Original Research Article

Frequency of hypophosphatemia in children presenting with sepsis in a tertiary care hospital: A cross-sectional study

Abstract

Aim: To determine the frequency of hypophosphatemia in children presenting with sepsis in a tertiary care hospital:

Study design: A cross-sectional study

Place and Duration: Department of Paediatric, Civil Hospital, Karachi, Pakistan from October 2020 to April 2021.

Methodology: A total of 190 children with clinical sepsis were included in the study. Serum phosphate level, CBC, CRP, and blood culture of all children were sent within 24 hours of admission. Serum phosphate level less than 2.5mg/dL was labeled hypophosphatemia. It was categorized as Mild, moderate and severe at level of 2-2.5 mg/dL), 1-2 mg/dL), and < 1 mg/dL respectively.

Results: Mean ± SD age of study participants was 2.69±3.19 years. Out of 190 patients 106 (55.8%) were male while 84 (44.2%) were female. Hypophosphatemia was found in 36 (18.9%) patients among them mild and moderate hypophosphatemia was noted in 18 (50%) of each category of patients.

Conclusion: This study concluded that hypophosphatemia was documented in considerable number of children who presented with clinical sepsis. To avoid the issues of a double burden of disease in these patients, strategies to prevent these diseases should be supported.

Keywords: Hypophosphatemia, Illness, Mortality, Outcome, Prognosis, Sepsis

Introduction

A dysregulated host response to infection causes sepsis, which is a life-threatening organ failure. Sepsis represents a significant socioeconomic burden worldwide [1]. Severe sepsis is one of the primary causes of admission to intensive care units (ICUS) [2-3]. The incidence and rate of hospitalization for severe sepsis is increasing every year. In studies published in the previous decade, the incidence of sepsis in all patients admitted to ICUs ranges from 9 to 37 percent, and severe sepsis remains a prominent cause of death. Severe sepsis mortality rates in patients admitted to intensive care units range from 30 to 50% [4-5].

Blood Culture remains the gold standard but has limitations due to final report after seven days. Hematological and inflammatory markers such as ESR, CRP, raised total leukocyte count, ANC, band cells, toxic granulations as indicator for sepsis but have certain limitations. Phosphate is a component of adenosine triphosphate, 2,3-diphosphoglycerate, and intracellular chemical messengers, among other intermediate molecules involved in critical physiological processes [6]. Hypophosphatemia (HP) has been linked to sepsis and has been suggested as a useful diagnostic tool [7]. During the first 24 hours of admission, patients with sepsis had a high rate of HP [7]. Phosphate (P) values of less than 2 mg/dl were particularly indicative of gram-negative sepsis. The exact process by which HP develops in sepsis is uncertain. The elimination of the illness was linked to an increase in P levels [8-10].

In the majority of cases, hypophosphatemia symptoms are nonspecific and include fatigue and irritability [11]. During childhood, the normal level of phosphorus in the blood changes. Normal blood phosphorus levels in children aged one to three years (3.8 mg/dl to 6.5 mg/dl), four to eleven years (3.7 mg/dl to 5.6 mg/dl), and twelve to fifteen years (3.7 mg/dl to 5.4 mg/dl) [12].

In the postoperative period of cardiac surgery, severe hypophosphatemia can lead to leukocyte dysfunction, and neuromuscular disturbances [13-15]. Children's sepsis played a role, with 37.37 percent having sepsis with a negative blood culture (NBC) and 30.30 percent having sepsis with a positive blood culture (PBC) (PBC). In both the PBC and NBC groups, hypophosphatemia was found in 80% of the septic patients [8].

In a study of Shazly A.N. El et al. they investigated that there are 34% sepsis cases in which 58.8% had hypophosphatemia while other 41.1% had normophosphatemia. Although a higher percentage of septic patients were hypophosphatemic, this finding did not reach statistical significance. [7]. Another study indicated that out of 8% of sepsis cases, 50% had HP and the other 50% had normophosphatemia, and that there was no significant connection between sepsis and previously recognized variables linked with hypophosphatemia [11]. The inefficiency of respiratory muscle contraction due to hypophosphatemia makes weaning patients from artificial ventilation difficult [11].

Patients with phosphate derangements primarily focus on the association of hypophosphatemia and the general critically ill population but in our part the local studies scarce and limited in the sepsis population. Several studies revealed that hypophosphatemia are common in severe sepsis [16-20]. Therefore, the aim of the study was to find out the frequency and severity of hypophosphatemia in children presenting with clinical sepsis.

Methodology:

This cross-sectional study was conducted at Department of Paediatric, Civil Hospital Karachi by non-probability consecutive sampling technique from October 2020 to April 2021. Permission was taken from the ethical review committee of the institute. The sample size was calculated by taking prevalence of hypophosphatemia in sepsis children P=(58.8%) [6] using margin of error(d)=7% the total calculated sample size was 190 patients with the help of WHO software for sample size calculation taking 95% confidence level. Children of either gender presenting with clinical sepsis form age 1 month to 15 years were included in the study. Children having chronic renal failure, congenital renal disease and severe malnutrition were excluded from the study. Hypophosphatemia was defined as the serum phosphate level less than 2.5mg/dL. It was categorized as Mild: 2-2.5 mg/dL, Moderate: 1-2 mg/dL and Severe :< 1 mg/dL. Patients were labeled as clinical sepsis if two or more of the following criteria were fulfilled: Axillary Temperature >38°C or <36°C, tachycardia or fast breathing, White blood cell count >12,000/mm2 , or 10% immature (band) forms, on complete blood count report.

Informed consent was taken from the care takers. Complete history and detailed examination of septic children were taken from all the patients at the time of admission. Serum phosphate level, CBC, CRP, and culture of all included children were sent within 24 hours of admission. The sepsis was diagnosed as per operational definitions. The final outcome i.e. Hypophosphatemia was labeled when the serum phosphate level was less than 2.5mg/dL. It was categorized as Mild, moderate and severe at the level of 2- 2.5 mg/dL, 1-2 mg/dL), < 1 mg/dL) respectively. Biasness and confounder were controlled by strictly following the inclusion criteria. All patients were given supportive and definitive management as per hospital protocols. All data was kept strictly confidential. The data was compiled and analyzed using SPSS version 21. For qualitative factors

such as gender, culture, hypophosphatemia, and levels of hypophosphatemia, frequencies and percentages were calculated.

Age, serum phosphate, axillary temperature, heart rate, respiration rate, white blood cell count, and CRP were all provided as mean SD quantitative variables. Stratification was used to control effect modifiers such as age, gender, axillary temperature, heart rate, respiration rate, white blood cell count, and CRP. The Chi-square test was used to determine whether category variables were related. The significance level was set at P 0.05.

Results:

In this study 190 patients were included to assess the hypophosphatemia in clinical sepsis children. Mean ± SD of age was 2.69±3.19. Mean ± SD of serum phosphate was 3.79±1.30. Mean ± SD of axillary temperature was 41.00±23.27. Mean ± SD of heart rate was 133.30±21.88 with. Mean ± SD of respiratory rate was 46.32±14.48. Mean ± SD of CBC was 14.13±8.65. Mean ± SD of CRP was 56.71±86.89. In distribution of gender, 106 (55.8%) were male while 84 (44.2%) were female. Positive blood culture was found in 38 (20%) patients while negative culture was found in 72 (80%) patients. Hypophosphatemia was found in 36 (18.9%) patients. Mild and moderate hypophosphatemia was noted in 18 (50%) patients of each category Stratification of age group, gender, axillary temperature, heart rate, respiratory rate, white blood cell (CBC) and CRP were done with respect to hypophosphatemia in order to found significant difference from.

Table 1: Descriptive statistics (Mean) of the study participants n=190

Age (Years)	2.69 ± 0.23
Serum Phosphate level (mg/dl)	3.79 ± 0.94
Axillary temperature (C)	41.00 ± 1.68
Hear Rate (bpm)	133 ± 1.58
Respiratory Rate (brpm)	46.32 ± 1.05
Complete Blood Count	14.13 ± 0.62
C Reactive Protein	56.71 ± 6.30

Table 2: Characteristics of study participants n = 190

Characteristics	**Number (%)**
Gender	
Male	106 (55.8)

Female	84 (44.2)
Blood C/S	
Positive	38 (20)
Negative	72 (80)
Hypophosphatemia	
Yes	36 (18.9)
No	154 (81.1)
Severity of hypophosphatemia	
Mild	18 (50)
Moderate	18 (50)

Table 3: Stratification of various factors with Hypophosphatemia n = 190

Variables	**Hypophosphatemia**	**P-value**

	Yes	**No**	
Age (years)			0.152
0-2	27 (14.3%)	96 (50.5%)	
>2	9 (4.7%)	58 (30.5%)	
Gender			0.975
Male	20 (10.5%)	86 (45.3%)	
Female	16 (8.4%)	68 (35.8%)	
Temperature (C)			0.682
38 - 40	35 (18.5%)	149 (78.4%)	
>40	1 (0.5%)	5 (2.6%)	
Heart Rate			0.136
90 - 120	11 (5.8%)	68 (35.7%)	
>120	25 (13.2%)	86 (45.3%)	
Respiratory Rate			0.343
25 - 40	13 (6.8%)	69 (36.4%)	
>40	23 (12.1%)	85 (44.7%)	
CBC			0.980
1 - 10	12 (6.3%)	51 (26.8%)	
>10	24 (12.6%)	103 (54.3%)	
CRP			**0.573**
0 - 50	24 (12.6%)	110 (57.9%)	
>50	12 (6.3%)	44 (23.2%)	

Discussion:

The mean age in our study findings was 2.69±3.19 years. Shazly AN EI, et al [6] noted a mean age of 14.3 years while Yoshimatsu S, noted as 18.6±12.3 months [11]. In distribution of gender,

106 (55.8%) were male while 84 (44.2%) were female. Shazly AN EI, et al [6] further reported to have 26 (52%) males and 24 (48%) females. The study of Yoshimatsu S, reported having 22 (46%) males and 26 (54%) females. Another study found to have 52% males and 48% females [21] whereas Brotfain E, et al noted to have 48 (64%) males and 27 (36%) females [22].

Hypophosphatemia was found in 36 (18.9%) patients in our study. The incidence of hypophosphatemia was noted in 21 (42%) cases in the findings of Shazly AN EI, et al [6] and 80% in Barak V, et al [7]. The study of Riedler CF noted in 41% cases [10]. A total of 5 children had hypophosphatemia throughout their PICU stay, despite the fact that more than half of our patients had hypophosphatemia at the time of admission [12] while Goldstein J noted in 56% [23] and Polderman KH reported the prevalence of 61% [24]. The findings of presence study show variation with broad range in comparison of previously conducted studies. As no follow-up in our study that is one of main reason with other possible residual confounders. In our study, stratification of confounders / effect modifiers with respect to hypophosphatemia, insignificant difference was noted in age group (P=0.152), gender (P=0.975), axillary temperature (P=0.682), heart rate (P=0.136), respiratory rate (P=0.343), CBC (P=0.980) and CRP (P=0.573). Hypophosphatemia is linked to a worse prognosis in critically ill adults and children, according to various studies (prolonged length of stay and the need for respiratory support, and higher mortality). However, there was inadequate information as to when hypophosphatemia becomes essential and requires treatment [25].

In an international investigation, 98 (46.4%) of the females had the average age of 10.51 days. The average phosphorus concentration was 4.39 0.67 mg/dL. Phosphorus levels in girls and boys were substantially different. The difference in mean phosphorus between positive and negative

blood culture patients was likewise significant. However, phosphorus levels were not linked with type of feeding, ESR, urine culture, or CRP status [26].

Conclusion:

It is to be concluded that hypophosphatemia was documented in considerable number of children in clinical sepsis. To avoid the issues of a double burden of disease in these patients, strategies to prevent these diseases should be supported. The sample population represents a single institutional experience; but the study sample can be generalized as the sample came from various areas of Pakistan.

Permission:

It was taken from the ethical review committee of the institute

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