydrogen ions (8).

The search for fast and reliable prognosis predictive parameters will always be needed for emergency services and research will continue. Phosphorus is a routine parameter in biochemistry tests in the emergency room and plays an important role in cellular metabolism. (5,9). That's why; Can plasma phosphorus levels play an important role in determining the prognosis of critically ill patients in emergency departments?

And also platelet (PLT), a basic component of blood, has an important role in pathological and physiological events such as inflammation and protection of the integrity of vascular endothelial cells, coagulation and thrombosis (10). PLT indices include PLT count, platelet distribution width (PDW), mean platelet volume (MPV) and plateletcrit (PCT) (11). MPV is the ratio of PCT to the number of PLT. PDW is equal to the PLT volume variation coefficient used to define the distribution of PLT volume (11). A decrease in plasma platelet count is an independent risk factor for critically ill patients in the Intensive Care Unit (ICU) (12).

In the study, a retrospective analysis of non-trauma patients who were admitted to ICUs from the ED was performed, and their demographic characteristics, initial laboratory values checked in the emergency room, and outcomes were analyzed. Because there remains uncertainty as to whether hypo/hyperphosphatemia is associated with mortality or may be markers of disease severity (5).

MATERIAL AND METHOD

This study was approved by the Karabük University Clinical Research Ethics Committee on 29/03/2017 with approval number 3/24. In this study, all patients admitted to the ICU from the ED between 2014 and 2016 were analysed retrospectively. In the study, 1926 patient files were scanned. After excluding patients who were pregnant, acute trauma patients, acute coronary syndrome, patients under 18 years of age and with missing parameters in their files, 1067 patients were included in the study. In the study, plasma glucose, phosphorus (P), thrombocyte (PLT), mean platelet volume (MPW) and Platelet Distribution Width (PDW) values were taken in the first blood examinations at admission to the ED and analysed. And the normal value range for plasma phosphorus measured in the hospital emergency biochemistry laboratory was 2.5-4.5 mg/dl (0.80-1.45 mmol/L). If the plasma phosphorus level was not measured in the first blood samples taken at admission, they were not included in the study. Hospitalization diagnoses are pulmonary (pneumonia, pulmonary embolism, pulmonary edema, chronic obstructive pulmonary diseases, sarcoidosis), internal (renal insufficiency, gastrointestinal bleeding, liver diseases, diabetic ketoacidosis, mushroom poisoning, warfarin overdose and oncological diseases), cardiac (heart failures, arrhythmias, valvular diseases, cardiac arrest), neurological (stroke, intracranial hemorrhages, coma and epileptic seizures), poisonings (inhaled poisoning due to carbon monoxide, thinner and nitrogen gas) and infections (sepsis, meningitis, encephalitis, Crimean-Congo hemorrhagic fever) collected in six groups. Demographic characteristics, initial laboratory values and outcomes of 1067 patients collected in six groups were analyzed retrospectively. Analyzes were performed with IBM SPSS Package Program version 24.0 (IBM Corporation, Armonk, NY, USA). ROC analyzes were performed with the ROC Curve Analysis Test. Statistical significance level was considered as $p<0.05$.

Table 1: Intensive Care Unit admission and outcomes by diagnostic groups

	Pulmonary diseases (31.0%)	Neurological diseases (22.1%)	Cardiac diseases (20.9%)	Internal medicine diseases (18.0%)	Poisonings (6.0%)	Infections (2.0%)	Total (100.0%)	p
Age, year [Median (Min-Max)]	75.00 (21-100)	72.00 (21-101)	67.50 (21-92)	72.00 (19-99)	43.00 (18-85)	75.00 (40-94)	72.00 (18-101)	<0.001*
Plasma glucose, mg/dL [Median (Min-Max)]	170.00 (44-566)	151.00 (74-717)	138.50 (68-686)	147.00 (9-800)	131.00 (69-334)	137.50 (20-780)	152.00 (9-800)	<0.001*
Phosphore, mg/dL [Median (Min-Max)]	4.15 (0.70-11.60)	3.40 (1.10-9.30)	3.50 (1.40-9.30)	3.80 (0.50-11.50)	3.10 (1.80-5.50)	3.15 (1.10-7.40)	3.60 (0.50-11.60)	<0.001*
Platelet, 10^3/µL [Median (Min-Max)]	216.00 (8.30-654)	209.00 (27-635)	218.50 (8.80-388)	236.50 (13-517)	222.15 (132-383)	193.00 (8-761)	218.00 (8-761)	0.467*
MPV, fl [Median (Min-Max)]	7.90 (4-14)	8.58 (4-93.37)	8.24 (5.46-16.30)	8.11 (5.17-18.80)	7.87 (5.45-14.82)	7.70 (5.38-84.05)	8.13 (4-93.37)	0.003*
PDW, % [Median (Min-Max)]	19.90 (2.78-48.65)	19.98 (2.20-24.64)	19.90 (12.80-23.89)	19.96 (0-31)	19.26 (12.50-24.80)	19.70 (15-21.60)	19.89 (0-48.65)	0.274*
Outcomes								<0.001**
Nonsurvivors (n/%)	140 (42.0%)	87 (36.6%)	23 (10.7%)	73 (37.4%)	0 (0.0%)	6 (27.3%)	329 (30.8%)	
Survivors (n/%)	179 (53.8%)	138 (58.0%)	134 (62.3%)	110 (56.4%)	54 (84.4%)	15 (68.2%)	630 (59.0%)	
Tranport external center ICU (n/%)	14 (4.2%)	13 (5.5%)	58 (27.0%)	12 (6.2%)	10 (15.6%)	1 (4.5%)	108 (10.2%)	
Total	333 (100.0%)	238 (100.0%)	215 (100.0%)	195 (100.0%)	64 (100.0%)	22 (100.0%)	1067 (100.0%)	

*Kruskal Wallis Test, ** Chi Square Test, PLT: platelet, MPV: mean platelet volume, PDW: Platelet Distribution Width, ICU: Intensive Care Unit

Table 2: Comparison of laboratory values of nonsurvivors and survivors patients

	Nonsurvivors	Survivors	Total	p
Age, year [Median (Min-Max)]	76.00 (21-100)	71.00 (18-101)	72.00 (18-101)	<0.001*
Plasma glucose, mg/dL [Median (Min-Max)]	160.50 (9-780)	147.00 (13-800)	152.00 (9-800)	0.006*
Phosphour, mg/dL [Median (Min-Max)]	4.00 (0.50-11.60)	3.50 (0.70-9.70)	3.60 (0.50-11.60)	<0.001*
PLT, 10^3/µL [Median (Min-Max)]	219.00 (8.30-654)	217.00 (27-761)	218.00 (8-761)	0.817*
MPV, fl [Median (Min-Max)]	8.22 (4-92.6)	8,10 (4.06-93.37)	8.13 (4-93.37)	0.562*
PDW, % [Median (Min-Max)]	20.00 (8.50-48.65)	19.84 (0.0-25.80)	19.89 (0-48.65)	0.827*

* Mann Whitney U Test, PLT: platelet, MPV: mean platelet volume, PDW: Platelet Distribution Width

Table 3. Cut-off point for blood phosphorus levels in patients transferred from the emergency department to the ICU and non-survival

	Diagnostic test					ROC Curve		p
	Cut-off	Sensitivity	Specificity	PPV	NPV	AUC	95% CL	
Fosfor	≥ 4.15	47.00	73.00	33.40	66.60	0.62	0.585-0.662	<0.001**

* PPV: Positive predictive value, NPV: Negative predictive value, AUC: Area Under the Curve, CL: Confidence limits, ** ROC Curve Analysis Test

RESULTS

The mean age of 1067 patients who met the criteria in the study was 69.16±15.61 years and 51.2% were male. Considering the reasons for hospitalization from the emergency service to the ICU; The most frequent hospitalizations were pulmonary with 31.0% (n=337), neurological with 22.1% (n=240) and cardiac with 20.9%. It was determined that 42.0% (n=140) of the cases caused by pulmonary disease, 37.4% (n=73) of cases caused by internal disease, and 36.6% (n=87) of cases caused by neurological resulted in nonsuvivors (**Table 1**).

While 42.6% (n=140) (most common) of the cases who died were due to pulmonary causes, 53.7% (n=58) of the cases referred were cardiac causes. It was determined that 62.3% (n=134) of the cases caused by cardiac causes were discharged with recovery (p<0.001) (**Table 1**). It was determined that the median age values and glucose and phosphorus values of the patients who died in the ICU were statistically significantly higher than those of the survivor patients (**Table 2**).

Cut-off point for blood phosphorus levels ≥ 4.15 mg/dL, sensitivity 47.0% specificity 73.0% area under the ROC curve±standard error (AUC±SE)=0.62±in patients hospitalized from the ED to the ICU and nonsurvivor 0.020 (p < 0.001) (**Table 3**, **Figure 1**).

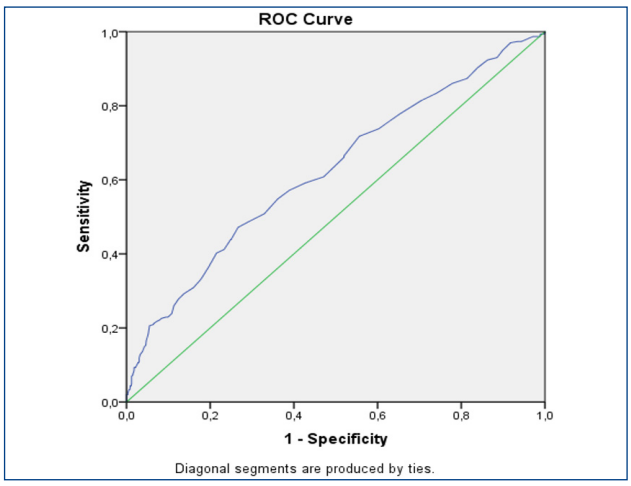

Figure 1. ROC curve graph of blood phosphorus levels

DISCUSSION

This retrospective study used plasma phosphorus levels in conjunction with emergency severity indices in critically ill patients in the ED. It also evaluates the prognosis of patients early by evaluating plasma phosphorus levels in the first blood samples taken at the first admission to the ED. Thus, the aim is to reduce the density of the ED and take rapid action with early intensive care consultation and contribute to the prognosis of patients. Peter Safar's words 'The most sophisticated intensive care often becomes unnecessarily expensive terminal care when the pre-ICU system fails' (13) in 1974 still maintain their importance. That's why research will always continue for the better.

In the study of Zhang S et al., 204 of 261 patients admitted to ICU were found 57 were nonsurvivor. When their etiologies were grouped, pulmonary diseases were the first in 26.5% of the survivors, followed by trauma in 12.3%, cardiac in 10.3% and neurological in 9.8%, respectively. It was determined that the most common cause of death was pulmonary diseases (13%), followed by trauma-related diseases (12.3%) (10). In our study, when the diseases admitted to ICU due to ED were grouped, it was determined that pulmonary diseases ranked first, followed by neurological diseases and cardiac. It is thought that the rate of pulmonary diseases were higher in our study due to the high density of Chronic Obstructive Pulmonary Disease (COPD) patients in the region where the study was scanned and the frequent pneumonia attacks. And also, in our study, ICU hospitalizations due to trauma were excluded, so they were not included in the list. It is also thought that one of the reasons for the difference in the deceased patient groups in our study may be due to the exclusion of acute coronary syndrome patients from the cardiac diseases group. No deaths due to poisoning were detected in our study, but 10 poisoning patients in our study were transported to a higher center and all survivors. In the study of Zhang S et al., it is also thought that the grouping of etiologies is relatively low since internal medicine diagnoses are separated within themselves (kidney failure, liver failure, gastrointestinal system, etc.) (10).

Broman et al.'s Cohort study compared patients with hyperphosphatemia and patients with an unstable phosphate profile in the ICU with patients with normophosphatemia.

180-day survival was found to be significantly lower in patients with hyperphosphatemia. Cox analysis found a significantly higher risk of death due to an increased risk of mortality compared to patients with normophosphatemia (5), which is also consistent with our study. It may be confusing that our study was divided into 6 main disease groups and that malignancy patients were only in the internal diseases group. At the same time, the fact that we analyzed it without taking into account other confounding factors that would affect phosphate levels is among the limitations of our analysis.

Despite many studies in the literature on hypophosphatemia associated with high mortality (14, 15), Jang et al. found that patients in the hypophosphatemia group had comparatively lower mortality (16).Studies have shown that hyperphosphatemia is associated with an increase in mortality in patients diagnosed with pneumonia in the emergency department (17,18). In our study, the plasma phosphorus level showed a statistical difference in the pulmonary diseases group, and the fact that it was the group with the highest number of patients dying as an outcome may be suggestive for new studies.

Thrombocytopenia is a common laboratory parameter that affects one-third of patients hospitalized in ICU (19). In the study of Efe et al., they found that the mortality rate of patients with low platelet, high MPV and PDW values was high. Furthermore, in Zhang S et al.'s study of MPV, patients with higher MPV and PDW were associated with higher mortality compared with those with normal MPV and PDW (10). There are also studies (20,21) finding that high MPV and PDW are associated with COPD and infections. MPV is a measure of PLT volume. In cases where PLTs are consumed excessively, mature PLTs will be released from the bone marrow and immature PLTs with larger volumes will also be present in the plasma. Thus, the elevation of both MPV and PDW explains why they are increased in critically ill patients (10,11,19). In our study, no significant statistical difference was found in PLT values between disease groups, nor was it found to be significant on mortality. This can be explained by the fact that the laboratory parameters taken in our study are the values at the first admission to the ED. However, MPV median value was statistically significant in neurological diseases compared to other groups, which can be attributed to the frequency of intracranial hemorrhages and ischemic infarcts among neurological diseases in this study.

Stress hyperglycemia is a frequently detected condition in patients admitted to the Emergency Department (22,23) and admitted to intensive care. In the study of Mantani et al., which included approximately 9 years of ICU data, it was concluded that hyperglycemia in non-diabetic ICU patients affected hospital mortality and length of hospital stay independently and in a dose-response manner (24). In our study, consistent with the literature, a statistically significant difference was found in the plasma glucose of the deceased compared to the living (even though it was the plasma glucose in the first blood sample taken in the emergency room). In addition, in this study, a statistically significant difference in plasma glucose was detected in the emergency department according to disease groups in pulmonary diseases compared to other groups.

CONCLUSION

It is not yet clear whether hypo-hyperphosphatemia is directly associated with death or merely an indicator of disease severity. Although the study has limitations, assumed that the phosphorus level pathologies of critically ill patients at the time of their first admission to the emergency department would negatively affect mortality. To clarify this issue, a large retrospective observational study is needed to determine whether patients with episodes of hypo-hyperphosphatemia have increased morbidity or mortality compared to patients with normal phosphate values. It can be predicted that phosphorus may be an important parameter in prognosis scoring in emergency departments in the future.

ETHICAL DECLARATIONS

Ethics Committee Approval: This study was approved by the Karabük University Clinical Research Ethics Committee on 29/03/2017 with approval number 3/24.

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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