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مرکز همایش‌های بین‌المللی روزبه

In The Name of God



Hypophosphatemia in ICU Patients

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Nephrology

2024



قطب علمی آموزشی نفرولوژی مرکز تحقیقات نفرولوژی

Group	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
1	1 H																	2 He
2	3 Li	4 Be											5 B	6 C	7 N	8 O	9 F	10 Ne
3	11 Na	12 Mg											13 Al	14 Si	15 P	16 S	17 Cl	18 Ar
4	19 K	20 Ca	21 Sc	22 Ti	23 V	24 Cr	25 Mn	26 Fe	27 Co	28 Ni	29 Cu	30 Zn	31 Ga	32 Ge	33 As	34 Se	35 Br	36 Kr
5	37 Rb	38 Sr	39 Y	40 Zr	41 Nb	42 Mo	43 Tc	44 Ru	45 Rh	46 Pd	47 Ag	48 Cd	49 In	50 Sn	51 Sb	52 Te	53 I	54 Xe
6	55 Cs	56 Ba	* 71 Lu	72 Hf	73 Ta	74 W	75 Re	76 Os	77 Ir	78 Pt	79 Au	80 Hg	81 Tl	82 Pb	83 Bi	84 Po	85 At	86 Rn
7	87 Fr	88 Ra	* 103 Lr	104 Rf	105 Db	106 Sg	107 Bh	108 Hs	109 Mt	110 Ds	111 Rg	112 Cn	113 Nh	114 Fl	115 Mc	116 Lv	117 Ts	118 Og
			* 57 La	58 Ce	59 Pr	60 Nd	61 Pm	62 Sm	63 Eu	64 Gd	65 Tb	66 Dy	67 Ho	68 Er	69 Tm	70 Yb		
			* 89 Ac	90 Th	91 Pa	92 U	93 Np	94 Pu	95 Am	96 Cm	97 Bk	98 Cf	99 Es	100 Fm	101 Md	102 No		



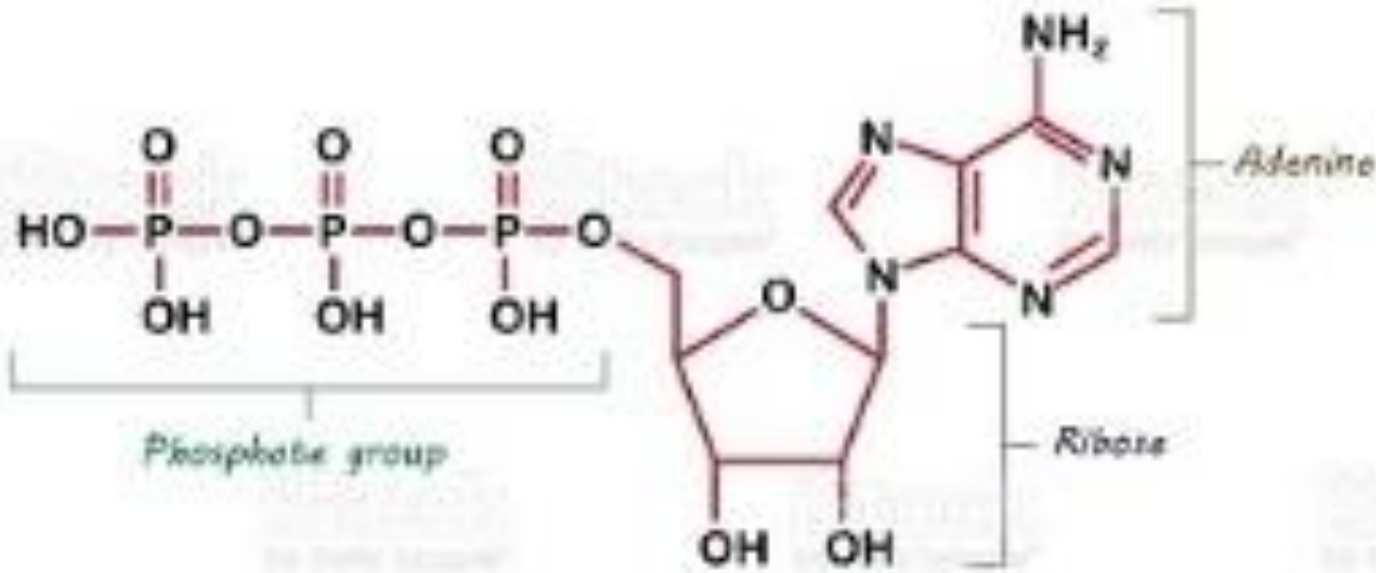
مردن من مردن یک برگ نبود
چشم فرستادی برام تا ببینم؛ که دیدم
انجیر میخواد دنیا بیاد، آهن و فسفرش کمه

جواب زنده بودنم مرگ نبود
گفتی بیا زندگی خیلی زیباست؛ دویدم
گفتی ببند چشمتو وقت رفتنه

شادروان حسین پناهی

Biology ● ● ●

Adenosine Triphosphate (ATP)



- Energy-carrier in all of living things
- Consist of nitrogenous base (adenine), sugar (ribose) and phosphate group



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فسفر

عدد اتمی ۱۵

عدد جرمی

۳۰/۹۷۳۷

Frequency and Risk Factors of Hypophosphatemia in Patients Admitted to Emergency Intensive Care Unit in Zagazig University Hospitals

Indian Journal of Critical Care Medicine: Peer-reviewed, Official Publication of Indian Society of Critical Care Medicine 2023 Vol. 27 Issue 4 Pages 277



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Inorganic phosphate (Pi) is a major electrolyte that participates in many functional & integral processes in the body. Low Pi levels may lead to multiple organ dysfunction. It is estimated to occur in 40–80% of ICU patients. However, it may be ignored in ICU.



A prospective cross-sectional study included 500 adult ICU cases in two groups; a group with normal Pi levels & a group with hypophosphatemia.

Results

56.8% had NL phosphate.

43.2% had low phosphate.

Hypophosphatemia group were associated with a significantly **higher** Acute Physiological & Chronic Health Evaluation (APACHE II) score, a longer hospital & ICU stay, a higher incidence of mechanical ventilation with a longer duration on it, & a significantly higher mortality rate.



Conclusion



Hypophosphatemia associated with
Higher APACHE II score,
Longer stay in the hospital and ICU,
Higher ratio of mechanical ventilation, & a
Higher mortality rate.

Hypophosphatemia on ICU admission is Associated with an increased length of stay in the ICU and Time under mechanical ventilation

H. Wozniak, A. Dos Santos Rocha, T. S. Beckmann, C. Larpin, N. Buetti, H. Quintard, et al.



Hypophosphatemia is frequently observed in the ICU & is associated with several impairments such as respiratory failure or infections. They hypothesized that hypophosphatemia on ICU admission is associated with a **prolonged duration of mechanical ventilation & ICU length of stay (LOS), particularly in COVID-19 patients.** This cross-sectional study analyzed data from **1226 patients** hospitalized in the ICU of the Geneva University Hospitals from August 2020 to April 2021.

Patients were categorized as having hypophosphatemia ($P \leq 0.8$ mmol/L) or non-hypophosphatemia ($P > 0.8$ mmol/L) on ICU admission.



Overall, 250 (20%) patients presented hypophosphatemia on ICU admission. In the univariable analysis, hypophosphatemic patients had longer ICU LOS than non-hypophosphatemic patients, 7.4 days (± 10.4) versus 5.6 days (± 8.3), ($p < 0.01$).

Hypophosphatemia

on ICU admission was

associated with a **prolonged duration of mechanical ventilation**, 7.4 days (± 11.2)

versus 5.6 days (± 8.9), ($p < 0.01$). **These**

associations were confirmed in the multivariable analysis ($p < 0.01$).



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In the subgroup of COVID-19 patients, a significant association

between hypophosphatemia & ICU LOS & duration of mechanical ventilation was also observed. In conclusion, hypophosphatemia on ICU admission is associated with a longer ICU LOS & time under mechanical ventilation, both in the general ICU population & in COVID-19 patients.



Hypophosphatemia and outcomes in ICU: a systematic review and meta-analysis

J. C. K. Sin, L. King, E. Ballard, S. Llewellyn, K. B. Laupland and A. Tabah

Journal of intensive care medicine 2021 Vol. 36 Issue 9 Pages 1025-1035



Hypophosphatemia is reported in up to **5% of hospitalized** & ranges from **20% to 80% in critically ill patients.**

They evaluated the effect of hypophosphatemia on **mortality** & **LOS** in ICU patients.

MEDLINE, EMBASE, Cochrane Library (Reviews and Trials), & PubMed were searched for articles in English. The **primary outcome** was **mortality** and **secondary outcome** was **LOS**. The quality of evidence was graded using a modified Newcastle-Ottawa Scale.

Results



Their search yielded **828 articles & ultimately included 12 studies with 7626 participants in the analysis. Hypophosphatemia was associated with increased hospital LOS (2.19 days [95% CI, 1.74-2.64]) & ICU LOS (2.22 days [95% CI, 1.00-3.44]) but not mortality (RR: 1.13 [95% CI, 0.98-1.31]; P=0.09).**

Conclusions



Hypophosphatemia in ICU was associated with **increased hospital & ICU LOS** but **not all-cause mortality**. Hypophosphatemia appears to be a **marker of disease severity**. Limited number of available studies & varied study designs did not allow for the ascertainment of the effect of severe hypophosphatemia on patient mortality.

Hypophosphatemia in critically ill patients with acute kidney injury on renal replacement therapies

V. Pistolesi, L. Zeppilli, E. Fiaccadori, G. Regolisti, L. Tritapepe and S. Morabito

Journal of Nephrology 2019 Vol. 32 Issue 6 Pages 895-908



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Hypophosphatemia is a common but often underestimated electrolyte derangement among ICU patients. Low P levels can lead to cellular dysfunction with potentially relevant clinical manifestations (muscle weakness, respiratory failure, lethargy, confusion, arrhythmias).

In critically ill patients with AKI, RRTs represent a well-known risk factor for hypophosphatemia, especially if the most intensive & prolonged modalities of RRT, such as CRRT or prolonged intermittent RRT, are used.



At that time,

No evidence-based specific guidelines was available for the treatment of hypophosphatemia in the critically ill; however, considering the potentially negative impact of hypophosphatemia on morbidity & mortality, strategies aimed at reducing its incidence & severity should be timely implemented in the ICUs.



In critically ill patients on RRT,
the most appropriate strategy

is to anticipate the **onset of hypophosphatemia** by
use of **phosphate-containing solutions for RRT**. The
present review is aimed at summarizing the most
relevant evidence concerning **epidemiology**,
prognostic impact, prevention & treatment of
hypophosphatemia in these patients with focus on
RRT-induced hypophosphatemia.



Hypophosphatemia and duration of respiratory failure and mortality in critically ill patients

CK Federspiel, TS Itenov, K Thormar, KD Liu, MH Bestle
Acta Anaesthesiologica Scandinavica, 2018



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Hypophosphatemia has been associated with **prolonged duration of respiratory failure & increased mortality in critically ill patients**, but there is **very limited evidence supporting the negative effects of low phosphate**. This study examined the association between hypophosphatemia at ICU admission & time to successful weaning & 28-day mortality.

A cohort study



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that included **all mechanically ventilated adult patients admitted to the ICU in 2013 at Nordsjællands Hospital**. Hypophosphatemia was defined as a **serum $iP < 0.80$ mmol/L**. Multivariate Cox-regression was used to evaluate the effect of hypophosphatemia on mechanical ventilation & 28-day mortality.

Of total of patients, 190 was eligible.

122 (64.2%) had iP levels measured

during the first 24h of admission, & of whom

25 (20.5%) were hypophosphatemic.

74% were successfully weaned from the ventilator within 28

days. Hypophosphatemia was not associated with this

outcome (HR: 0.56; 95% CI: 0.30-1.04; P = .067).

All-cause 28-day **mortality** was **32.6%** & Hypophosphatemia

was also not associated with 28-day mortality (HR: 1.64; 95% CI:

0.65-4.17; P = .447).



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Hypophosphatemia

at ICU admission **was not**

associated with prolonged respiratory failure nor mortality. Further studies are warranted, where phosphate is measured systematically on all patients to elucidate the effect of low phosphate on relevant outcomes.



قطب علمی آموزشی نفرولوژی مرکز تحقیقات نفرولوژی

Efficacy and safety of a phosphate replacement strategy for severe hypophosphatemia in the ICU

E. Engwerda, M. Van den Berg, M. Blans, A. Bech and H. De Boer

Neth J Med 2018 Vol. 76 Issue 10 Pages 437-441



قطب علمی آموزشی نفرولوژی مرکز تحقیقات نفرولوژی

Experience with **P replacement** is **limited** in **severe** hypophosphatemia. This study compares the efficacy & safety of an individualized regimen of **serum P < 0.4 mmol/l** treatment in ICU patients to patients with **moderate** hypophosphatemia (0.4-0.6 mmol/l).

A retrospective cohort included

36 patients with **severe** &

35 patients with **moderate** hypophosphatemia.

Supplementation dose was calculated according to the equation:

P dose (in mmol)=

0.5 x body weight x (1.25–[serum P]).

Na-K-phosphate was infused at a rate of **10 mmol/h**. Blood samples were taken at baseline & the next morning at 06.00 hrs.



Serum P rose to > 0.40 mmol/l in all patients with severe hypophosphatemia



& to > 0.60 mmol/l in 56% of patients with severe hypophosphatemia & in 86% of patients with moderate hypophosphatemia (p= 0.01).

Mild hyperphosphatemia was observed in one patient only (1.53 mmol/l), hyperkalemia was observed in three patients (all three had severe hypophosphatemia, average potassium after supplementation was 5.2 ± 0.2 mmol/l) & serum Ca levels remained unchanged in both groups.

Conclusion



Individualized P replacement was effective & safe for both moderate & severe hypophosphatemia, but was more accurate in moderate hypophosphatemia.

Hypophosphatemia in critically ill patients with acute kidney injury treated with hemodialysis is associated with adverse events

C. Lim, H. K. Tan and M. Kaushik

Clinical kidney journal 2017 Vol. 10 Issue 3 Pages 341-347



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Hypophosphatemia in critically ill patients **may be exacerbated** by RRT. This study aimed to identify **risk factors & adverse outcomes** associated with **hypophosphatemia** in ICU patients treated with **RRT for AKI**.



A secondary analysis of data from a single-center prospective cohort of medical & surgical ICU patients with RRT for AKI between 18 December 2010 and 3 April 2013.

& RRT laboratory, Demographic, comorbidity & lab data were retrieved from patient case notes & electronic medical records.

Outcomes assessed were hypophosphatemia ($P < 0.94$ mmol/L) during RRT, ICU mortality, & duration of mechanical ventilation & vasopressor support.

Results



Of 96 patients received acute RRT, 25 (26.0%) developed **hypophosphatemia**. On multivariate logistic regression, serum P at RRT initiation [adjusted OR 0.29, 95% CI (0.09, 0.91), P = 0.03] was independently associated with **hypophosphatemia** during acute RRT.

Patients with **hypophosphatemia** during RRT required **longer ventilatory support** [median 12 (interquartile range: 8, 17) days VS 5 (3, 9) days, P < 0.001] & **vasopressor support** [5 (4, 15) days VS 2 (2, 6) days, P = 0.003] compared with those without hypophosphatemia but **there was no significant difference in ICU mortality** [5 patients (20.0%) VS 24 patients (33.8%), P = 0.20]. **Hypophosphatemia** during RRT was independently associated with **prolonged mechanical ventilation (≥ 7 days)** [adjusted OR 14.0, 95% CI (1.37, 143.90), P = 0.03].

Conclusion



Hypophosphatemia is common during acute RRT for critically ill patients & was associated with adverse clinical outcomes.

Analysis of hypo-and hyperphosphatemia in an intensive care unit cohort

M. Broman, A. M. Wilsson, F. Hansson and B. Klarin

Anesthesia & Analgesia 2017 Vol. 124 Issue 6 Pages 1897-1905



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Blood P levels are vulnerable to fluctuations & changes in P levels are often neglected.
The aim of this study was to evaluate whether deviations in phosphate levels correlate to higher 180-day overall mortality or morbidity.

4656 patients with 19,467 iP values

treated at the adult ICU at Skåne University Hospital, Lund, Sweden

during 2006–2014 were retrospectively divided into a **control group** & **3 study groups: hypophosphatemia, hyperphosphatemia, & a mixed group** showing both hypo/hyperphosphatemia.

Sex, age, disease severity represented by maximal organ system Sequential Organ Failure Assessment score, renal Sequential Organ Failure Assessment score, lowest ionized Ca value, & diagnoses classes were included in a **Cox hazard model** to adjust for **confounding factors**, with time to death in the first 180 days from the ICU admission as outcome.



RESULTS



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When compared to normophosphatemic controls, the **hyperphosphatemic** study group was associated with **higher risk of death** with a HR of 1.2 (98.3% CI 1.0–1.5, P=. 0089). **Mortality** in the **hypophosphatemic** or mixed study group **did not differ from controls**. The mixed group showed **markedly longer ventilator times & ICU stays compared to all other groups**.

CONCLUSIONS



Phosphate alterations in ICU patients are **common & associated with worse morbidity & mortality. Many underlying pathophysiologic mechanisms may play a role. A rapidly changing phosphate level or isolated hypo or hyperphosphatemia should be urgently corrected.**

Hypophosphatemia in critically ill patients

S. Suzuki, M. Egi, A. G. Schneider, R. Bellomo, G. K. Hart and C. Hegarty

Journal of critical care 2013 Vol. 28 Issue 4 Pages 536. e9-536. e19



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The aim of this retrospective observational **study in ICU** in an Australian university teaching hospital enrolling **2730** was to **assess the association of P concentration with key clinical outcomes** in a heterogeneous cohort of critically ill patients.

adult critically ill patients.

Results



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They studied **10504 P measurements** with a mean value of **1.17 mmol/L** (measurements every **28.8 hours** on average).

Hyperphosphatemia ($iP > 1.4$ mmol/L) occurred in **45%** & **Hypophosphatemia** ($iP \leq 0.6$ mmol/L) in **20%**.

ICU nonsurvivors had **lower minimum P concentrations** than did survivors ($P = .009$).

Similar results were seen for **hospital mortality**. But, on multivariable logistic regression analysis, hypophosphatemia was not independently associated with ICU mortality (adjusted OR, 0.86 [95% CI, 0.66-1.10]; P = .24) & hospital mortality (OR, 0.89 [0.73-1.07]; P = .21). Even when different cutoff points were used for hypophosphatemia ($iP \leq 0.5, 0.4, 0.3, \text{ or } 0.2 \text{ mmol/L}$), hypophosphatemia was not an independent risk factor for ICU & hospital mortality. In addition, timing of onset & duration of hypophosphatemia were not independent risk factor for ICU & hospital mortality.



Conclusions



Hypophosphatemia behaves like a **general marker of illness severity** & not as an independent predictor of **ICU or in-hospital mortality** in critically ill patients.

Approach to hypophosphataemia in intensive care units—a nationwide survey

D. Geerse, A. Bindels, M. Kuiper, A. Roos, P. Spronk and M. Schultz
hospital 2012 Vol. 21 Pages 31



Evidence-based guidelines for monitoring of serum P levels & for the treatment of hypophosphataemia in critically ill patients **are lacking**. The aim of this survey was to evaluate current practice with respect to **diagnosis & treatment of hypophosphataemia** in critically ill patients among ICU physicians in the **Netherlands**.



A survey was conducted among all hospitals with an ICU in the **Netherlands**. A **questionnaire** was sent, with questions on practice regarding serum P **monitoring & treatment of hypophosphataemia**. Respondents returned the questionnaire either by **mail** or through a **web-based** survey.

Results



A response was received from **67/89 ICUs (75%)**. Respondents mentioned **RRT, sepsis & malnutrition**, as well as **surgery** involving **cardiopulmonary bypass** as the most important causes of **hypophosphataemia** in ICU patients. Of all respondents, **46%** reported to measure serum P levels on a daily basis, whereas in **12%** serum P levels were measured only on clinical indication.

Less than half of the respondents had some sort of guideline for correction of hypophosphataemia. In a vast majority (79%), correction of hypophosphataemia was reported to start with serum P levels < 0.60 mmol/l. **IV administration of phosphate** was the preferred method of correction, with widely variable dosages and speeds of infusion. Complications of IV phosphate were reported to occur infrequently.



Conclusion



There is **large variability** in the way serum P is monitored & **hypophosphataemia** is treated in critically ill patients in the Netherlands.

Take home Messages

Pi is a major electrolyte that participates in many functional processes.

Hypophosphatemia occurred in 40–80% of ICU patients. However, it may be ignored in ICU.

Is associated with Higher APACHE II score, **Longer stay in the hospital** and ICU, Higher ratio of mechanical ventilation, & a Higher mortality rate.

In **COVID-19** patients, a significant association between hypophosphatemia & **ICU LOS** & duration of mechanical ventilation was also observed.

Appears as a marker of **disease severity**, cellular dysfunction, **muscle weakness**, respiratory failure, **lethargy**, confusion & **arrhythmias**.



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