

HYPOPHOSPHATAEMIA IN CRITICALLY ILL CHILDREN

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ABSTRACT

BACKGROUND

To estimate the prevalence of hypophosphataemia and outcome associated with this disturbance in children admitted to PICU.

METHOD

In this prospective cohort study, 102 children admitted consecutively to a paediatric intensive care unit (PICU) were monitored regarding their phosphorus serum levels during the first 7 days of admission. Age, gender, diagnosis at admission, malnutrition, starvation period, length of stay, and outcome were analysed as independent variables for hypophosphataemia.

RESULTS

Most of our patients (56%) developed hypophosphataemia during their PICU stay. The number of starvation days, days on mechanical ventilation, and survival to discharge were significantly associated with hypophosphataemia. The worst outcomes correlated well with this abnormality.

CONCLUSION

Hypophosphataemia was commonly observed in our PICU and was associated with the presence of respiratory diseases, infections, and increased starvation days and ventilation days. These factors might be considered as risk factors for hypophosphataemia in critically ill children.

KEYWORDS

Hypophosphataemia, PICU, Critically Ill Children.

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INTRODUCTION

Phosphorus in the form of inorganic or organic phosphate is a major component of all tissues and is essential for many functions within the body. It is a vital constituent of bone and cell membranes and of molecules such as adenosine triphosphate (ATP), nicotinamide adenine dinucleotide (NAD), cyclic adenosine monophosphate (cAMP) and cyclic guanosine monophosphate (cGMP); it is essential for energy storage and metabolism and it is important for cell signalling and enzyme activation.^[1]

Most phosphorus is in bone or is intracellular, with <1% in plasma. More than any other electrolyte, the phosphorus concentration varies with age. The teleologic explanation for the high concentration during childhood is the need for phosphorus to facilitate growth. There is diurnal variation in the plasma phosphorus concentration with the peak during sleep.^[2] Hypophosphataemia is a metabolic disturbance with potential serious complications and is often unrecognized in critically ill children (CIC).^[3]

Three main mechanisms lead to hypophosphataemia: long-term low intake, decreased absorptive state, intracellular redistribution, and increased renal tubular losses.^[4-8] Symptoms of hypophosphataemia tend to be nonspecific in the majority of cases and include fatigue and irritability. However,

severe hypophosphataemia (Less than 1.0 mg/dL) may lead to more serious problems^[4] such as reduced diaphragmatic contractility,^[9] cardiac arrhythmias,^[10] myocardial reduction, and severe congestive cardiac insufficiency in the postoperative period of cardiac surgery.^[11] Leukocyte dysfunction^[10] and neuromuscular disturbances.^[8]

The aim of this study was to estimate the prevalence of hypophosphataemia in children admitted to our PICU.

MATERIALS AND METHODS

All infants and children admitted to Kempegowda Institute of Medical Sciences PICU during the period from January 2014 through December 2014 were enrolled. Children aged 1 month to 18 years admitted to paediatric intensive care unit for 3 days or more were included. Neonates and those suffering from chronic renal failure, renal tubular defects, and hyperparathyroidism were excluded. The study was explained and consents were obtained from all parents or legal guardians before enrolment.

Initial evaluation included history and clinical examination. Then, routine laboratory investigations were done as per our PICU protocols such as complete haemogram, erythrocyte sedimentation rate, C-reactive protein, serum electrolytes, serum aminotransferases, blood urea nitrogen, serum creatinine as well as the appropriate bacterial cultures wherever necessary.

Serum phosphorus levels were measured using the blood sample taken for routine examination at admission initially, then patients with chronic renal failure, neonates were excluded. Patients staying for 3 days or more were now taken into consideration (Remaining were excluded) and again sera phosphorus levels repeated between the third and fifth day in the PICU. Serum phosphorus levels were repeated between

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seventh and tenth day if PICU stay was extended. Two millilitres of whole blood were collected by venepuncture under strict aseptic precaution and sent to biochemistry laboratory for assessment of serum phosphorus levels. Determination done by CALORIMETRIC method. Data was collected regarding age, gender, clinical diagnosis, serum phosphorus level, medicines in use, nutritional state, starvation time, and mechanical ventilation.

Hypophosphataemia was defined if sera levels <3.8 mg/dL in <2 yrs. and <3.5 mg/dL in >2 yrs. children. Special emphasis on monitoring serum phosphorus levels during the first 7 days of admission (Within first 6 hrs of admission after 3 days and after 7 days if the stay was more than that).

The prevalence of hypophosphataemia was calculated based on the number of children who had below normal sera phosphorus levels divided by the total number of children studied during the first 7 days of hospitalization.

RESULTS

Of 610 children admitted to the intensive care unit over the study period, 102 fulfilled the inclusion criteria. 93 had been discharged and 9 died. The mean serum phosphorus level was (4.58 mg/dL for day 1; 3.58 mg/dL for day 3, and 2.43 mg/dL for 7 days). The main characteristics of the patients were shown.

Variables	Number	Hypophosphataemia	Normophosphataemia
Age (yrs.)	5.065 (mean)		
Sex			
Female	45 (44.1%)	21 (46.67%)	24 (53.33%)
Male	57 (55.9%)	36 (63.15%)	21 (36.8%)
Total	102	57 (56%)	45 (44%)
Diagnosis			
Respiratory diseases	27(26.4 %)	15(55.5%)	12(44.5%)
Infections	39(38.2%)	24(61.5%)	15(38.5%)
Sepsis	6(5.9%)	2(33.3%)	4(66.6%)
CNS	6(5.9%)	4(66.7%)	2(33.3%)
Poisoning	6 (5.9%)	2 (33.3%)	4 (66.6%)
Others	16 (15.7%)	10 (62.5%)	6 (37.5%)
Starvation (days)	3.36		
Mechanical lung ventilation (days)	4		
Ventilated patients	18	15 (83.3%)	3 (16.7%)

Table 1: Main Clinical and Biochemical Characteristics of the Patients

Regarding the admission diagnoses of patients participating in the study, the majority were suffering of infections such as dengue fever, enteric fever, Rickettsial infections. Next common being the respiratory disorders as pneumonias, bronchiolitis, bronchial asthma, pleural effusion,

interstitial lung diseases. Eighteen percent (n=18) of all children were mechanically ventilated. Eighty three percent of ventilated children were hypophosphatemic (n=15 vs n=3). Hypophosphatemic patients tended to spend more days being ventilated.

	Number of Patients	Hypophosphataemia	Normophosphatemia
Discharged	93 (91.2%)	49 (52.7%)	44 (47.3%)
Expired	9 (8.8%)	8 (88.9%)	1 (11.1%)

Table 2: Outcome of the study

Hypophosphataemia, metabolic disturbance found in most of the patients having a prolonged stay in paediatric intensive care. However, this abnormality most frequent occurred in the dead patients, almost 90% of all the dead patients suffered from hypophosphataemia.

DISCUSSION

The prevalence of hypophosphataemia in our prospective study was 56% (57 cases) of all the admissions meeting inclusion criteria. In the present study, 56% of patients presenting with respiratory disorders were hypophosphatemic. The adding-on effect of hypophosphataemia to their respiratory problems might be attributed to the fact that hypophosphataemia was known to lead to muscle weakness and hypotonia.

Hypophosphatemic patients were more likely to be ventilated and to spend more days on ventilation than normophosphatemic patients. This might be explained by the fact that hypophosphataemia causes deficiency in the intermediary compounds for energy production such as

adenosine triphosphate and 2,3-diphosphoglycerate and alterations in energy metabolism, which may lead to respiratory muscle weakness and consequent worsening of respiratory insufficiency.^[9]

Barak et al^[12] found an association between hypophosphataemia and early sepsis and elevated blood cytokine levels following analysis of 3 groups of patients (Sepsis with positive blood culture, sepsis with negative blood culture, and infection), comparing them with 25 healthy participants in the first 24 hours after hospital admission. The authors concluded that concentrations of cytokines together with those of phosphorus can be used as prognostic markers in the assessment of patients with sepsis. Similar findings had been reported by Shoenfeld et al^[13].

The demand for nutrients such as phosphorus usually greater in children because it is needed for the formation of new tissues, a state that puts a critically ill patient with severe malnutrition at higher risk of developing hypophosphataemia, a point emphasized by the present study. To prevent potential complications related to hypophosphataemia, it is essential to

identify patients at risk to frequently monitor phosphorus serum levels and to supplement when required.^[14]

Our review of the literature concerning hypophosphataemia in critically ill children and adolescents identified few studies, restricted to case reports, which detailed low phosphorus serum levels associated with bone tumour^[15], refeeding of seriously malnourished patients.^[14,16] and severe head trauma.^[17] Two recent studies on hypophosphataemia in the paediatric age group were also found. A retrospective study concerning 68 children with kwashiorkor showed 76% of patients to have phosphorus serum levels less than 3 mg/dL and revealed an association between severe hypophosphataemia (<1 mg/dL) and mortality.^[10]

A prospective study assessed the relationship between serum levels of phosphorus and C-reactive protein (CRP) in children with acute infection. The prevalence of hypophosphataemia ranged from 4.4% to 45% depending on the type of infection and correlated negatively with CRP value. Hypophosphataemia occurred during the phase of rising CRP levels, resolving when CRP levels fell, and thus was considered a frequent but transient phenomenon.^[18] In the present study, serum CRP values were not obtained in all patients, thus a relationship between the magnitude and duration of hypophosphataemia and the magnitude and/or duration of acute metabolic stress could not be established.

Study Limitations

Because of the exclusion of some patients with a short ICU stay, severe diseases that could possibly have evolved with hypophosphataemia may have been overlooked.

CONCLUSION

Hypophosphataemia is frequent in children admitted to PICU who are critically ill. It was more prevalent in those with respiratory failure, those with infections, those with more starvation days. More length of stay and worse outcome were associated with hypophosphataemia. Our study highlights the importance of serum phosphorus level as predictive for the course of illness and outcome.

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