

## Original Research Article

# Changes in serum phosphorous level during inpatient treatment of children with severe acute malnutrition

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## ABSTRACT

**Background:** SAM children have increased requirements for phosphorus during recovery. If requirements are not met, they may develop refeeding hypophosphatemia leading to increased morbidity and mortality. However, no much studies known about the effect of current therapeutic diets (F-75 and F-100) on serum phosphate in SAM children.

**Methods:** Prospective observational study, in which measuring serum phosphate at admission, at end of stabilization phase and at discharge in SAM children between 6-59 months.

**Results:** Among 35 children enrolled, mean serum phosphate was  $4.3 \pm 0.6$  mg/dl at admission,  $4.1 \pm 0.8$  mg/dl at end of stabilization phase and  $4.4 \pm 0.7$  mg/dl at discharge. 17% of children had hypophosphatemia at admission, 31% at end of stabilization phase and 17% at discharge. mean weight gain in hypophosphatemia and normophosphatemia groups are  $1.3 \pm 1.46$  mg/kg/day and  $2.51 \pm 2.63$  mg/kg/day ( $p=0.1$ ) respectively. Mean duration of stay in hypophosphatemia and normophosphatemia groups are  $11.6 \pm 1.26$  and  $10.26 \pm 1.54$  days respectively ( $p=0.016$ ).

**Conclusions:** Hypophosphatemia was common among children with SAM at admission and increased at end of stabilization phase. Serum phosphate remains subnormal in about 1/5<sup>th</sup> of the children at discharge. This could be problematic for further recovery as phosphorus is needed for catch-up growth and bioavailability of phosphorus is low in local diets. Hence, authors suggest phosphorus supplementation in SAM children.

**Keywords:** Phosphorus, Hypophosphatemia, Severe acute malnutrition

## INTRODUCTION

Severe acute malnutrition (SAM) accounts for 33% of under-five mortality. As per WHO guidelines Sam children are treated with a starter F75 diet (containing 75 calories ) initially for 3-7 days and later with a catch up F100 diet (containing 100 calories). During refeeding due to anabolism and insulin release increased cellular uptake of electrolytes like potassium, magnesium including phosphorous occurs. This leads to hypophosphatemia, hypokalemia, hypomagnesemia with resultant increased mortality and morbidity. Clinical features of these biochemical changes are nonspecific and may be misinterpreted as sepsis. Serum electrolytes are not

routinely monitored, hence adequate content in diet is essential to prevent depletion. Potassium and magnesium supplements are routinely supplemented. But for phosphorous diet is the main source.<sup>1,2</sup>

The World health organization's (WHO) recipe for preparation of F-75 and F-100 from locally available ingredients contain 300 ml and 900ml of skimmed milk per 1000 mL of F-75 and F-100, respectively. Assuming a phosphorus content of skimmed milk of 217 mg/250 ml, a child fed 130mL of locally prepared F-75 per kg per day during stabilization, gets 35mg/kg/day of phosphorus and a child fed 200mL/kg/day of F-100 during rehabilitation, gets 156mg/kg/day of phosphorus. Locally

prepared F-75 thus provide limited amounts of phosphorous during stabilization, and substantially less than the 60mg/kg/day recommended by WHO.<sup>3-5</sup> This combination of a high proportion of energy from carbohydrate and the low phosphorus content may be problematic.

In previous studies, the frequency of hypophosphatemia was found to be 72.9%-93% when SAM children are fed with locally prepared F75 (which contains substantially less phosphate than WHO recommended 60mg/kg/day).<sup>3-5</sup> In contrast use of premixed F75 with extra added phosphorous salt as per UN specifications which provides a phosphorous intake of 73mg/kg/d seems to prevent refeeding hypophosphatemia.<sup>6</sup>

Hence, authors aimed to know the serum phosphorous level during nutritional rehabilitation of SAM children using locally prepared F75 (containing 35mg/kg of phosphorous). The aims and objectives of the study were: to know the changes in serum phosphorous level in SAM children at admission, at the end of stabilization phase and at discharge, to know the frequency of hypophosphatemia in SAM children, to compare the average weight gain (mg/kg/day), time to discharge in SAM children with and without hypophosphatemia.

## METHODS

A prospective observational study conducted at Nutritional Rehabilitation Center (NRC), Vani vilas Hospital attached to Bangalore Medical College and Research Institute, Bengaluru between Jan 2018-july 2018.

### Inclusion criteria

- Patients willing to give written informed consent
- SAM children requiring admission to nutritional rehabilitation center aged between 6 months-5 years.

### Exclusion criteria

- SAM children less than 6 months
- SAM children with any underlying chronic illness as secondary cause of malnutrition.

After obtaining institutional ethics committee clearance and written informed consent, the in-patients of nutritional rehabilitation center fulfilling the inclusion/exclusion criteria were enrolled in the study. All children in the group were managed according to WHO SAM guidelines. Patients were monitored daily for weight gain. Serum phosphorus was measured at three time points namely-at admission, at end of stabilisation phase and at discharge in all children. At each of 3 time points 1ml of blood is taken in vacutainer and centrifuged using Beckman counter au 480 and serum phosphorus is estimated by SISKE and SUBBOWS method. According

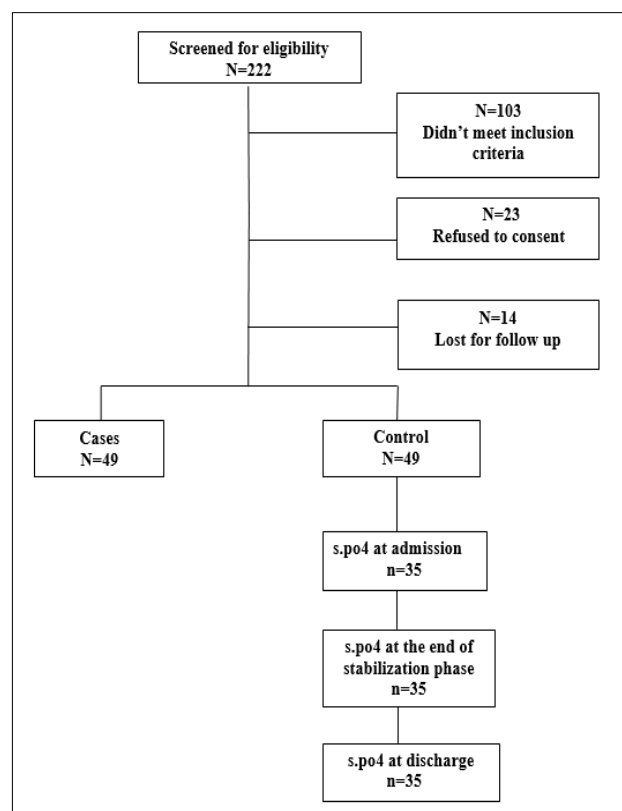
to the Nelson textbook of pediatrics, authors defined plasma phosphate concentration  $>3.7$ ,  $2$  to  $<3.7$ ,  $1$  to  $<2$ , and  $<1$ mg/dL as non- hypophosphatemia, mild Hypophosphatemia, moderate Hypophosphatemia, and severe Hypophosphatemia respectively.<sup>7</sup> Hyperphosphatemia was defined as serum phosphorus  $>6.5$ mg/dl in children  $<4$ years and  $>5.6$ mg/dl in children  $>4$  year.

### Statistical analysis

Descriptive statistics are presented for relevant baseline patient characteristics. Continuous variables are expressed as mean $\pm$ SD and were analyzed using a student's t test; categorical variables are expressed as proportions and were analyzed using chi-square test. p value  $<0.05$  was considered statistically significant.

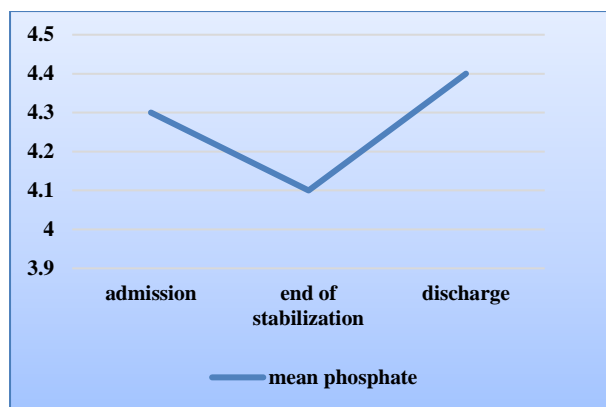
## RESULTS

Total of 222 children who were admitted with SAM to NRC during study period were screened for eligibility. About 103 children did not meet the inclusion criteria and guardians of 23 children refused to participate in the study.



**Figure 1: Flow of participants in the study.**

The control group formed present study group. Among this enrolled group of 49 children, 11 of them lost were lost for follow-up and in 3 children all three samples could not be collected. Remaining 35 children could complete the study (Figure 1).



**Figure 2: Mean phosphorus level.**

Remaining 98 children were randomized into case group (receiving phosphorous supplement n = 49) and control group (receiving regular treatment as per SAM guidelines n=49).

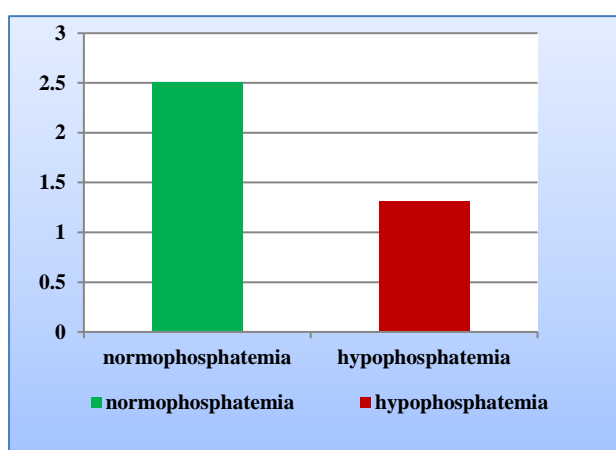
The mean S-phosphorus level was  $4.3 \pm 0.6$  mg/dl at admission,  $4.1 \pm 0.8$  mg/dl at end of stabilization phase and  $4.4 \pm 0.7$  mg/dl at discharge (Figure 2).

17% of children had hypophosphatemia at admission, 31% at end of stabilization phase and 17% at discharge. A total of 11 children had hypophosphatemia. There was no difference in mean age, sex distribution, comorbid condition in SAM children with hypophosphatemia and Normophosphatemia (Table 1).

**Table 1: Comparison of diagnosis, weight gain and duration of stay in both the groups.**

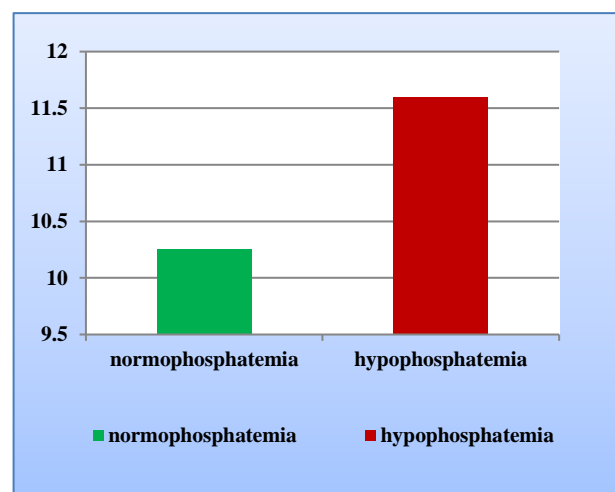
	Normophosphatemia N=24	Hypophosphatemia N=11	P value
Mean age	17.6 $\pm$ 11.8	18.5 $\pm$ 11.7	0.3
Male	12 (50%)	5 (45%)	0.8
Female	12 (50%)	6 (55%)	0.8
MUAC Mean $\pm$ SD	11.3 $\pm$ 0.6	11.2 $\pm$ 0.7	0.8
Anemia	5 (14%)	3 (8%)	0.6
AGE	5 (14%)	4 (11%)	0.3
LRTI	5 (14%)	3 (8%)	0.6
Others	9 (25%)	1 (28%)	0.08
Weight gain gm/kg/day	2.51 $\pm$ 2.63	1.3 $\pm$ 1.46	0.1
Duration of stay(days)	10.26 $\pm$ 1.54	11.6 $\pm$ 1.26	0.01

The mean weight gain in hypophosphatemia and normophosphatemia groups are  $1.3 \pm 1.46$  mg/kg/day and  $2.51 \pm 2.63$  mg/kg/day ( $p=0.1$ ) respectively (Figure 3).



**Figure 3: Weight gain (mg/kg/day).**

The mean duration of stay was significantly more in hypophosphatemia group when compared to normophosphatemia groups ( $11.6 \pm 1.26$  vs  $10.26 \pm 1.54$  days;  $p=0.016$ , Figure 4).



**Figure 4: Duration of stay (days).**

## DISCUSSION

To our knowledge, this is the first study to present data on S-phosphate in children stabilized with locally prepared F-75 and F100 and to present data on changes in P-phosphate during the transition phase.

### S-phosphate at admission

Authors found that in present study 17% of children had hypophosphatemia at admission. The prevalence of hypophosphatemia at admission in malnourished children has been reported as 86% by Kimutai et al,<sup>7</sup> 72.9% by Shoshimatsu et al,<sup>3</sup> 37% by Namusoke et al,<sup>8</sup> respectively.<sup>3,4,8</sup> This variation may be due to differences in dietary intake, cut off limits for hypophosphatemia and laboratory method of estimation.

### Changes during treatment

Mean S phosphate decreased by 0.2mg/dl and 31 % of children had hypophosphatemia at the end of stabilization phase. This could be due to decreased phosphate content of F 75 (260 mg/l) in present study. Similar fall in mean S phosphate at the end of stabilization phase has been reported by Kimutai et al, shoshimatsu et al, who have used locally prepared diet probably low in phosphorous content (the phosphorous content of which is not revealed in their articles).<sup>3,4</sup> Hence, authors suggest supplementing phosphorous during F75 therapy.

Although further randomized trials are required to decide whether it is beneficial. Mean S phosphate increased by 0.3mg/dl and 17 % of children had Hypophosphatemia at discharge in present study. Authors used F100 containing 781 mg phos/L. Shoshimatsu et al, (using standard Dhaka protocol- phosphorous content not known) have reported hypophosphatemia in 14% at discharge.<sup>4</sup>

When using premix F100 containing 579 mg phosphorus/L as per new UN specification the prevalence of hypophosphatemia at discharge was 6% as per Namusoke et al.<sup>8</sup> This variation could be due to loss of follow up at discharge (40-48%) in both these studies. However, in present study authors have analyzed only those for whom S phosphorous is available at all three points of time. The bioavailability of the phosphorous salt in children with SAM is unknown, but might be low due to decreased gastric acidity, and it is not clear if it is well absorbed.

In present study the hypophosphatemic children had lesser mean weight gain but it was not significant statistically. They had a significantly increased duration of stay. Lodha et al, have reported that Hypophosphatemia was common in critically ill children and was associated with prolonged length of stay and increased duration of mechanical ventilation and a serum phosphate <2.5mg/dL was associated with increased mortality.<sup>9</sup> Santana Meneses et al, have reported hypophosphatemia in 61% during first 10 days of PICU stay and malnutrition was a risk factor for hypophosphatemia.<sup>10</sup>

Hence authors suggest phosphorous supplementation for the children during stabilization and rehabilitation phase to avoid hypophosphatemia and to achieve better average

weight gain and to reduce the duration of the stay in hospital. Further randomized trial is required to prove this. Strength and limitations of this study were the first study in India to describe the pattern of s-phosphate in children with SAM receiving treatment locally prepared milk based F75, F100 according to WHO protocol.

There was no selection bias as authors have analyzed S phosphate of children in whom all the three results were available. Present study has few limitations. First, the observational design precludes conclusions about causality, second with the modest sample size, the power to detect differences was limited.

### CONCLUSION

Hypophosphatemia was common among children with SAM at admission, and still subnormal in about 17% of the children at discharge. This could be problematic for further recovery as phosphorus is needed for catch-up growth and local diets are likely to be low in bioavailable phosphorus.

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*Conflict of interest: None declared*

*Ethical approval: The study was approved by the Institutional Ethics Committee*

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