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Phosphate Disturbance in Critically Ill Children in Zagazig University Pediatric Intensive Care Unit

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ABSTRACT

Background: Phosphorus is very important for normal cellular structure (cell membrane and nucleic acids). Phosphorus has an important role in the cell metabolism, ATP production, and homeostasis.

Objectives: The aim of the work was to determine the prevalence and some of risk factors of hypophosphatemia in sick children, and to evaluate the prognostic effect of serum phosphorous level on the outcome in terms of morbidity and mortality in critically ill children during their stay in the pediatric intensive care unit.

Patients and methods: This prospective cohort study included a total of 50 critically ill children, attending at Department of Biochemistry and Pediatric Intensive Care Unit (PICU), Department of Pediatrics, Zagazig University Hospitals. This study was conducted between April 2017 to August 2018. Patients age ranged from 2 months to 129 months and according to serum phosphorus level cases were classified into those with hypophosphatemia and others with normal phosphate level. The severity of illness was determined by using SOFA score.

Results: Revealed that there was statistically significant decrease in phosphorus level at day 1 and day 3 between hypophosphatemia and normal phosphate level groups. The prevalence of hypophosphatemia was 46% at first day of admission and 70% at third day of admission. Significant increase of PTH and total bilirubin in hypophosphatemia group, and significant decrease of calcium in hypophosphatemia group compared to normophosphatemia group. The cases were followed and compared regarding; morbidity (need for mechanical ventilation, and length of PICU stay), degree of organ failure (SOFA score) and their outcome (discharge from PICU or death).

Conclusion: It could be concluded that hypophosphatemia is considered a common co-morbidity in critically ill children in PICU. Hypophosphatemia more prevalent in those with respiratory problems, and higher SOFA score.

Keywords: Hypophosphatemia, SOFA score, PICU, PTH.

INTRODUCTION

Electrolytes disturbance develops frequently in critically ill children during the course of stay in the pediatric intensive care unit (PICU), hypophosphatemia is one of the most frequently encountered electrolyte disorders in the PICU [(1)]. Hypophosphatemia refers to any serum phosphorus level <3.8 mg/dl for children below 2 y old and <3.5 mg/dl for children more than 2 y old [(2)].

Critically ill children are at high risk for developing hypophosphatemia due to the presence of several causative factors, the mechanisms of hypophosphatemia in pediatric intensive care units may be due to decreased absorption, increased renal loss or internal redistribution of inorganic phosphate due to alkalosis [(3)].

Regardless of the continuous monitoring of the serum levels of electrolytes: sodium, potassium, and calcium ions in critically ill children admitted to PICUs, phosphorus is not routinely investigated in these patients, hypophosphatemia occurs in 45% of all hospitalized cases in the PICU patients [(4)].

Low serum level of phosphorus cause problems in patients admitted to the pediatric intensive care units (PICUs); hypophosphatemia is associated with cardiac dysfunction, respiratory failure, delayed weaning from the ventilator, prolonged hospital stay and hematological disorders. Low concentrations of serum phosphorus is an important cause of myopathy and rhabdomyolysis, and is a life-threatening factor that causing death in children with protein energy malnutrition disorders [(5)].

The prevalence of hypophosphatemia is higher in critically ill children than in adults, and it is commonly present during admission. There is an association between correction of low phosphorus level and improvement in the clinical outcome [(1, 6)].

Therefore, the present study was conducted to determine the prevalence and some of risk factors of hypophosphatemia in sick children, and to evaluate the prognostic effect of serum phosphorous level on the outcome in terms of morbidity and mortality in critically ill children during their stay in the pediatric intensive care unit.

SUBJECTS AND METHODS

This prospective cohort study included a total of 50 critically ill children, attending at Department

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of Biochemistry and Pediatric Intensive Care Unit (PICU), Department of Pediatrics, Zagazig University Hospitals. Written informed consent of all the parents of subjects was obtained. This study was conducted between April 2017 to August 2018.

Ethical approval

Approval of the ethical committee was obtained.

Patients age ranged from 2 months to 129 months with median 12.5 months, 32 (64%) were males and 18 (36%) were females and following their outcome till discharged from PICU. According to serum phosphorus level our cases were classified to cases with hypophosphatemia and cases with normal phosphate level.

Inclusion criteria:

1. Critically ill children admitted to PICU.
2. Children age > 1 month to 14 years.
3. An expected PICU-stay >24 hours.

Exclusion criteria:

1. Acute renal injury at time of admission.
2. Familial hypophosphatemia.
3. Refractory renal rickets.
4. Underlying parathyroid disorders.
5. Death within 24 h of PICU admission and discharge to ward within 24h.

All the participating patients in this study were subjected to the following:

A) Full history taking:

- Name, age, sex, order in family, perinatal history, postnatal and history of NICU admission.
- Presentation: For critical illness (respiratory support as need for mechanical ventilation, cardiovascular instability, need for adrenergic agents, neurologic state assessed by modified Glasgow coma score, pallor).
- Manifestations for hypophosphatemia: Respiratory, cardiovascular, hematologic and/or neuromuscular.
- Past history of previous admission, disease, drug intake and operations
- Family history: similar condition, consanguinity and socioeconomic state.
- History of drugs given related to hypophosphatemia**.**
- In Zagazig University PICU routinely giving glycophos in TPN (1ml /100 ml IV fluids) to critically ill who can't start enteral feeding. In cases of hypophosphatemia the critically ill children with serum phosphorus <1.5 mg\dl given glycophos in a dose of 1ml/kg/12h till serum phosphorus reach >2.5 mg/dl.
- Follow up to the cases: (a) Duration of PICU stay for >6 days was taken as cutoff to define prolonged PICU stay. (b) Need for mechanical ventilation. (c) Follow up their outcome.

B) Thorough Clinical Examination:

1. **Complete general examination:** Vital signs and appearance, activity.
2. **Complete local examination:** Cardiovascular system. Central nervous system and musculoskeletal system. Respiratory system and abdominal examination for organomegaly or ascites.
3. **Scoring systems**: These systems applied in our study to critically ill children. Including:
   i. **Glasgow coma scale (GCS)**: used to describe the consciousness level [(7)]**.**
   ii. **Sequential Organ Failure Assessment (SOFA):** in the first 24 h after admission to assess morbidity, the degree of organ failure and hence the SOFA score is also related to mortality, the mortality rate increased with increasing scores for each organ [(8)].

C) Laboratory investigations:

1. Complete Blood picture (CBC) measured by Sysmex-K-21.
2. Prothrombin time (PT), Partial thromboplastin time (PTT), International normalized ratio (INR) measured by vitrous 350 analyzer.
3. Serum Albumin and bilirubin.
4. Renal function tests (Serum urea and creatinine) and alkaline phosphatase (Cobas-6000).
5. Arterial /venous PH, paO2 and FIO2. (ABL 800 flex)
6. Serum calcium (Mindray CL 1000i).
7. Serum phosphorus D1 and D3 (hypophosphatemia was defined as any serum phosphate <3.8 mg/dl for children younger than 2 y and <3.5 mg/dl for children 2y or older) colorimetric method (Hitachi Modular P800, Cobas, Roche).
8. Urine sample for estimation of urinary Phosphorus and Creatinine (Hitachi Modular P800, Cobas, Roche). Mention the type of urine sample, if it is random, morning or 24 hours samples.
9. **(TmP/GFR)**: This index represents the blood concentration of phosphate, above which kidney excretes most of the phosphate and below which most of it is reabsorbed. Normal TmP/GFR range for children is 2.8–4.4 mg/dl. Inappropriately

high renal phosphate excretion was defined as TmP/GFR < 2.8 mg/dl [3].

Walton and Bijvoet normogram: was used to calculate TmP/GFR with the help of serum phosphate and Tubular reabsorption of phosphate (TRP). TRP = 100 – Fractional excretion of phosphate. Fractional excretion of phosphate (FePO4) was calculated using the equation: (Urine Phosphate × Serum Creatinine)/ (Plasma Phosphate × Urine Creatinine) × 100. **Tmp/GFR =** TRP × plasma phosphate.

10. Serum Parathyroid hormone (PTH) baseline (Mini vidas).

Statistical analysis:

Recorded data were analyzed using the statistical package for social sciences, version 20.0 (SPSS Inc., Chicago, Illinois, USA). Quantitative data were expressed as mean± standard deviation (SD). Qualitative data were expressed as frequency and percentage. Independent-samples t-test of significance was used when comparing between two means. Chi-square (x^2) test of significance was used in order to compare proportions between two qualitative parameters. The confidence interval was set to 95% and the margin of error accepted was set to 5%. The p-value was considered significant as the following: P-value <0.05 was considered significant. P-value <0.001 was considered as highly significant. P-value >0.05 was considered insignificant.

RESULTS

This study included 50 children; their age ranged from 2 to 129 months.

Table (1): Socio-demographic characteristics and SOFA score of the studied group:

Variable	**The studied group (50) mean ± SD**	
Age (months):	23.6±29.2	
SOFA score	6.8±2.1	
Variable	**NO (50)**	**%**
Sex:		
Male.	32	64.0%
Female.	18	36.0%
SOFA grades:		
Mild.	18	36.0%
Moderate.	19	38.0%
Severe.	13	26.0%

This table shows that median age of the study group is (12.5 m) ranged from (2-129 months) and (64.0%) of them are males. This table shows that SOFA score of the study group is (6.8±2.1) ranged from (4-12) and (38.0%) have moderate SOFA classification followed by mild (36%) and sever (26%).

Table (2): Comparison between children with hypophosphatemia and normal phosphate level in the studied group regarding age, sex and causes of admission:

Variable	**Hypophosphatemia group (23) mean ± SD**	**Normal phosphate level group (27) mean ± SD**	**test**	**p-value**
Age (years)	21.7±13.8	23.6±15.7	M.W 0.2	0.8
Sex:	**No** (23) %	**No** (27) %		
Male	20 87.0	12 44.4	**FET**	**0.003***
Female	3 13.0	15 55.6		
Cause of admission:	**No** (23) %	**No** (27) %		
CNS diseases	6 26.1	8 29.6		
CVS diseases	3 13.0	3 11.1	1.3	
Chest diseases	8 34.8	11 40.7		0.8
GIT& Liver	4 17.4	2 7.4		
Other causes	2 8.7	3 11.1		

FET= Fischer Exact test. M.W= Mann-Witenny U test * p-value <0.05 is significant.

In this table, there is statistically significant increase incidence of hypophosphatemia in males but as regard age and causes of admission, there is no statistically significant difference between hypophosphatemia and normal phosphate level groups.

Table (3): Comparing Phosphorus at day1 and day3 between children with hypophosphatemia and normal phosphate level in the studied group:

Variable	Hypophosphatemia group (23) mean ± SD	Normal phosphate level group (27) mean ± SD	t-test	p-value
Phosphorus day 1 *(mg/dl)*	3.4±0.3	4.8±0.7	8.4	**0.001****
Phosphorus day 3 *(mg/dl)*	3.1±0.4	4.2±0.6	3.2	**0.002***

M.W= Mann-Witenny U test * p-value <0.05 is significant. * * p-value <0.001 is highly significant.

In this table, there is statistically significant decrease in phosphorus level at day1 and day 3 between hypophosphatemia and normal phosphate level groups.

Table (4): Comparing grades of SOFA score between children with hypophosphatemia and normal phosphate level in the studied group:

Variable	Hypophosphatemia group No (23)	%	Normal phosphate level group No (27)	%	test	p-value
SOFA score						
Mild (18)	3	16.7	15	83.3	FET	**0.001****
Moderate (19)	9	47.4	10	52.6		
Severe (13)	11	84.6	2	15.4		

FET= Fischer Exact test. ** p-value <0.001 is highly significant.

In this table, there is statistically significant difference between hypophosphatemia and normal phosphate level groups in SOFA score. Severe grade is more prevalent in the hypophosphatemic group (84.6%) and mild score is more prevalent in normal phosphate level group (83.3%).

Table (5): Comparing drug used in PICU at day 3 between children with hypophosphatemia and normal phosphate level in the studied group:

More than one drug may be used by one patient.

Variable Drugs	%	Hypophosphatemia group No (35)	%	Normal phosphate level group No (15)	%	χ^2	p-value
Dopamine (18)	36	16	88.9	2	11.1	**40.5**	**0.001****
Steroids (15)	30	12	80.0	3	20.0		
β2 agonist (20)	40	16	80.0	4	20.0		
Omeprazole/Rantidine (9)	18	8	88.9	1	11.1		
Acyclovir (9)	18	8	88.9	1	11.1		
Furosemide (16)	36	13	81.3	3	18.7		
Epanutin (13)	26	11	84.6	2	15.4		

** p-value <0.001 is highly significant.

In this table, there is statistically significant increase in number of hypophosphatemic patients according to drug used in PICU.

Table (6): Comparing mechanical ventilation and length of stay between children with hypophosphatemia and normal phosphate level in the studied group:

Variable	Hypophosphatemia group No (23)	%	Normal phosphate level group No (27)	%	χ^2	p-value
Mechanical ventilation						
No (31)	9	39.1	22	81.5	**9.5**	**0.002***
Yes (19)	14	60.9	5	18.5		
PICU LOS						
<6 days (20)	4	17.4	16	59.3	**FET**	**0.001****
>6 days (30)	19	82.6	11	40.7		

FET= Fischer Exact test. * p-value <0.05 is significant. * * p-value <0.001 is highly significant.

In this table, there is statistically significant increase in length of stay and use of mechanical ventilation in hypophosphatemic group.

Table (7): Comparing outcome between children with hypophosphatemia and normal phosphate level in the studied group:

Variable	Hypophosphatemia group No (23) %	Normal phosphate level group No (27) %	test	p-value
Outcome				
A live (39)	14 60.9	25 92.6	**FET**	**0.05***
Died (11)	9 39.1	2 7.4		

FET= Fischer Exact test. * p-value <0.05 is significant.

In this table, there is statistically significant increase of died patient in hypophosphatemic group, as 39.1% of hypophosphatemic group died compared to normophosphatemic group 7.4% died.

DISCUSSION

In this prospective study, hypophosphatemia was common in critically ill children. The prevalence of hypophosphatemia among critically ill children admitted to PICU was (46%) as we detect 23 cases out of 50 critically ill children on admission, by follow up of our cases at day 3 we found that 4 cases returned to normal values of serum phosphate and 12 new cases developed hypophosphatemia the prevalence of hypophosphatemia was increased to (70%), which nearly similar to the study done by **Shah *et al.*** [3] with prevalence 71.6 % in the first 10 days of admission. Our prevalence lower than a retrospective study conducted by **Souza de Menezes *et al.*** [9] as they have found prevalence of 76%. However, prevalence of hypophosphatemia was slightly higher than previous studies reported by **Santana e Meneses *et al.*** [6], **Kilic *et al.*** [1] and **El Shazly *et al.*** [10] as they found prevalence of (61%), (60%) and (62%) respectively.

According to our study we found that median (range) serum phosphate measurements in the studied group in D1; was 4.2 (2.1-6.9), which decreased in D3 to 3.4 (2.8-5.5) but without significant difference similarly to **Shah *et al.*** [3] estimated phosphate level at D1 and D3, the median (range) serum phosphate concentrations on D1 and D3, were 3.7 (2.9, 4.4) mg/dl and 3.2 (2.5, 3.9) mg/dl respectively. It was also agreed with **Rady and Khalek** [11] as the mean serum phosphorus level was (3.5 mg/dl for day1; 3.7 mg/dl for day 7).

Santana e Meneses *et al.* [6] reported that serum phosphorus levels did not vary significantly in children hospitalized within the PICU for at least 10 days, serum phosphorus level measures taken, with values of 4.2 ± 2.3 mg/dl at admission (measurement 1), 3.7 ± 1.4 mg/dl between the fourth and sixth day of hospitalization (measurement 2), and 3.8 ±1.3 mg/dl between the seventh and tenth day of PICU stay (measurement 3).

Comparison of phosphorus between day 1 and day 3 in children with hypophosphatemia and normal phosphate level, there was significant decrease in phosphate level between two groups D1 3.4±0.3 mg/ dl vs. 4.8±0.7; D3 3.1±0.4 vs. 4.2±0.6 mg/dl.

As regard the demographic data this study included 50 critically ill children, their median age 12.5 months (range2-129 m), (64%) of them were males and (36%) were females. The median age of hypophosphatemic group was 18 months. Our result detected that incidence of hypophosphatemia was significantly higher in males (87%) than females (15%), with no statistically significant difference between hypophosphatemic and non hypophosphatemic groups as regarding age. However, **Basri *et al.*** [12] found that hypophosphatemia was more common in female patients (67%) compared to male patients (33%), while **Shahsavarinia *et al.*** [4] found no significant difference in the incidence of hypophosphatemia regarding sex; in males (54.2%), and (45.8%) in females.

According to the causes of admission in our hypophosphatemic cases, there were no statistically significant difference and this agree with **Shah *et al.*** [3] who found no association between hypophosphatemia and causes of admission. But we found that in hypophosphatemic children chest problems account for 34.8 %, which were the highest percentage of the causes of admission followed by CNS causes 26.1%, then GIT & Liver problems 17.4%, then CVS about 13%, and the other causes represent 8.7%. This agree with **Shahsavarinia *et al.*** [4] and **Rady and Khalek** [11], who found that (56%) and (57.8%) respectively of patients presenting with respiratory disorders were hypophosphatemic. Similarly, **Santana e Meneses *et al.*** [6], found that patients diagnosed with respiratory disease were more likely to have hypophosphatemia than other subjects. The adding-on effect of hypophosphatemia to their respiratory problems might be attributed to the fact that hypophosphatemia is known to lead to muscle weakness and hypotonia [11].

The critical illness and degree of organ failure assessed using SOFA score [8]. According to this; SOFA score of our patients was (6.8±2.1) ranged from (4-12), 18 patients (36%) had mild score, 19 patients

(38%) had moderate score and 13 patients (26%) had severe score. Sepsis had the highest SOFA score (8.2±2.6), then cardiomyopathy (8±2), then Inborn error of metabolism had score (8), followed by congenital heart disease (7.6±0.89), then plan C dehydration (7.2±2.8), after that disturbed conscious level (7.2±1.9) then pneumonia (7.1±2.3), then status epileptics (6.5±1.7), then stridor had the score (6), then DKA and bronchiolitis had the same score (5), lastly GBS had the lowest score (4).

As regarding the SOFA score there was statistically significant difference between cases with hypophosphatemia and cases with normal phosphate level, with a significant negative correlation between SOFA score and phosphorus level. Sever score was presented with high percentage (84.6%) in hypophosphatemic patients while mild score was more presented in patients with normal phosphate level (83.3%). This run parallel to **Rady and Khalek** [(11)] who showed that PIM score values were significantly higher in hypophosphatemic children. In contrary, **Kilic *et al.*** [(1)] and **El Shazly *et al.*** [(10)] who used the PELOD score for assessment of critical illness and organ failure, they found no association between hypophosphatemia and PELOD score this may be due to the difference between the components of scores.

Our study revealed a significant association between drugs used in PICU and hypophosphatemia. In contrast, **Rady and Khalek** [(11)] found that none of the drugs known to deplete serum phosphorus levels as a side effect to their use (catecholamines, antacids, anticonvulsants, steroids, diuretics), showed association with hypophosphatemia.

In this study conducted in Zagazig University PICU we assessed the level of PTH as it is one of the phosphaturic hormones, the median was 9.8 ng/l. In comparison between hypophosphatemic and non-hypophosphatemic group there was significant difference as PTH was significantly higher in the hypophosphatemic group and showed significant negative correlation with phosphorus. **Bech *et al.*** [(13)] found that, although the mean serum levels of PTH was above the upper normal limit of healthy subjects, PTH had no significant impact on hypophosphatemia. On the other hand, **Shah *et al.*** [(3)] found that there was no difference in parathyroid hormone (PTH) levels between the two groups.

Disturbances in phosphate homeostasis are often linked to abnormalities in calcium and bone metabolism, therefore, this aspect was also evaluated in the present study; Total calcium 8.7±0.6 mg/dl, Alkaline phosphatase 154.7±63.5 U/L and the level of serum calcium, was significantly lower in the hypophosphatemic than normophosphatemic group (8.4 ± 0.6 vs. 8.9 ± 0.4) with significant positive correlation with phosporus. This run parallel with **Bech *et al.*** [(13)], and disagree with **Kilic *et al.*** [(1)] who found that there was no association between hypophosphatemia and electrolyte disturbances in the PICU. In our study there was no significant difference at alkaline phosphatase between all patients.

The arterial blood gases (ABG) for our study group were within normal PH 7.3±0.1, Hco3 19.8±8.3, Po2 77.9±22.7, Pco2 43.6±16.6. There was no significant difference between the hypophosphatemic and non-hypophosphatemia groups regarding Po2, Pco2, Hco3 and PH. In the study conducted by **Shah *et al.*** [(3)] trend towards increased pH was seen in hypophosphatemic group but it failed to reach the statistical significance, but **Basri *et al.*** [(12)] found significant association between higher PH and hypophosphatemic patients. PH was significantly predictive of serum phosphate levels. A correlation of PH with serum phosphate levels is related to the physiologic changes during alkalosis that may lower serum phosphate levels via transcellular shift. **Suzuki *et al.*** [(14)] found an association between hypophosphatemia and alkalemia; as during hypophosphatemia alkalosis was significantly higher in patients with hypophosphatemia (50% vs 33%).

Our results revealed a significant association between hypophosphatemia and the use of mechanical ventilation as in our study 19 patients (38%) were on mechanical ventilator, 14 patients (60%) of them were hypophosphatemic. In agree with our study **El Shazly *et al.*** [(10)] and **Rady and Khalek** [(11)] revealed that hypophosphatemic patients were more likely to be ventilated and to spend more days on ventilation than normophosphatemic patients. In contrast **Souza de Menezes *et al.*** [(9)] found that there was no significant association between hypophosphatemia and use of mechanical ventilation.

Hypophosphatemia affects the length of PICU stay, this might be explained by the effect of hypophosphatemia that can trigger myocardial dysfunction, low ATP for proper respiratory muscles contraction [(3)].

In our study there was highly significant association between hypophosphatemia and prolonged PICU LOS [in this study duration of PICU stay for patient >6 d was taken as cutoff to define prolonged PICU stay]. In our study there were 30 patients stay >6 days, 19 (82.6%) of them were hypophosphatemic while 11 (40.7%) patients were normophosphatemic, and 20 patients stay <6 days 16 (59.3%) of them were normophosphatemic while 4 (17.4%) were hypophosphatemic. **Kilic *et al.*** [(1)] and **Shah *et al.*** [(3)] found a significant association between hypophosphatemia and PICU LOS. Similarly, **Rady and Khalek** [(11)] found in comparing the duration of stay at PICU, those with the normal serum phosphorus

level were discharged earlier than those with hypophosphatemia.

Our results revealed significant association between hypophosphatemia and mortality during study period as 11 patients died during the study 9 of them (39%) were hypophosphatemic while, 92.6% who survived were normophosphatemic and this agreed with the studies conducted by **Suzuki *et al.* [(14)]**, **Shor *et al.* [(15)]** and **Sakhawey *et al.* [(16)]** they found that Intensive care unit mortality rate was significantly higher in patients who presented with hypophosphatemia at ICU admission or developed hypophosphatemia on the day of ICU admission compared with patients without hypophosphatemia.

In Zagazig University PICU routinely giving glycophos in TPN (1ml /100 ml IV fluids) to critically ill who cannot start enteral feeding. In cases of hypophosphatemia the critically ill children with serum phosphorus <1.5 mg/dl given glycophos in a dose of 1ml/kg/12h till serum phosphorus reach 2.5 mg/dl.

CONCLUSION

It could be concluded that hypophosphatemia is considered a common co-morbidity in critically ill children in PICU. Hypophosphatemia more prevalent in those with respiratory problems, and higher SOFA score. One of the important mechanisms responsible for hypophosphatemia is decreased tubular reabsorption and thus, increased excretion of phosphate. PTH have a role in hypophosphatemia as one of the phosphaturic hormones. Hypophosphatemia can affect the outcome by more length of stay and worse outcome were associated with hypophosphatemia and increased mortality.

REFERENCES

11. **Kilic O, Demirkol D, Ucsel R *et al.* (2012):** Hypophosphatemia and its clinical implications in critically ill children: a retrospective study. J Crit Care, 27: 474-479.
12. **Assadi F (2010):** Hypophosphatemia: an evidence-based problem-solving approach to clinical cases. Iran J Kidney Dis., 4(3): 195-201.
13. **Shah SK, Irshad M, Gupta N *et al.* (2016):** Hypophosphatemia in critically ill children: risk factors, outcome and mechanism. The Indian J Pediatr., 83(12-13): 1379-1385.
14. **Shahsavarinia K, Motazedi Z, Mahmoudi L *et al.* (2016**): Hypophosphatemia in critically ill children. J Anal Res Clin Med., 4(3): 153-157.
15. **Maduell F, Navarro V, Alos M *et al.* (2003):** Intradialysis hemolysis secondary to hypophosphatemia. Nefrologia, 23(1): 85-88.
16. **Santana e Meneses JF, Leite HP, De Carvalho WB *et al.* (2009):** Hypophosphatemia in critically ill children: prevalence and associated risk factors. Pediatr Crit Care Med., 10(2): 234-238.
17. **Kirkham FJ, Newton RJC, Whitehouse W (2008):** Pediatric coma scales, DMCN. wiley.com › abs › j.1469-8749.2008.02042.x
18. **Vincent JL, Moreno R, Takala J *et al.* (1996):** The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure. n behalf of the working group on sepsis-related problems of the European Society of intensive care medicine. Intensive Care Med., 22 (7): 707-710.
19. **Souza de Menezes F, Leite HP, Fernandez J *et al.* (2006):** Hypophosphatemia in children hospitalized within an intensive care unit. J Intensive Care Med., 21(4): 235-239.
20. **El Shazly AN, Soliman DF, Assar EH *et al.* (2017):** Phosphate disturbance in critically ill children: Incidence, associated risk factors and clinical outcomes. Ann Med Surg., 21: 118-123.
21. **Rady HI, Khalek KA (2014):** Prevalence and risk factors of hypophosphatemia in pediatric intensive care unit. J Anesth Crit Care, 1(5): 00033.
22. **Basri MN, Janattul AJ, Azrina MR *et al.* (2012):** Hypophosphatemia in the intensive care unit: incidence, predictors and management. IMJM., 11(1): 31-36.
23. **Bech A, Blans M, Telting D *et al.* (2013):** Incidence and aetiology of renal phosphate loss in patients with hypophosphatemia in the intensive care unit. Intensive Care Med, 39:1785-1791.
24. **Suzuki S, Egi M, Schneider AG *et al.* (2013):** Hypophosphatemia in critically ill patients. J Crit Care, 28(4): 536-539**.**
25. **Shor R, Halabe A, Rishver S *et al.* (2006):** Severe Hypophosphatemia in Sepsis as a Mortality Predictor. Ann Clin Lab Sci., 36(1): 67-72.
26. **Sakhawey A, Alawady S, Razek A (2015):** Effect of phosphate level on the outcome of critically ill patients in the intensive care unit. J Am Sci., 11: 82- 88.