Original Research Article

Estimation of serum folate and vitamin B12 levels in children with severe acute malnutrition

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ABSTRACT

Background: Severe acute malnutrition is the important health issue children affected in India. It is often associated with Iron, Vitamin B12 and Folic acid and other micronutrient deficiencies. These reports of declining trend of Iron and folic acid deficiency with implementation of national anemia control programme. Estimation of Serum Folate and Vitamin B12 levels in SAM children aged 6-60 months with anemia was the objective of the study.

Methods: A hospital based observational study on 80 children admitted to nutritional rehabilitation center were suffering from severe acute malnutrition (SAM) in the age group of 6-60 months enrolled in the study during the period November 2018 to May 2019. Data was collected using a predesigned and pretested proforma, containing details of feeding, socio-economic and development history. Blood samples were sent for measurement of plasma vitamin B12 and serum folate levels. Statistical analysis was done using SPSS version 20.0.

Results: Out of 80 children, majority were between the age group of 24-60 months and majority were boys (53.8%). Mean Vitamin B12 and folic acid levels being 384.61 and 8.95 respectively. 45% and 3.8% had vitamin B12 and folic acid deficiencies respectively. Majority of neurological changes and developmental delays were noted in B12 deficient group. Of the 36, B12 deficient children, majority had moderate anaemia (40.2%), normal total count (41.7%), 60% had neutropenia, 44.4% had lymphocytosis, majority had normocytic (30.9%) anemia.

Conclusions: There was a moderate to high prevalence of vitamin B12 deficiency among malnourished children. Folate deficiency was found only in few. Efforts should be directed to prevent its deficiency in pregnant and breastfeeding women and their infants with special attention on malnourished children. B12 and folate deficiency shall be considered in all cases with SAM irrespective of blood indices. Treatment will have impact on prognosis of child.

Keywords: Anemia, Folate deficiency, Severe acute malnutrition, Vitamin B12 deficiency
status, inadequate intake and poor absorption. Vitamin B12 and Folate deficiency leads to megaloblastic anemia, poor growth and increased infections, in addition vitamin B12 deficiency leads to irreversible neurological damage to developing brain.\textsuperscript{10,12} Prevalence of Vitamin B12 deficiency found to be 30% in a data from the National Nutrition Survey 1999.\textsuperscript{1} The decreasing trend in Iron & Folate deficiency could be due implementation of the National Anaemia Control Programme where mother and children receive iron and folic acid tablets regularly.\textsuperscript{13}

There are limited studies on changing trend of Vitamin B12 deficiency in patients with SAM. This study has been undertaken to estimate the serum folate and vitamin B12 status in malnourished children. Based on these levels, micronutrients can be supplemented/treated in appropriate dosages and forms.

**METHODS**

It is a hospital based Observational cross sectional study on 80 severely malnourished children admitted in nutritional rehabilitation center (NRC) of our hospital over a study period of 18 months from July 2017 to June 2019. Children aged of 6-60 months were enrolled in the study. As soon as the SAM children admitted to NRC, Department of pediatrics Vanivilas hospital, BMCRI. When diagnosis fitting to severe acute malnutrition criteria. Children details were entered in a case form, designed for NRC.

Investigations were carried out as per SAM guidelines. Those are CBC, urine routine, culture sensitivity, serum albumin, serum electrolytes, X ray chest. Beside which serum folate and vitamin B12 levels were estimated and findings were noted. The final outcome in terms of deficiency and their correlation with demographic, clinical profile and neurologic changes were noted.

**Inclusion criteria**

- Parents / Guardians willing to give written informed consent.
- Children diagnosed as primary SAM.
- Age group of 6- 60 months.

**Exclusion criteria**

- Patients not willing to give informed assent.
- Children <6months and >5 years will be excluded.
- Anemia due to acute blood loss.
- All children with non-nutritional anemias (malignancies, Hemolytic anemia, Aplastic anemia).
- Children diagnosed to have secondary SAM.
- Those who have received iron, vitamin B12, folate and blood transfusion prior to admission.

Ethical clearance was taken from the Ethical Committee of the institution before starting the study. Patients were enrolled after written and informed consent from their parents. Patients fulfilling the inclusion criteria will be included in the study.

**Statistical analysis**

Data will be entered in Microsoft excel and will be exported into SPSS version 211.0. Data will be analysed by descriptive statistics for statistical association between variables will be use suitable parametric and non-parametric tests p<0.05 will consider statistical significant.

**RESULTS**

Eighty children suffering with Severe Acute Malnutrition (SAM) aged 6-60 months were studied. Mean age of study children was 51.6months. 43 (53.8%) cases were males, 37(46.3%) cases were females. Of the 36 (45%) vitamin B12 deficient children, 32(88.9%) belong to upper lower socioeconomic status and 3(8.3%) to lower middle socioeconomic status (Table 1 and 2).

| Vitamin B12 | Levels | Frequency | Percent |
|-------------|--------|-----------|---------|
|            | <100   | 36        | 45      |
|            | 100-200| 19        | 23.8    |
|            | >200   | 44        | 55      |

Statistically 36 (45%) SAM children had vitamin B12 deficiency (vitamin B12 levels<100pg/ml), and 19 (23.8%) had borderline vitamin B12 levels (100-200pg/ml).\textsuperscript{13} Folic acid deficiency is seen in 3(3.8%) children (Table 3). Mean Vitamin B12 and folate levels being 384.61 and 8.95 respectively.

Among the children with vitamin B12 deficiency, 23(63.9%) were still predominantly on breast feeding and 23(63.9%) had delayed introduction of complementary feeding (beyond 6 months).Of the B12 deficient children, 6(16.7%) had neuroregression, 2(5.6%) had neuroregression with Infantile tremor syndrome, 1(2.8%) had Infantile tremor syndrome and 10(27.7%) had delayed milestones. 4(23.50%) had macrocytic anemia (MCV >100fl) 10(27.8%) had thrombocytopenia (Table 4).\textsuperscript{13}

**DISCUSSION**

In the present study, males outnumbered females. This can be explained by differential health seeking behavior of parents where male child is still preferred in India. Similar results were also obtained in another hospital based study by Yadav SS et al.\textsuperscript{14} We found vitamin B12 deficiency 36(45%), more prevalent than folic acid deficiency 3(3.8%). Over the last few years, the number of cases of vitamin B12 deficiency are increasing as
compared to folic acid deficiency. In a study by Chhabra A et al, they concluded that nutritional megaloblastic anaemia occurs commonly in malnourished children; the commonest age is 3-18 months. These children were exclusively breast fed by mothers who have had poor cobalamine levels and undernourished.

**Table 2: Demographic and clinical profile of vitamin B12 and Folic Acid deficient group of SAM children with anemia.**

| Deficient group | Vitamin B12 (N=36) | Folic acid (N=3) | p value |
|-----------------|---------------------|-----------------|---------|
| Age             |                     |                 |         |
| 0.6 - 1 year    | n=10               | n=0             | 0.29    |
| 1- 5 years      | n=26               | n=3             |         |
| Gender          |                     |                 |         |
| Male            | n=18               | n=1             | 0.579   |
| Female          | n=18               | n=2             |         |
| Residence       |                     |                 |         |
| Urban           | n=14               | n=2             | 0.03    |
| Rural           | n=22               | n=1             |         |
| Socioeconomic status |               |                 |         |
| Upper middle    | n=1               | n=1             | 0.381   |
| Upper lower     | n=32              | n=34            |         |
| Lower           | n=3               | n=4             |         |
| Diet            |                     |                 |         |
| Vegetarian      | n=20              | n=0             | 0.064   |
| Mixed           | n=16              | n=3             |         |
| Predominantly BF even after 6M |     |                 |         |
| Yes             | n=23              | n=2             | 0.923   |
| No              | n=13              | n=1             |         |
| Late initiation of complementary feeds | |                 |         |
| Yes             | n=23              | n=0             | 0.031   |
| No              | n=13              | n=3             |         |
| Immunization    |                     |                 |         |
| Up to date      | n=30              | n=6             | 0.442   |
| Incomplete      | n=6               | n=0             |         |
| Milestones      |                     |                 |         |
| Appropriate for age | n=15           | n=3             | 0.052   |
| Delayed         | n=21              | n=0             |         |
| Hyperpigmentation |                 |                 |         |
| Yes             | n=25              | n=0             | 0.016   |
| No              | n=11              | n=3             |         |

**Table 3: Distribution of anemia in SAM children.**

| Deficient Group | Frequency | Percent |
|-----------------|-----------|---------|
| Vitamin B12     | 36        | 45.0    |
| Folic acid      | 3         | 3.8     |
| Others          | 41        | 51.3    |
| Total           | 80        | 100.0   |

**Table 4: Neurologic changes in Vitamin B12 and folic acid deficient group among SAM Children with anemia.**

| Deficient group | Neurologic changes | Neuroregression | Neuroregression with ITS | ITS | Delay | No | Total | \( \chi^2 \) value | p value |
|-----------------|--------------------|-----------------|--------------------------|-----|-------|----|-------|------------------|---------|
| Vitamin B12     | 6                  | 2               | 1                        | 10  | 17    | 36 | 6.70% | 5.60%            | 2.80%   | 2.77% | 47.20% | 100.00% | 3.088 | 0.686 |
| Folic acid      | 0                  | 0               | 0                        | 0   | 3     | 3  | 0.00% | 0.00%            | 0.00%   | 100.00% | 0.00%  | 100.00% | 3.088 | 0.686 |
| Total           | 6                  | 2               | 1                        | 10  | 20    | 39 | 15.40%| 5.10%            | 2.60%   | 27.77% | 51.30% | 100.00% | 3.088 | 0.686 |

In a study by Yahikomba T et al on assessment of iron, folate and vitamin B12 status children with SAM children aged 6-60 months concluded that prevalence of cobalamine deficiency in SAM children is much more than folate deficiency. The decrease in folic acid deficiency could be due to implementation of the
National Anaemia Control Programme where mother and children receive iron and folic acid tablets regularly. Moreover, breast milk is an important source of folate and this may account for the positive effect of breast feeding in these children.  

In the present study vitamin B12 deficiency was found to be significantly higher in children of lower socioeconomic status families, those born to vegetarian mothers feeding their babies, exclusively on breast milk even beyond 6 months of age. Therefore, dietary history of both mother as well the child is equally important and stress should be given to follow appropriate infant and young child feeding (IYCF). Hematologic parameters showed no difference in prevalence of anemia, mean hemoglobin levels or mean total leucocyte or differential leucocyte counts among the B12 deficient and B12 sufficient children except the lower mean platelet count and higher mean corpuscular volume found in B12 deficient children which are known to be features of vitamin B12 deficiency. Lower sample size, follow up of developmental delay cases were the few limitations.

CONCLUSION

There was a moderate prevalence of vitamin B12 deficiency 36(45%) among malnourished children. Folate deficiency was found only in few 3(3.8%). Efforts should be directed to prevent its deficiency in pregnant and breastfeeding women and their infants with special attention on malnourished children. Deficiency was more common in young children, lower socio-economic status class, those on exclusive breast feeding and/or having delayed initiation of complementary feeding. It has a clear association with adverse developmental outcome. We did not find significant folate deficiency among these children. Improving the status of these nutrients (folate, and vitamin B12) might reduce the burden of childhood anemia and improve the neuronal development of these children.

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