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Cobalamin and folate status in malnourished children

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ABSTRACT

Background: Vitamin B12 and folate are essential micronutrients which are critical especially during infancy and early childhood as these are periods of rapid growth, development, and increased demand. Malnutrition further increases the risk of these micronutrient deficiency due to poor socioeconomic status, inadequate intake and poor absorption. Aim of present work was to study the cobalamin and folate status in malnourished children.

Methods: A hospital based observational study on 80 children suffering from severe acute malnutrition (SAM) aged 6-60 months. Detailed socio-economic, feeding and development history with complete anthropometric evaluation was done. Blood samples sent for measurement of plasma vitamin B12 and serum folate levels. Statistical analysis was done using SPSS version 20.0.

Results: Mean age of SAM children was 17.25±12.60 months. 30 (37.5%) had vitamin B12 deficiency (vitamin B12 levels<100pg/ml) and 9 (11.25%) had borderline vitamin B12 levels (100-200pg/ml). Folate deficiency was found in only 7 (8.75%) children. Mean vitamin B12 and folate levels were found to be 353.65±330.76pg/ml, 11.18±4.17ng/ml respectively. Among vitamin B12 deficient children, majority (26, 86.66%) belong to lower socio-economic status, 17 (56.66%) were still predominantly on breast feeding and 11 (36.66%) had delayed introduction of complementary feeding. Among B12 deficient children 23 (76.66%) had delayed development (DQ <70). 100% of B12 deficient children were anemic with majority (21,70%) having severe anemia. 17 (56.66%) B12 deficient children also had associated thrombocytopenia (PC <1.5 lakh/cumm).

Conclusions: There was a 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.

Keywords: Folate deficiency, Malnutrition, Vitamin B12 deficiency

INTRODUCTION

Vitamin B12 and folate are essential micronutrients which are critical especially during infancy and early childhood as these are periods of rapid growth, development, and increased demand. During infancy and childhood, deficiency of folate and vitamin B12 can result in megaloblastic anemia, poor growth, and increased infections, additionally vitamin B12 deficiency can potentially cause irreversible neurologic damage to

the developing brain. 1-3 Vitamin B12 is exclusively found in animal-derived foods such as meat, eggs, fish and milk, and its deficiency is mainly due to inadequate dietary intake of these foods. 4 A mother's strict vegetarian diet may be associated with vitamin B12 deficiency both in the mother as well as the newborn. 5 Folate deficiency mainly results from a low intake of green leafy vegetables, legumes and meat. 6 Malnutrition further increases the risk of micronutrient deficiency due to lack of availability, poor socioeconomic status, inadequate intake and poor absorption and false beliefs

associated with their diet and eating habits. Malnutrition is India's silent crisis. It has some of the highest rates of child morbidity and mortality in under-fives in the world. One out of every five children in India under the age of five years is wasted.7 India has 132 million under five children. Of these 132 million children, it is expected that 9 million children, are suffering from severe acute malnutrition. This is almost 50 percent of children with severe acute malnutrition (SAM) worldwide.⁷ According to recent data released by NFHS 4, carried out in 20015-16, 35.7% of children under the age of 5 years in India are underweight, 21% are wasted, 7.5% are severely wasted and 38.4% stunted.8 These data are even more unacceptably high in Udaipur district of Rajasthan where 52% of children under the age of 5 years are underweight, 29.9% are wasted, 11.4% are severely wasted and 47.5% are stunted.9

Vitamin B12 is a water-soluble vitamin and is necessary for the production of tetrahydrofolate, essential for DNA synthesis. Vitamin B12 deficiency usually presents with manifestations such as hypotonia, developmental delay, regression, irritability, developmental movements and failure to thrive.10 Vitamin B12 deficiency in infants is usually from mothers with low B 12 levels or insufficient diet of cobalamin rich nutrients. In the nervous system, vitamin B12 acts as a coenzyme in the methyl malonyl-CoA mutase reaction, which is necessary for myelin synthesis. Vitamin B 12 deficiency therefore results in defective myelin synthesis, leading to central and peripheral nervous system dysfunctions like bilateral peripheral neuropathy or degeneration (demyelination) of the posterior and pyramidal tracts of the spinal cord and (subacute combined degeneration of cord), less frequently, optic atrophy or cerebral symptoms. 11 The patient presents with paresthesia, muscle weakness, or difficulty in walking and sometimes dementia, psychotic disturbances, or visual impairment. Long-term nutritional cobalamin deficiency in infancy leads to poor brain development and impaired intellectual development. 10,11 Folic acid deficiency results in megaloblastic anemia, glossitis, listlessness and growth retardation. Cerebral folate deficiency manifests at 4-6 months of age with irritability, microcephaly, developmental delay, cerebellar ataxia, pyramidal tract signs, choreoathetosis, ballismus, seizures and blindness due to optic atrophy.¹²

The diagnosis of cobalamin or folate deficiency has traditionally depended on the recognition of the relevant abnormalities in the peripheral blood and analysis of the blood levels of the vitamins. Normal serum levels range from 160–200 pg/ml to 1000 pg/ml. In patients with megaloblastic anemia due to cobalamin deficiency, the level is usually <100 pg/ml. Values between 100 and 200 pg/ml are regarded as borderline. The serum cobalamin level is sufficiently robust, cost-effective, and most convenient to rule out cobalamin deficiency in the vast majority of patients suspected of having this problem. Serum methylmalonate and homocysteine have been

introduced and recommended for the early diagnosis of cobalamin deficiency, even in the absence of hematologic abnormalities or subnormal levels of serum cobalamin. The normal range of serum folate is from 5 -20 ng/ml. The serum folate level <3ng/ml is labelled as folate deficiency. The red cell folate assay is a better indicator of chronic deficiency.¹²

METHODS

It is a hospital based descriptive study on 80 severely malnourished children admitted in malnutrition treatment center of our hospital over a study period of 12 months from July 2015 to June 2016. Children aged of 6-60 months age group were enrolled in the study. Children having secondary malnutrition (e.g. congenital heart disease, congenital malformations, malabsorbtion syndromes, genetic and chromosomal malformations) were excluded from the study. A detailed socioeconomic, feeding and development history was obtained. Detailed anthropometric measurements were taken using standard methods. Children were classified according to weight for length/height Z score (WHZ) criteria as per WHO child growth standards charts (Multicentre Growth Reference Study, MGRS) as Z score of < -3SD as severe acute malnutrition.¹³ Development was assessed in all the domains (gross and fine motor, social and language milestones) and development quotient (DO) was calculated as average age at attainment / observed age of attainment X 100. A DO below 70% was taken as delayed, 70-90 as borderline and 90-110 as normal.¹⁴ Blood samples were collected at the time of admission for measurement of plasma vitamin B (12) and serum folate levels. Vitamin B12 levels were estimated by electrochemiluminiscence (ECL) procedure using COBAS e411 analyzer. Vitamin B12 cut off value below 100 pg/ml was considered deficient, value between 100-200 pg/ml as borderline and above 200pg/ml as sufficient. Folate deficiency is defined as a serum folate concentration <3ng/ml.

Statistical analysis

Statistical analysis was done using SPSS version 20.0 (Chi-square test, T-test, percentage, mean and standard deviation). Proper 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.

RESULTS

Eighty children suffering with Severe Acute Malnutrition (SAM) aged 6-60 months were studied. Mean age of study children was 17.25±12.60 months. 46 (57.5%) were male and 34 (42.5%) were female. 30 (37.5%) SAM children had vitamin B12 deficiency (vitamin B12 levels<100pg/ml) and 9 (11.25%) had borderline vitamin B12 levels (100-200pg/ml).

Table 1: Distribution of study children according to deficiency cut off for vitamin B12 and serum folate.

Investigation	Deficiency cut off	SAM	
		No.	%
Vit B12	<100	30	37.5
(279-996	100 -<200	9	11.25
pg/ml)	≥200	37	51.25
Serum Folate	<3	7	8.75
(5-20 ng/ml)	≥3	73	91.25

Folate deficiency was found in 7 (8.75%) children. Mean vitamin B12 and folate levels were found to be 353.65±330.76pg/ml, 11.18±4.17ng/ml respectively in

severely malnourished children. Mean vitamin B12 levels in B12 deficient children was 43.52 ± 19.84 pg/ml.

Mean age of vitamin B12 deficient children was 11.40±4.22 months. Of the 30 (37.5%) vitamin B12 deficient children, 26 (86.66%) belong to lower socioeconomic status and 4 (13.33%) to middle socioeconomic status.

Among the vitamin B12 deficient children 17 (56.66%) were still predominantly on breast feeding and 11 (36.66%) had delayed introduction of complementary feeding (beyond 6 months). 29 (96.66%) of B12 deficient children were underweight and 22 (73.33%) were stunted.

Table 2: Different parameters studied in vitamin B12 deficient and folate deficient group.

Parameters	Vitamin B12 deficient group	Folate deficient group	P value
Mean age	11.40±4.22 months	23.57±18.52 months	< 0.05
Mean B12 levels in deficient children (pg/ml)	43.52±19.84	370.12±255.62	< 0.05
Mean folate levels in deficient children (ng/ml)	10.16±5.59	2.52±0.69	< 0.05
Lower socioeconomic status	26 (86.66%)	3 (42.85%)	< 0.05
Predominantly breast feeding even after 6 months of age	17 (56.66%)	2 (28.57%)	< 0.05
Late initiation of complementary feeding	11 (36.66%)	5 (71.4%)	< 0.05
Underweight	29 (96.66%)	7 (100%)	>0.05
Stunted	22 (73.33%)	5 (71.4%)	>0.05
Delayed development (DQ <70)	23 (76.66%)	6 (62.55%)	>0.05
Severe anemia (Hb <7g/dl)	21 (70%)	3 (42.85%)	< 0.05
Macrocytic anemia (MCV >100fl)	16(53.33%)	1 (14.2%)	< 0.05
Thrombocytopenia (PC <1.5 lakhs)	17(56.66%)	2 (28.57%)	< 0.05

Among the B12 deficient children 7 (23.33%) had borderline DQ, 23 (76.66%) had delayed development (DQ <70) and none had normal DQ. 100% of B12 deficient children were anemic with 21 (70%) having severe anemia, 6(20%) having moderate and 3(10%) having mild anemia. 16 (53.33%) had macrocytic anemia (MCV >100fl), 10 (33.33%) had microcytic and 5 (16.66%) had normocytic anemia. 17 (56.66%) among B12 deficient children had associated thrombocytopenia (PC <1.5 lakh/cumm). All these parameters were similarly evaluated for folate deficient children as shown in Table 2.

DISCUSSION

In the present study, males out numbered 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. ¹⁵ We found vitamin B12 deficiency to be more prevalent than folic acid

deficiency. Over the last few years the cases of vit B12 deficiency are more commonly seen as compared to folic acid. In a study by Chhabra A et al in 2012, they concluded that nutritional megaloblastic anaemia occurs commonly in malnourished children; the commonest age is 3-18 months. These children are generally exclusively breast fed by mothers who are undernourished and have poor cobalamine levels. In a study by Yahikhomba T et al on assessment of iron, folate and vitamin B12 status children with SAM aged 6-60 months concluded that prevalence of vitamin B12 deficiency in SAM is much more than folate deficiency. The same common of the control of the case of the case

The decrease in folic acid deficiency could be due 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 fact 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 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.

Another interesting fact in our study was finding of significantly lower DQ scores in vitamin B12 deficient children. Vitamin B12 are associated with lower cognitive scores. Similar results were found by Agarwal N et al who concluded clear association of vitamin B12 deficiency with impaired neurodevelopmental status in children.

Folate deficient children in present study did not show significant abnormalities in the studied parameters (young age, lower SES, faulty feeding, severe anemia, macrocytic anemia and platelet counts) except for having near same percentage of children having underweight, stunting, late initiation of complementary feeding and delayed development (lower DQ scores) as that found in vitamin B12 deficient group (Table 2).

CONCLUSION

This analysis revealed a high prevalence of vitamin B12 deficiency among malnourished children aged 6 to 60 months. 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 development outcome.

Malnutrition in mother and preferential vegetarian diet with low vitamin B12 levels in mothers could be the associated factors. We did not find significant folate deficiency among these children.

Based on these findings, the study concludes that efforts should be directed to prevent cobalamin deficiency in pregnant and breastfeeding women predominantly on vegan diets and their infants which can be done by giving supplements, food fortification and dietary modification. Special attention should be given to malnourished children as they are already compromised in their intake as well as their in absorptive capacities which runs an unending vicious cycle.

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