

## Original Research Article

# Clinico-epidemiology and assessment of folate and vitamin B12 status in severe acute malnourished children: a hospital-based observational study in the rural area of Uttar Pradesh

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## ABSTRACT

**Background:** Severe acute malnutrition (SAM) is a serious health problem in children in India. Vitamin B12 and folate are crucial micronutrients along with others required for rapid growth and development during infancy and early childhood, whereas their deficiencies contribute to malnutrition. The study aimed to evaluate iron, folate and vitamin B12 status in hospitalized SAM children aged between 6-59 months and their clinical, epidemiological profile.

**Methods:** A hospital-based observational study on 159 children with SAM in the age group 6-59 months who were enrolled in the study based on anthropometric indicators after written informed consent from parents. The clinical, demographic profile and pertinent details of each patient were collected using standardized proforma and the blood samples were collected. Serum ferritin level was done in all anaemia cases, while vitamin B12 and folic acid (FA) were done only in children with macrocytic or dimorphic anaemia. For statistical analysis, SPSS 20.0 software was used.

**Results:** Mean age of admitted children was 23.77±13.95 months belonging mainly to lower socioeconomic scale and joint families with preferential vegetarian diet. 39.62% SAM patients were between 6-12 months of age at the time of admission. The most common associated infections were GI infections (gastrointestinal tract) in 52.20%. Out of all cases, 93.71% of SAM patients were anaemic. 39.59% cases had macrocytic anaemia followed by microcytic anaemia in 30.20%. Of the 91 cases with macrocytic/dimorphic anaemia (based on MCV and morphology), vitamin B12 and FA levels were done, 92.30% and 61.53% had a deficiency of vitamin B12 and FA, respectively. Overall out of all admitted patients, 52.83% of SAM children had vitamin B12 deficiency and folate deficiency was found in 35.22% of children.

**Conclusions:** SAM children had a high prevalence of vitamin B12 and folate deficiency. Efforts should be made to prevent deficiency of such micronutrients in pregnant and breastfeeding mothers and their infants. Treatment can affect a child's prognosis.

**Keywords:** Anthropometric, Clinical-demographic, Folate, Severe acute malnutrition, Vitamin B12

## INTRODUCTION

Nutritional-related health issues have been prominent in infants and young children (especially those under the

age of five) in Asian economies such as India for decades, which is a major concern for children's health.<sup>1-3</sup> Globally, childhood malnutrition or undernutrition continues a significant public health issue, leading to

increased morbidity, mortality and disease risk and delayed recovery despite nutritional rehabilitation.<sup>4-7</sup>

In India, an estimated 8.1 million (7.5%) children under the age of 5 are affected by SAM and are responsible for nearly 0.6 million deaths and 24.6 million DALYs (disability adjusted life years).<sup>8,9</sup> Data provided under national family health survey 4 (NFHS 4, 2015-16) revealed underweight prevalence rate was 35.8% and 63%, 58% and 16% of the children were underweight, wasted and stunted, respectively.<sup>10</sup>

Several reports have been shown that vitamin B12 and FA, the 2 micronutrients play a dynamic role in malnutrition in children. Undesirable consequences of vitamin B12 deficiency are increasingly recognized such as slowed growth, developmental retardation and cognitive impairment.<sup>5,15</sup> As a result, ferritin, vitamin B12 and FA supplementation have been a primary focus of national government and foreign agency initiatives to reduce malnutrition (to improve child health).<sup>11,12</sup> However, research on cases with SAM and hospital-based surveys conducted over the last two to three decades have revealed a global increase in the prevalence of vitamin B12 deficiency.<sup>5,13-15</sup>

With this background, the authors undertook this study to evaluate hematopoietic factors' status in children with SAM in rural areas, which was poorly understood. This hospital-based study's primary objective was to determine the serum ferritin, folate and vitamin B12 status in these children. The secondary objective was to evaluate the clinical-epidemiological profile of SAM patients.

## METHODS

The present study was conducted at the department of paediatrics, Hind Institute of Medical Sciences, Ataria, Sitapur District, UP, India and approved by the ethical committee on 25 May 2019, IEC/IRB no.: HIMS/IRB/2019-20/05. This study was conducted on a sample size of 159 children (diagnosed cases of SAM) aged between 6 and 59 months admitted to the department of paediatrics after written informed consent from parents.

### Inclusion criteria

Children 6-59 months age group with presence of any of the following criteria for SAM like weight for length/height <-3 standard deviation (SD) of median WHO child growth standards, mid-upper-arm circumference <11.5 cm or presence of bilateral pedal oedema were included in the study.<sup>11,16</sup>

### Exclusion criteria

Children with cerebral palsy, malabsorption, chronic systemic disorders, thalassemia, heart disease, congenital

malformations and other non-nutritional causes of SAM were excluded from the study.

A detailed history of SAM patients was noted on a proforma including personal profile, presenting complaints, diet, immunization, development, socio-demographic details of their parents, anthropometry was done followed by biochemical analysis.

Blood was collected for investigations. Complete blood counts and red cell indices performed using automated Sysmex K-1000 (done in the department of pathology/biochemistry). Red cell morphology was assessed on peripheral blood smear using a Romanowsky stain (done in the department of pathology). Levels of serum ferritin, FA and vitamin B12 were done by ELISA using the ENZO Life sciences Kit (standard range-iron deficiency was labelled when serum ferritin concentration was <12 ng/ml, folate deficiency if folate concentration <10 nmol/l and vitamin B12 deficiency if serum vitamin B12 concentration <203 pg/ml.<sup>17,18</sup> Vitamin B12 and FA were done only in SAM patients with macrocytic/dimorphic anaemia.

### Statistical analysis

The statistical studies were carried out using the statistical package for social sciences version 20.0 software. The findings are presented using the mean and standard deviation (SD). Chi-square test was used to compare the categorical variables. P values <0.05 was considered as significant.

## RESULTS

In our study, a total of 159 cases were enrolled from May 2019 to 2020, out of which 67.29% were male. The mean age of admitted patients was 23.77±13.95 months. 39.62% children were between 6-12 months of age at the time of admission. Of all admitted patients, 98 (61.63%) were up to 24 months of age.

As shown in Table 2, most cases, that is, 139 (87.42%), were Hindus and belonged to joint family, that is, 132 (83.01%) with preferential vegetarian diet. 118 (74.21%) SAM patients belonged to lower socioeconomic scale (III and IV). Majority of mothers, 133 (83.64.3%) of SAM children were illiterate and fathers were illiterate in 59 (37.10%) cases. The majority of patients, that is, 139 (87.42%) had incomplete immunization status according to age and 16 (10.69%) patients were not immunized at all. Merely 4 (2.51%) patients were fully vaccinated as per age.

Exclusive breastfeeding remained an average of 3.5±1.87 months. Only 57 (35.84%) children were exclusively breastfed till 6 months of age. 105 (66.03%) children were given mixed feeds (breastmilk with top feed) under the age of 6 months.

**Table 1: Age and sex distribution of study population.**

Characteristics of patients	Number of patients, N (%)
<b>Sex</b>	
Male	107 (67.29)
Female	52 (32.70)
<b>Age (in months)</b>	
6-12	63 (39.62)
13-24	35 (22.01)
25-36	21 (13.20)
37-48	23 (15.90)
49-59	17 (10.69)

**Table 2: Socio-demographic distribution of SAM along with dietary factors, N (%).**

Socio-demographic distribution	Number of patients, N (%)
<b>Religion</b>	
Hindu	139 (87.42)
Muslim	20 (12.57)
<b>Type of family</b>	
Joint	132 (83.01)
Nuclear	27 (16.98)
<b>Socioeconomic status (modified BG Prasad scale updated January 2018)</b>	
Class I (upper middle)	12 (7.54)
Class II (middle)	29 (18.23)
Class III (lower center)	56 (35.20)
Class IV (lower)	62 (38.99)
<b>Father's educational status</b>	
Illiterate	59 (37.10)
Primary school	68 (42.76)
Middle school	26 (16.35)
Secondary school	6 (3.77)
<b>Mother's educational status</b>	
Illiterate	133 (83.64)
Primary school	12 (7.54)
Middle school	9 (5.66)
Secondary school	5 (3.14)
<b>Awareness about malnutrition</b>	
Yes	40 (25.15)
No	119 (74.84)
<b>Dietary practice of mother/family</b>	
Vegetarian	136 (85.53)
Combined (with meat/fish/eggs)	23 (14.46)
<b>Immunization status</b>	
Unimmunized	16 (10.69)
Incomplete	139 (87.42)
Complete	4 (2.51)
<b>Feeding practices</b>	
Prelacteal feeds	32 (20.12)
Colostrum given	98 (61.63)
<b>Exclusive breastfeeding (in months)</b>	
Up to 1	59 (37.10)
Up to 2	65 (40.88)
Up to 3	53 (33.33)
Up to 4	41 (25.78)
Up to 5	69 (43.39)

Continued.

Socio-demographic distribution	Number of patients, N (%)
Up to 6	57 (35.84)
Mixed feeds during 6 months of age	105 (66.03)
<b>Complimentary feeding</b>	
Delay in initiation	108 (67.92)
Adequacy of complementary feeds	68 (42.76)

**Table 3: Distribution of patients according to presenting clinical features/symptoms.**

Sr. No.	Presenting clinical features/symptoms	Number of patients, N (%)
1.	Fever	146 (91.82)
2.	Loss of appetite	119 (74.81)
3.	Cough	99 (62.26)
4.	Loose motion	83 (52.20)
5.	Hair changes	79 (49.68)
6.	Skin changes	63 (39.62)
7.	Vomiting	59 (37.10)
8.	Abdominal distension	44 (27.67)
9.	Ear discharge	21 (13.20)
10.	Convulsion	12 (7.54)
11.	Bleeding	8 (5.03)
12.	Tremor	2 (1.25)

**Table 4: Distribution of patients according to co-morbidities.**

Sr. No	Comorbidities	Number of patients, N (%)
1.	Anaemia (Hb <11g/dl)	149 (93.71)
	Mild (10.0-10.9 g/dl)	37 (24.83)
	Moderate (7.0-9.9 g/dl)	52 (34.89)
	Severe (< 7.0 g/dl)	60 (40.26)
2.	Acute gastroenteritis	83 (52.20)
3.	Acute respiratory infections	62 (38.99)
4.	Hypothermia	59 (37.10)
5.	Signs of vitamin A deficiency	55 (34.59)
6.	Electrolyte imbalance	44 (27.67)
7.	Developmental delay	36 (22.64)
8.	Septicemia	27 (16.98)
9.	Hypoglycemia	23 (14.46)
10.	Skin infections and infestations (scabies)	21 (13.21)
11.	Cognitive impairment	11 (6.91)
12.	Urinary tract infection	5 (3.144)
13.	Measles	4 (2.51)
14.	Malaria	3 (1.88)
15.	Tuberculosis	1 (0.62)
16.	HIV infection	1 (0.62)

**Table 5: Age distribution with mean weight of children (sex distributed).**

Age (in months)	Mean of weight (in kg)±SD						Welch t test; p value
	On admission		Total at admission	On discharge		Total at discharge	
	M (N=107)	F (N=52)		M (N=107)	F (N=52)		
6-12	6.96±1.98	6.2±1.23	7.21±0.53	6.29±2.14	6.14±0.23	6.32±0.17	<0.0001
13-24	6.71±1.08	5.82±0.58	6.00±0.07	7.91±0.47	7.62±0.47	7.8±0.27	<0.0001
25-36	8.95±1.89	7.6±2.32	6.80±0.71	8.95±0.98	7.79±0.51	8.18±0.88	<0.0001
37-48	8.9±2.74	7.46±0.50	7.82±0.50	9.62±1.23	9.12±1.97	9.32±0.23	<0.0001
49-59	10.2±2.95	9.98±2.27	10.76±1.48	13.2±1.56	13±0.90	13.65±0.35	<0.0001

\*Data are expressed in mean, SD.

**Table 6: Distribution of SAM patients based on 3 criteria: (weight/height) z score, mid-upper arm circumference (MUAC) and pedal oedema.**

SAM indicator	Number of patients (N=159)		P value
	On admission (%)	On discharge (%)	
<b>Weight/height &lt;-3 SD (z score)</b>	113 (71.06)	49 (30.81)	<0.05
<b>MUAC (&lt;11.5 cm)</b>	104 (65.41)	36 (22.64)	<0.05
<b>Nutritional oedema</b>	14 (8.80)	5 (3.14)	<0.05

MUAC: mid-upper arm circumference.

**Table 7: Distribution of malnourished children (gender) with the type of anaemia (including biochemical association).**

Type of anaemia (based on morphology)	Number of patients (N=149)		Total N (%)	P value	Low ferritin (ng/ml) (%)	Low vit. B12 level (pg/ml) N (%)	Low folate (ng/ml) N (%)
	Male N=105 (%)	Female N=44 (%)					
<b>Dimorphic</b>	25 (23.33)	7 (15.90)	32 (21.47)	<0.05	19 (59.37)	28 (87.50)	23 (71.87)
<b>Normocytic</b>	8 (7.84)	5 (11.36)	13 (8.75)	<0.05	0	-	-
<b>Microcytic</b>	26 (24.76)	19 (43.18)	45 (30.20)	<0.05	41 (91.11)	-	-
<b>Macrocytic</b>	46 (45.09)	13 (29.54)	59 (39.59)	<0.05	6 (10.17)	56 (94.91)	33 (55.93)

**Table 8: Serum ferritin at admission and discharge.**

Biochemical parameters	Number of patients (N=149)		P value
	Mean biochemical±SD		
	On admission	On discharge	
<b>Ferritin (ng/ml)</b>	6.19±0.82	8.02±1.02	0.001

Data are expressed as mean (SD); p value <0.05 significant; normal serum ferritin >12 ng/ml.

**Table 9: Serum vitamin B12 and FA concentrations.**

Biochemical parameters	Number of patients (n=91)		t test	P value
	M (N=72)	F (N=19)		
<b>Vitamin B12 level (pg/ml)</b>	120.28±19.37	116.06±16.45	-1.57	0.06
<b>Folic acid (nmol/l)</b>	6.97±0.85	5.93±0.55	-2.22	0.01

Data are expressed as mean (SD); p value <0.05 significant; normal range serum vitamin B12 >203 ng/ml; normal serum folate >10 nmol/l.

There was a delay in initiation of complementary feeding in 108 (67.92%) children after six months. The mean age at which semi-solid complimentary food was introduced was 9.52±2.30 months. The complementary feeds' adequacy according to infant and young child feeding (IYCF) guidelines was seen only in 68 (42.76%) children.

As shown in Table 3, fever was the most common presenting clinical complaint in 146 (91.82%) of all admitted patients, followed by loss of appetite in 119 (74.81%), cough in 99 (62.26%) and loose motion in 83 (52.20%) patients. Skin and hair changes were seen in 63 (39.62%) and 79 (49.68%) patients, respectively.

The most common co-morbidities in SAM patients were anaemia in 149 (93.71%) followed by acute gastroenteritis in 52.20% and respiratory infections in 38.99% patients. Out of 149 of SAM patients with anaemia, 60 (40.29%) were having severe (<7.0 g/dl), 52 (34.89%) having moderate (7.0-9.9 g/dl), and 37 (24.83%) having mild anaemia (10.0-10.9 g/dl). Signs of vitamin A deficiency were seen in 55 (34.59%) patients.

The overall mean weight at the admission time for these children was 7.61±1.45 kg and 9.05±2.78 kg at discharge respectively (after 14.67±3.69 days of hospital stay). A statistically significant difference was observed between the mean weight at discharge and the mean weight at admission for the study group (p<0.0001) (Table 5). The

study group's overall average weight gain during their stay at the hospital was  $9.05 \pm 5.33$  g/kg/day.

Out of 159 admitted children, 113 (71.06%) children were severely malnourished according to criteria weight/height z score  $< -3$  SD, 104 (65.41%) and 14 (8.80%) children had MUAC  $< 11.5$  cm and nutritional oedema, respectively. At the time of discharge after nutritional rehabilitation, 49 (30.81%), 36 (22.64%) and 5 (3.14%) children respectively were still severely malnourished according to these criteria. t test was applied and the difference between children severely malnourished at the time of discharge as compared with admission was observed to be statistically significant ( $p < 0.05$ ).

Out of 149 children with anaemia, majority had severe anaemia (40.26%), 34.89% children had moderate anaemia and 24.83% had mild anaemia. Based on mean corpuscular volume (MCV) and RBC morphology, SAM patients were labelled as microcytic, normocytic, macrocytic or dimorphic. Majority of the children had macrocytic anaemia (39.59%), followed by microcytic in 30.20%. There was a significant difference in the type of anaemia in genders ( $p > 0.05$ ) as shown in Table 7.

Out of 149 patients with anaemia, 66 (44.29%) had low serum ferritin. The mean ferritin level in these children was  $6.19 \pm 0.82$  ng/ml when they were admitted and  $8.02 \pm 1.02$  ng/ml, when they were discharged (slightly increased). For this study sample, there was a statistically significant difference between the mean ferritin level at discharge and the mean ferritin level at admission ( $p < 0.05$ ), indicating the statistically significant change at the hospital (Table 8).

In the 91 cases of macrocytic and dimorphic anaemia where vitamin B12 and FA levels were measured, 84 (92.30%) had low levels of vitamin B12 (serum vitamin B12  $< 203$  ng/ml), while 56 (61.53%) had folate deficiency (serum folate  $< 10$  nmol/l) (Table 9). Overall out of all admitted patients, 52.83% of SAM children had vitamin B12 deficiency and folate deficiency was found in 35.22% of children.

## DISCUSSION

This is the first study to evaluate serum ferritin, vitamin B12 and serum folate levels in admitted SAM children specifically in rural area of Uttar Pradesh, India to the best of the authors' knowledge and thorough web search. SAM is still a significant social and health concern in children aged 6 to 59 months and it is among the leading causes of paediatric morbidity, hospitalization and mortality in India, but this disease can be prevented and treated.<sup>12-18</sup>

In our study, the mean age of admitted patients was  $23.77 \pm 13.95$  months. Majority of children, 98 (61.63%), were within 6-24 months of age and it was supported by

studies of Choudhary et al and Mamidi et al where the majority of patients (96% and 71% respectively) were below 24 months.<sup>19,20</sup>

In our study, maternal and paternal illiteracy rates were 133 (83.64%) and 59 (37.10%), respectively which is one of contributing factor for SAM. Chowdhury et al and Goyal et al described higher illiteracy rates of the mothers and fathers (89.3% mothers and 66.2% fathers) and (60.6% mothers and 39.4% fathers), respectively which was similar to our study.<sup>2,19</sup>

We observed that in this present study majority of parents of admitted SAM children (35.20%) belonged to lower socioeconomic strata (class IV) (based on modified BG Prasad scale updated January 2018). Similarly, Goyal et al, Chowdhury et al and Devi et al reported a higher percentage of parents 96%, 83.6%, 76%, 89.8% belonging to lower socioeconomic strata, respectively in their studies indicating that low purchasing power, food scarcity and unequal distributions put children in poor communities at risk of malnutrition.<sup>2,19,23</sup>

In our study, 10.69% (16) of children were unimmunized and 87.42% (139) were incompletely immunized for age. The percentages were 6.35 versus 85.71%, 42.7% versus 44% and 24% versus 62.3% in studies by Chowdhury et al and Dasgupta et al, respectively, thus, incomplete immunization can be a contributing factor with SAM.<sup>19,24</sup> In our study only, 2.51% of SAM children were fully immunized as per the medical records.

Exclusive breastfeeding was given in only 35.84% of SAM patients, while 66.03% were mixed fed up to 6 months. The percentages were 32% and 35% in the study by Devi et al.<sup>23</sup> Aprameya et al reported exclusive breastfeeding in 20.9% and bottle feeding in 58.2% cases.<sup>25</sup> In our study delayed initiation of complementary feeds was seen in 67.92% of admitted children similar to 63.5% in Chowdhury et al study.<sup>19</sup>

Anaemia (93.71%) and acute gastroenteritis (52.20%) were the most common comorbidity, followed by acute respiratory infections (38.99%) in our study. Chowdhury et al and Kumar et al also described similar findings.<sup>19,26</sup>

Out of 159 admitted children, 113 (71.06%) children were severely malnourished according to criteria weight/height z score  $< -3$  SD, 104 (65.41%) and 14 (8.80%) children had MUAC  $< 11.5$  cm and nutritional oedema, respectively. At the time of discharge after nutritional rehabilitation, 49 (30.81%), 36 (22.64%) and 5 (3.14%) children respectively were still severely malnourished according to these criteria. Difference between children severely malnourished at the time of discharge as compared with admission was observed to be statistically significant ( $p < 0.05$ ), which was similar to other studies emphasizing the role of nutritional rehabilitation centres.<sup>2,24,27</sup>

Macrocytic anaemia was the most common form of anaemia in our study with 39.59% of SAM children having it, followed by microcytic anaemia with 30.20%. Our findings were close to those of Dwivedi et al who found macrocytic anaemia in 33% cases.<sup>28</sup> This may be due to the fact that most of these children had anisocytosis and displayed features of dimorphic anaemia which was treated with iron at the first stage, leading to a relative recovery of iron stores and deficiency of vitamin B12 or folate resulting in macrocytosis.

In the 91 cases of macrocytic and dimorphic anaemia where vitamin B12 and FA levels were measured, 84 (92.30%) had low levels of vitamin B12 (serum vitamin B12 <203 ng/ml), while 56 (61.53%) had folate deficiency (serum folate 10 nmol/l) (Table 9). Overall, 52.30% of SAM children had vitamin B12 deficiency, and folate deficiency was found in 35.22% of children.

In macrocytic anaemia, the most common deficiency was vitamin B12 (94.91%), followed by FA and ferritin in 55.93 and 10.17 % of children. In dimorphic anaemia, the most common deficiency was vitamin B12 (87.50%), FA and ferritin in 71.87% and 59.37% of children. In microcytic anaemia, ferritin was low in (91.11%) children.

Several recent studies have revealed a high prevalence of vitamin B12 and FA deficiency in SAM children.<sup>12,28-31</sup> Kumar et al also found that 14.4% of the SAM patients were vitamin B12 deficient and folate deficiency in 15% of children.<sup>26</sup> Vitamin B12 deficiency was found to be significantly higher in children with low socioeconomic families, particularly those born to vegetarian mothers who breastfed their babies exclusively even after 6 months of age with delayed initiation of complimentary feeding. As a result, both the mother's and the child's dietary histories are equally significant, and particular attention should be paid to infant and young child feeding (IYCF).<sup>15,28-31</sup>

In this study, in our hospital, NRC (nutrition rehabilitation centres) team members had provided knowledge and awareness to mothers of SAM children about different facts including personal hygiene, basic nutrition concepts, complimentary food preparation and preparation of nutritious food from the available foods items.

There were some limitations in this research. First, since this was a hospital-based analysis, the results cannot be generalized to the general population. Second, since this was a cross-sectional observational study, it was impossible to assess the effect of diet, social status or other co-morbid illnesses on SAM. Finally, the lack of a control group and long term follow up data made it much more challenging to study the treatment plan and complications.

## CONCLUSION

Based on the findings of this report, we conclude that the issue of severe malnutrition is multifaceted. In malnourished children aged 6 to 59 months, a rising incidence of ferritin, vitamin B12 and FA deficiency was discovered. SAM children, those from lower socioeconomic classes, who were exclusively breastfed even after 6 months of age with delayed initiation of complementary feeding were more likely to be deficient, leading to an adverse development outcome. Malnourished mothers with preferential vegetarian diet in mothers could be the associated factors. We found a significant folate deficiency among these children. Consequently, we should concentrate our efforts on preventing its deficiency in pregnant and breastfeeding mothers and their infants, with a particular focus on malnourished children. Strengthening these nutrients' status (folate and vitamin B12) in SAM children in the hospital can reduce nutritional anaemia and improve neuronal development.

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