Indian J Pediatr
DOI 10.1007/s12098-014-1600-7

ORIGINAL ARTICLE

Assessment of Iron, Folate and Vitamin B12 Status in Severe Acute Malnutrition

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Received: 4 March 2014 / Accepted: 30 September 2014

Abstract
Objectives To assess iron, folate and vitamin B12 status in hospitalized children aged between 6 mo to 5 y with severe acute malnutrition and its correlation with their clinico-epidemiological profile.
Methods The study was conducted on 50 children with severe acute malnutrition. Anthropometric measurements were taken to determine their nutritional status. The demographic profile and relevant information of individual patient were collected by using structured proforma and an informed consent was taken for enrolling the children into the study. Serum ferritin, folate and vitamin B12 was estimated using electrochemiluminiscence (ECL) method.
Results Seventy eight percent patients had weight/height (WT/HT) Z score<−3 standard deviation (3SD), 72 % with mid upper arm circumference (MUAC) <11.5 cm and 22 % of them had edematous malnutrition. Anemia was prevalent in 47(94 %) and there was significant correlation between WT/HT<−3SD and vitamin B 12 deficiency (p=0.015). Significantly higher number of these patients had vitamin B12 deficiency as compared to folate and iron deficiency (p=0.0006 each).
Conclusions Vitamin B12 deficiency was more common than iron and folate deficiencies in these patients with severe acute malnutrition.

Keywords Severe acute malnutrition · Ferritin · Folate · Vitamin B12

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Published online: 24 October 2014

Introduction

Severe acute malnutrition (SAM), still has a high prevalence, especially in South-East Asia. Globally, there are estimated 20 million children suffering from SAM; less than 2 million received treatment in 2011, and one million die each year with SAM [1]. In 2005–2006, among all the children under 5y of age 48 % were stunted, 43 % were underweight and 20 % were wasted [2].

The prevalence of anemia is reported to be high in children with SAM and iron deficiency anemia was found to be the commonest [3–5]. There are limited data on the status of hematopoietic factors in patients with severe acute malnutrition. Hence, this cross sectional study was conducted with the primary objective to assess the serum ferritin, folate and vitamin B12 concentrations in these children. Secondary objective was to correlate the hematopoietic factor status to the clinico-epidemiological profile of these patients.

Material and Methods

It was a hospital based cross sectional study on 50 children with severe acute malnutrition, aged 6 mo to 5 y, admitted in Bal Chikitsalaya, RNT Medical College, Udaipur (Rajasthan). WHO criteria was used to define severe acute malnutrition [6]. Those children who had organic cause of malnutrition, were critically sick or were already on hematinics before admission were excluded. Detailed history of these patients including personal profile, presenting complaints, feeding, immunization, development, socio-demographic details of their parents, anthropometric measurements and systemic examination were recorded on a proforma; and frequencies of various co-morbid conditions in study population were assessed.

Two ml of peripheral venous blood sample was taken in an EDTA vial for determination of complete blood count, 2 ml in

plain vial for C reactive protein (CRP) and 3 ml in another plain vial for serum ferritin, folate and vitamin B12 estimation.

Serum ferritin, folate and vitamin B12 were estimated by electrochemiluminiscence (ECL) method using VIT B12 600, FOL III 618 and FERRITIN 381 ELECSYS kits for COBASe411 analyzer, Roche diagnostics GmBH Germany distributed by Roche diagnostics GmBH, Sandhofer Strasse 116 Manheim. Iron deficiency was labeled when serum ferritin concentration was<12 ng/ml, or <30 ng/ml if the CRP was positive [7, 8], folate concentration<10 nmol/L [9] and serum vitamin B12 concentration<150 pmol/L (203 pg/ml) [9].

A written informed consent was taken from either of the parents. The protocol was reviewed and approved by the clearance from Institutional Ethics Committee.

Statistical analyses were performed using SPSS for Windows, version 16.0. Karl Pearson coefficient has been used for studying the correlation. Association of malnutrition with hematopoietic factor deficiency was found out by Chi-square test and Yate's correction has been applied for frequencies less than five. A '*P*' value of less than 0.05 was considered significant.

Results

Fifty percent of the patients were in the aged group 6–12 mo and in majority (88 %) of them, no complementary feeding was started. Anemia was present in 47 (94 %) patients of which 8 % had mild (Hb 10–10.9 g/L), 40 % moderate (Hb 7–9.9 g/L) and 46 % were severely (Hb<7 g/L) anemic [10]. Sixteen (32 %) children had pneumonia, 14(28 %) had diarrhea and only 4 (8) and 3(6 %) had malaria and nutritional tremor syndrome (NTS) respectively (Table 1). There was significant correlation between WT/HT<−3SD and vitamin B12 deficiency (p=0.015). Significantly higher number of these patients had vitamin B12 deficiency (34 %) as compared to folate and ferritin (iron) deficiency (6 % each) (p=0.0006 each) (Table 2).

Table 1 Characteristics of the study children

Category	Number (%)
Sex	
Male	29(58)
Female	21(42)
Age (mo)	
6–12	25(50)
13–24	13(26)
25–60	12(24)
Birth order	
1st	14(28)
2nd	14(28)
3rd	9(18)
4th or more	13(26)
Immunization (EPI)	
Complete	9(18)
Incomplete	22(44)
Unimmunized	19(38)
Development	
Normal	2(4)
Delayed	47(94)
Regressed	1(2)
Socioeconomic	
Upper middle	1(2)
Lower middle	7(14)
Upper lower	39(78)
Lower lower	3(6)
Caste	
ST	44(88)
SC	3(6)
OBC	1(2)
GEN	2(4)
Feeding pattern	
EBF	25(50)
PBF	16(32)
M&CF	9(18)
Clinical findings	
WT/HT<−3SD	39(78)
MUAC<11.5 cm	36(72)
Edematous	11(22)
Co-morbidities	
Anemia	47(94)
Pneumonia	16(32)
Diarrhea	14(28)
Malaria	4(8)
NTS	3(6)
Others	4(8)

EBF Exclusive breastfeeding; *PBF* Predominantly breastfeeding; *M*&CF Milk and complementary feeding; *MUAC* Mid upper arm circumference; *WT/HT* Weight by height; *3SD* 3 standard deviations; *NTS* Nutritional Tremor Syndrome

Discussion

To the best of authors' knowledge and thorough web search this is the first study to assess the status of serum ferritin and serum folate in children with SAM. In the index study only 20 (40 %) patients had micronutrient deficiencies whereas anemia was highly prevalent (94 %). This could be due to anemia of chronic diseases or a false impression of low prevalence of iron deficiency anemia with high values of serum ferritin, it being an acute phase reactant [11]. Other conditions like worm infestation and protein energy malnutrition may also be the reason for the high prevalence of anemia [12]. The high prevalence of anemia is reported by Thakur et al. (moderate to severe anemia in 81.1 %) [13], Kumar et al. (88.5 %) [3]

Table 2 Differences in baseline variables by serum hematopoietic factor concentrations in the study population

Characteristics	Serum ferritin < 12 ng/ml (*n*=3)	Serum folate < 10 nmol/L (*n*=3)	Serum vitamin B12 < 203 ng/ml (*n*=17)
Age (mo)			
06–12 (*n*=25)	1	1	8
13–24 (*n*=13)	1 (0.687)	1 (0.687)	5 (0.657)
25–60 (*n*=12)	1	1	4
Sex			
Male (*n*=29)	3 (0.248)	2 (1.000)	9 (1.000)
Female (*n*=21)	0	1	8
Feeding patterns			
EBF (*n*=25)	2	1	9
PBF (*n*=16)	1 (0.678)	1 (0.687)	5 (0.324)
M&CF (*n*=9)	0	1	3
Edema			
Edematous (*n*=11)	1 (1.000)	2 (1.000)	5 (0.089)
Non-edematous (*n*=39)	2	1	12
MUAC			
<11.5 cm (*n*=36)	3 (0.248)	3 (0.248)	13 (0.052)
>11.5 cm (*n*=14)	0	0	4
WT/HT			
<−3SD (*n*=39)	3 (0.248)	3 (0.248)	14 (0.015)
>−3SD (*n*=11)	0	0	3
Anemia			
Normal Hb (*n*=3)	0	0	2
Mild (*n*=4)	1 (0.953)	1 (0.953)	0 (0.052)
Moderate(*n*=20)	1	1	7
Severe (*n*=23)	1	1	8
Serum ferritin			
<12 ng/ml (*n*=3)		1 (1.000)	1 (0.0006)
>12 ng/ml (*n*=47)		2	16
Serum folate			
<10 nmol/L (*n*=3)	1 (1.000)		1 (0.0006)
>10 nmol/L (*n*=47)	2		16
Serum vitamin B12			
<203 ng/ml (*n*=17)	1 (1.000)	1 (1.000)	
>203 ng/ml (*n*=33)	2	2	

EBF Exclusive breastfeeding; *PBF* Predominantly breastfeeding; *M*&CF Milk and complementary feeding; *MUAC* Mid upper arm circumference; *WT/HT* Weight by height; *3SD* 3 standard deviations. Figures in parenthesis represent *P* values

and RCH-2 (96.78 % of under-nourished children) [4]. In the earlier studies [5] on hematopoietic micronutrient levels in anemic children, iron deficiency was found to be the commonest whereas in the index study on SAM patients, vitamin B12 deficiency was more common (34 %) than ferritin and folate (6 % each). Only one patient had combined folate and vitamin B12 deficiency. Only 8.8 % CRP negative patients had low serum ferritin whereas none of the CRP positive patients had serum ferritin below 30 ng/ml. This could be due to presence of infection in these patients and routine iron folic acid supplementation to the pregnant and lactating mothers, whereas higher vitamin B12 deficiency rate could be due to low maternal vitamin B12 levels in predominantly vegetarian community where no vitamin B12 supplementation is routinely given. Vitamin B12 deficiency is well recognized in exclusively breastfed infants of vitamin B12 deficient mothers [14]. Concentrations of vitamin B12 in breast milk reflect maternal vitamin B12 stores [15], and maternal vitamin B12 stores are depleted in up to one-third of rural Indian women [16]. A study in rural Karnataka by Pasricha et al. also found that concentrations of ferritin and vitamin B12 were decreased in toddlers who continued to receive breast milk [17]. Folate concentrations in breast milk are generally high [18] and independent of maternal stores [19] thus, prolonged breastfeeding in most of the index patients might be protective from folate deficiency. The adverse neurological outcome in the form of delayed and regression of milestones in these patients can be attributed to vitamin B12 deficiency [20].

Kumar et al. also found that 14.4 % of the SAM patients were serum vitamin B12 deficient. A study of about 2482 children aged 6–30 mo in New Delhi reported vitamin B12 deficiency in 28 % and folate deficiency in 15 % of children [21]. An earlier study of 100 anemic children who lived in a Delhi slum showed that 14.4 % of children had vitamin B12 deficiency alone, 22.2 % of children had combined vitamin B12 and iron deficiency, and 2.2 % of children had folate deficiency [22]. In 51 urban toddlers in Pune, the prevalence of vitamin B12 deficiency was 14 % [23]. Chandra et al. also documented 20 % folate deficiency and 32 % serum vitamin B12 deficiency in children [24].

The results of the index study should be considered within its strengths and limitations. The measurement of holotranscobalamin and metabolites such as homocysteine and methylmalonic acid are more sensitive indicators than serum vitamin B12. Pre-analytic hemolysis of blood samples might also be a factor for higher folate values. The measurement of breast milk micronutrient contents might have also strengthened the results. Absence of a comparative group is also another setback of the study. Finally, the authors recruited only a small sample size to understand the prevalence and determinants of micronutrient deficiency in this group of children.

Conclusions

In conclusion, serum vitamin B12 deficiency was more common than deficiencies of iron and folate in these SAM patients. The index findings provide a framework for the development of strategies to improve the micronutrient status, mainly that of vitamin B12 in this specific population and to disseminate knowledge regarding timely introduction of complementary feeding. In national nutritional anemia prophylaxis program, vitamin B12 supplementation should also be given along with iron and folic acid to prevent hematological as well as non hematological manifestations of vitamin B12 deficiency.

Acknowledgments The authors acknowledge the kind help from the HOD, department of Biochemistry.

Conflict of Interest None.

Source of Funding None.

References

1. Report on the IAEA technical meeting on ‘severe acute and moderate malnutrition in South East Asia’ (jointly with IMTF), 27–29 May 2013, Bangkok, Thailand, p. 1.
2. National Family Health Survey 3, 2005–2006. Mumbai India: International Institute of Population Science; 2006. p. 269.
3. Kumar R, Singh J, Joshi K, Singh HP, Bijesh S. Co-morbidities in hospitalized children with severe acute malnutrition in Rewa district. Indian Pediatr. 2014;51:125–7.
4. Nutritional status of children and prevalence of anemia among children, adolescent girls and pregnant women. District level household survey on reproductive and child health 2002–04. p. 27.
5. Ejaz MS, Latif N. Stunting and micronutrient deficiencies in malnourished children. J Pak Med Assoc. 2010;60:543–7.
6. WHO-country office for India, NRHM. Facility based care of severe acute malnutrition. March 2011.
7. WHO/UNICEF/UNU. Iron deficiency anaemia: assessment, prevention, and control. A guide for programme managers. Geneva, Switzerland: World Health Organization; 2001.
8. WHO; CDC. Assessing the iron status of populations: including literature reviews: report of a Joint World Health Organization/ Centers for Disease Control and Prevention Technical Consultation on the Assessment of Iron Status at the Population Level. 2nd ed. Geneva, Switzerland: World Health Organization & Centers for Disease Control and Prevention; 2004.
9. De Benoist B. Conclusions of a WHO Technical Consultation on folate and vitamin B12 deficiencies. Food Nutr Bull. 2008;29:S238–44.
10. http://www.who.int/vmnis/indicators/haemoglobin.pdf page 3.
11. http://www.who.int/vmnis/indicators/serum_ferritin.pdf page 1.
12. Alderman H, Shekar M. Nelson textbook of paediatrics. 19th ed. Chapter 43, Nutrition, food security, and health. p. 172.
13. Thakur N, Chandra J, Pemde H, Singh V. Anemia in severe acute malnutrition. Nutrition. 2014;30:440–2.
14. Allen LH. Vitamin B12 metabolism and status during pregnancy, lactation and infancy. Adv Exp Med Biol. 1994;352:173–86.
15. Allen LH. Multiple micronutrients in pregnancy and lactation: an overview. Am J Clin Nutr. 2005;81:1206S–12S.
16. Menon KC, Skeaff SA, Thomson CD, Gray AR, Ferguson EL, Zodpey S, et al. Concurrent micronutrient deficiencies are prevalent in nonpregnant rural and tribal women from central India. Nutrition. 2011;27:496–502.
17. Pasricha SR, Shet AS, Black JF, Sudarshan H, Prashanth NS, Biggs BA. Vitamin B-12, folate, iron, and vitamin A concentrations in rural Indian children are associated with continued breastfeeding, complementary diet, and maternal nutrition. Am J Clin Nutr. 2011;94:1358–70.
18. Mackey AD, Picciano MF. Maternal folate status during extended lactation and the effect of supplemental folic acid. Am J Clin Nutr. 1999;69:285–92.
19. Allen LH. B vitamins: proposed fortification levels for complementary foods for young children. J Nutr. 2003;133:3000S–7S.
20. Black MM. Effects of vitamin B12 and folate deficiency on brain development in children. Food Nutr Bull. 2008;29:S126–31.
21. Taneja S, Bhandari N, Strand TA, Sommerfelt H, Refsum H, Ueland PM, et al. Cobalamin and folate status in infants and young children in a low-to-middle income community in India. Am J Clin Nutr. 2007;86:1302–9.
22. Gomber S, Kumar S, Rusia U, Gupta P, Agarwal KN, Sharma S. Prevalence & etiology of nutritional anaemias in early childhood in an urban slum. Indian J Med Res. 1998;107:269–73.
23. Hanumante NM, Wadia RS, Deshpande SS, Sanwalka NJ, Vaidya MV, Khadilkar AV. Vitamin B12 and homocysteine status in asymptomatic Indian toddlers. Indian J Pediatr. 2008;75:751–3.
24. Chandra J, Jain V, Narayan S, Sharma S, Singh V, Kapoor AK, et al. Folate and cobalamin deficiency in megaloblastic anemia in children. Indian Pediatr. 2002;39:453–7.