Journal of Pediatric Neurology & Medicine

Agarwal N, et al.,, J Pediatr Neurol Med 2016, 1:1
DOI: 10.4172/2472-100x.1000103

Research Article OMICS International

Epidemiology and Neurodevelopmental Correlates of Cobalamin Deficiency in Hospitalized North Indian Infants

Neha Agarwal[1], Chandrakanta[1], S Koonwar[1], AA Mahdi[2] and Rashmi Kumar[1*]

[1]*Departments of Pediatrics, King George's Medical University, Lucknow, India*

[2]*Departments of Biochemistry, King George's Medical University, Lucknow, India*

[*]**Corresponding author:** Rashmi Kumar, Department of Pediatrics, King George's Medical College, Lucknow, India, 226024, Tel: 9415408777; E-mail: rashmik2005@gmail.com

Received date: Nov 25, 2015; **Accepted date:** Feb 01, 2016; **Published date:** Feb 08, 2016

Abstract

Vitamin B_{12} deficiency has been associated with neurodevelopmental disorders in infants. Role of maternal and infant diet and other epidemiological features have not been reported from India.

Objective: To compute the prevalence of vitamin B12 deficiency in hospitalized children 2 months to 2 years of age and compare demographic, clinical, dietary and developmental status between those found deficient and sufficient.

Methods: The first 3 children aged 2 months to 2 years hospitalized to the Pediatric Medicine wards of King George's Medical University Hospital, Lucknow on a predecided weekday were enrolled for study and subjected to a proforma driven work up. Those with history of vitamin supplements were excluded. Vitamin B12 and folate levels were measured by chemiluminiscence method. Vitamin B12 cut off value below 200 pg/ml and folic acid cut off value of <3 ng/ml were considered deficient. Neurodevelopmental status was assessed by Vineland Social Maturity Scale. Demographic data, dietary history of mother and child, anthropometry, clinical features and neurodevelopmental status were compared between the 2 groups.

Results: A total of 91 children [mean age 9.64+/- 4.42 months; 57.1% male] were enrolled, of which 17 [18.7%; 95% CI 11.3-28.2] were vitamin B12 deficient. No child was folic acid deficient. Vitamin B12 deficient children were significantly more likely to belong to lower socioeconomic status, be exclusively breast fed infants of vegetarian mothers with higher mean corpuscular volume and mean corpuscular hemoglobin concentration but lower mean platelet count. They also had higher odds of having a developmental quotient [DQ]<70 [OR=7.8; 95% CI 2.4-24.8; p=0.000] and significantly lower mean DQ [p=0.018].

Conclusion: Clear association of vitamin B_{12} deficiency with maternal and infant diet and impaired neurodevelopmental status was found which has important implications for millions of children in this country.

Keywords: VitaminB_{12} deficiency; Cobalamin; Epidemiology; Neurodevelopmental status; Folate deficiency; Maternal diet

Introduction

Vitamin B12 is a water soluble vitamin which is found as cobalamin in food. This essential nutrient is present only in animal-derived foods, such as meat, fish, eggs and milk. Nutritional deficiency is therefore common in people having strict vegetarian diets. Other causes of B12 deficiency are pernicious anemia [deficiency of intrinsic factor], selective B12 malabsorption, gastric or distal ileal surgical procedures and diphyllobothrium latum infection [1,2]. In infants, the cause of cobalamin deficiency are generally low cobalamine level in mother due to any of the above causes, leading to low levels in breast milk. Babies who are exclusively or predominantly breast fed for long periods are more likely to become deficient.

Cobalamin has a role in two enzymatic processes in mammalian cells - the methionine synthase reaction and methylmalonyl CoA mutase reaction. In the former, homocysteine is converted to methionine allowing for the "recycling" of 5-methyl-tetrahydrofolate to N5,10 methylene- tetrahydrofolate which is needed for DNA formation. Concurrently, homocysteine accumulates while methionine decreases, leading to a decrease in S-adenosyl methionine. Decreased methionine and S-adenosyl methionine may limit many methylation reactions including those involving DNA and myelin basic protein. In the methyl malonyl CoA mutase reaction, methyl malonyl CoA, derived from propionic acid, is converted to succinyl CoA. Thus, vitamin B12 deficiency results in accumulation of methyl malonic acid.

Classically, severe Vitamin B12 deficiency was known to cause megaloblastic anemia. However, it is also recognized to be a cause of neurological disorders and dementia in the elderly [3]. The mechanism of these effects on the nervous system poorly understood, but cobalamine is a necessary cofactor for synthesis of RNA and DNA. Severe vitamin B12 deficiency manifests as diffuse, uneven, degeneration of white matter in the brain, spinal cord, and peripheral nerves. Poor cobalamine status leads to deficiency of S-adenosyl methionine and reduced S-adenosyl methionine-dependent

transmethylation reactions could affect myelination of neurons and levels of neurotransmitters in specific brain areas [4,5].

Jadhav et al. published the first report of nutritional Vitamin B_{12} deficiency in early life describing a syndrome of apathy, developmental regression, involuntary movements and alteration in skin pigmentation that manifested in infants. The babies were well till 6-12 months of age after which they failed to thrive, became lethargic, hypotonic and showed developmental regression with or without involuntary movements [6]. Following this, over the last four decades, there have been many case reports from other countries, of neurodevelopmental delay, regression and brain atrophy in infants found to be severely vitamin B12 deficient [7-16]. These cases were breast fed babies whose mothers had severe vitamin B12 deficiency either secondary to strict vegetarian or 'vegan' diets, pernicious anemia or gastrointestinal surgical procedures. Apart from this there are also case series of vitamin B12 deficiency in association with seizures, neuropathy, ataxia and West syndrome in infancy [17,18].

Large sections of the Indian population have a lacto-vegetarian diet in which milk but not eggs and meat are consumed. However, due to poverty and high cost of these foods, women of lower socioeconomic status, even if omnivorous and lactating, are unlikely to consume milk or meat frequently or in significant amounts. So this is a 'near-vegetarianism' imposed by poverty [19]. Cobalamin and folate status were found to predict mental development scores in north Indian children [20]. Prevalence of vitamin B12 deficiency in Guatemalan infants was predicted by maternal vitamin B12 deficiency and infant diet, but there is no similar data from India [21]. Given the high proportion of the Indian population having vitamin B12 deficient diets, this micronutrient deficiency could well emerge as an important preventable cause of neurodevelopmental disorders in Indian infants. It was therefore proposed to study the prevalence, epidemiology and risk factors for vitamin B12 deficiency in hospitalized infants in northern India, and association with neurodevelopmental disorders.

Patients and Methods

This cross sectional study was conducted in the pediatric wards of King George's Medical University Hospital, Lucknow, in northern India between September 2014 and August 2015. This is a state run teaching hospital which caters to the poor and seriously sick population from Lucknow and surrounding districts of the north Indian state of Uttar Pradesh. The first 3 infants between the ages of 2 months and 2 years hospitalized on one predecided week day were enrolled for study. Those who had received any vitamin supplements within the previous 2 months were excluded. Enrolled children underwent a detailed work up according to predesigned data collection form. The variables noted included demographic data such as family characteristics such as rural or urban residence, parent education and socio-economic status, anthropometric data, clinical data such as detailed developmental history, dietary history of baby as well as mother, besides a full systemic and neurologic examination. Socioeconomic status was assessed by the modified Kuppuswamy Scale [22]. Anthropometry was described according to the WHO MGRS Scale [23]. In addition, developmental assessment was done by Vineland Social Maturity Scale [VSMS] – [Malin's adaptation (Malin)] and developmental age and quotient were computed. Laboratory variables were complete blood counts measured by automated coulter counter, serum vitamin B_{12} and folate levels [24]. The levels of vitamin B12 and folic acid were measured by chemiluminiscence method [25]. Vitamin B12 level less than 200 pg/dl and folate level less than 3 ng/ml were taken as deficient [26]. Prevalence of Vitamin B_{12} and folate deficiency were computed. The final diagnosis of the child was noted. Demographic, anthropometric, laboratory and neurodevelopmental features were compared between vitamin B_{12} deficient and sufficient children by univariate analysis, using Student's 't' test for continuous variables and Chi square test for categorical variables. Epi–info software was used for analysis. .

Ethical Approval for the study was obtained from the Ethics Committee of King George's Medical University, Lucknow. Informed consent was taken from parent of the child. Results of vitamin B_{12} assays were communicated to the treating team so that those found deficient could be appropriately treated.

Results

Over the study period a total of 91 children were enrolled according to the inclusion and exclusion criteria outlined. The diagnoses in the enrolled children are shown in Table 1a and Table 1b. Table 2 describes the vitamin B12 and folate levels in hospitalized infants. No infant was found to be folate deficient. Prevalence of vitamin B_{12} deficiency was 18.7% [95% CI 11.3-28.2] and was highest in the age group between 9 and 12 months [8/23 or 34.8%]. Table 3 compares the demographic, anthropometric and neurodevelopmental features between vitamin B_{12} deficient and sufficient children. Significantly lower socioeconomic status exclusive breast feeding and maternal vegetarianism were noted in the vitamin B12 deficient group. Mean DQ was significantly lower in vitamin B12 deficient children and vitamin B_{12} deficient children had high odds of having DQ less than 70 [Odds ratio 7.8; 95% CI [2.4-24.8]]. Table 3 compares the hematologic and biochemical parameters in these two groups. Significant differences were found between mean platelet counts [lower in vitamin B12 deficient group], mean corpuscular volume, mean corpuscular hemoglobin and mean corpuscular hemoglobin concentration [higher in vitamin B12 deficient group].

Discussion

Cobalamin and folate status are well proven to be associated with mental development in children [20]. Vegetarianism, whether imposed by self or by poverty [near vegetarianism, as happens in large parts of the developing world] is associated with low vitamin B12 levels [19]. Macrobiotic diets consumed by nursing mothers in the developed countries is shown to result in vitamin B12 deficient state in their infants[7-11] Vitamin B12 deficiency in Guatemalan mothers was associated with low B12 status in their infants [21]. In India also, given the high proportion of vegetarianism, poverty and lack of access to animal foods, it may be anticipated that such prevalence would be high. Neurodevelopmental effects of vitamin B12 deficiency may be long lasting or even permanent [19,27]. Vitamin B12 deficiency could be as an important easily preventable cause of developmental delay and regression in Indian infants and therefore warrants study. We therefore set out to study prevalence, risk factors and correlates of vitamin B_{12} deficiency in Indian infants. Our study confirms that maternal vegetarianism and exclusive breast feeding in our population are associated with low vitamin B_{12} status in infants with adverse developmental effects.

Strengths of the study were the standard inclusion and exclusion criteria used and standardized work up followed. The inclusion and exclusion criteria used ensured an unbiased selection of subjects. Vitamin B_{12} level was tested by the standard method of

chemiluminiscence and automated [Coulter counter] bloods counts were done in all patients. A standard cut off for vitamin B12 of 200 pg/ml was used. The person doing the developmental assessments did not know the vitamin B12 levels.

There were some limitations of our study. Firstly, we only studied prevalence in a hospital based population. A community based study would yield the true picture of prevalence. However, community based prevalence would more or less only apply to the particular community studied and it would be very difficult to convince parents to let the field team draw a blood sample from their infant. Hospital based studies would give some idea of prevalence in the community also. Secondly, parameters like methymalonic acid in blood or urine and serum homocysteine levels which are considered supportive evidence of vitamin B12 deficiency were not part of this study. They would have lent more weight to the study had they been done. Such metabolite testing could have identified many more asymptomatic vitamin B12 deficient children [19]. Vitamin B12 and folic acid levels could not be done in mothers. Since there were differences in socioeconomic status the lower DQ may be explained to some extent by this. Cobalamin deficiency is known to be associated with apathy and mental defects. Bayley Scale of Infant Development could not be used because it involves testing the infants, which could not be done as many of the children were admitted due to acute illness. Vineland Social Maturity Scale involves only asking the caregiver about the child's abilities. So it could be used in such children. Finally, since cross sectional design was used, time relationships could not be defined and at best we can say that an association between vitamin B12 deficiency and neurodevelopmental problems was found.

Prevalence of vitamin B12 deficiency was found to be 18.7% which is lower than found in an earlier community based study in 12-18 month old north Indian children [20]. Prevalence in the present study was highest in the age group between 9 and 12 months. Vitamin B12 deficiency was found to be significantly higher in babies of lower socioeconomic status families, born to vegetarian mothers feeding their babies exclusively on breast babies beyond 6 months of age. We used the modified Kuppuswamy Scale of socioeconomic status [SES] – a widely used scale in India based on education, occupation and income of the family head. In Table 2, it is seen that the lowest SES are more likely to be vitamin B12 deficient, where as the middle classes were vitamin B12 sufficient and there were no upper class patients seen. Our study thus corroborates earlier work which had shown that diet is a strong and sensitive determinant of vitamin B12 status and intake of animal foods or supplements promptly corrects the deficiency [28]. Anthropometry was not significantly different between vitamin B12 deficient and sufficient groups. A picture of anemia and pigmentary disturbances, but adequate general nutrition is known to occur with vitamin B12 deficiency [6,19]. Recently, Strand et al., have shown that improved vitamin B12 status led to increased mean weight for age z scores in a double blind randomized placebo controlled trial, however [29].

Hematologic parameters showed no difference in prevalence of anemia, mean hemoglobin levels or mean total leucocyte or differential leucocyte counts but lower mean platelet count and higher mean corpuscular volume, mean corpuscular hemoglobin and hemoglobin concentrations. The latter are suggestive of megaloblastic anemia which is known to be a feature of vitamin B12 deficiency.

Another interesting finding in our study was that folate deficiency was not found in even a single infant. This could represent a type 2 error as sample size was small. Alternatively, the folate trap phenomenon may cause falsely high folate levels [20], obscuring the assessment of folate status in these subjects. Both folate and vitamin B12 are associated with lower cognitive scores but folate is present in plant foods and in vegetarian diets while vitamin B12 is not. Breast milk is an important source of folate and this fact may account for the positive effect of breast feeding on cognition that has been observed in several observational studies [20,30]. Conversely, vitamin B12 status has been shown to be poorer in breast fed babies [20]. Breast feeding therefore can have opposite effects on status of different micronutrients in infants but the sum total effect on cognition may be positive.

This small study therefore reiterates that vitamin B12 deficiency is not uncommon in Indian infants. It is strongly related to maternal and infant diet and has a clear association with adverse developmental consequences. This deficiency is eminently preventable by simple supplementation, food fortification or dietary modification. These facts have implications for millions of children in the developing world.

System involved	Diagnosis	Total no. of patients
Respiratory system	Pneumonia	20
	Bronchiolitis	3
	Pleural effusion	5
	Pulmonary tuberculosis	2
	Bronchial asthma	3
Cardiovascular system	Congenital heart disease with congestive heart failure	4
	Congenital heart disease with total anomalous pulmonary venous connection	2
	Dilated cardiomyopathy	2
	Myocarditis	2
Central nervous system	Acute encephalitis syndrome	4
	Bacterial meningitis	4
	Right sided hemiparesis	1
Renal system	Nephrotic syndrome	4
Hematological system	Acute lymphoblastic leukemia	3
	Testicular malignancy with intraabdominal tumor with paraparesis	1
	Hemophagocytic syndrome	1
	Severe anemia cause under evaluation	3
Hepatobiliary system	Chronic hepatitis	2
	Extrahepatic portal venous obstruction	2
	Acute hepatitis	2
	Follow through case of hepatic encephalopathy	1
	Infantile cholestasis	3

Others	Severe acute malnutrition	5
	Cellulitis	3
	Pyrexia of unknown origin	3
	Fever with rash under evaluation	4
	Rickettsia	2
	Post measles severe acute malnutrition with pulmonary tuberculosis	1
Total (N)		91

Table 1a: Diagnoses of enrolled patients [N=91].

	Highest level	Lowest level	Median	Mean + SD	Prevalence of deficiency [%; 95% CI]
Vitamin B12* [pg/ml]	2000	30	340	409.79+315.98	17 [18.7; 95% CI 11.3-28.2]*
Folic acid ** [ng/ml]	21.7	4.5	15	14.69+4.94	0**

Table 1b: Vitamin B12 and folate levels in the study population.

Demographic characteristics	n [%]	Vitamin B_{12} status		OR [95 % CI]	P value
		Deficient [n=17]	Sufficient [n=74]		
Mean age [in months]		9.64 ± 4.42	10.72 ± 6.53	_	0.518[1]
Males	52	8 [47]	44 [59]	0.6 [0.2-1.74]	0.351[2]
Rural	73	16 [94.1]	57 [77]	4.7 [0.5-38.6]	0.678[2]
Socioeconomic status*	0	0 [0.0]	0 [0.0]	_	0.001[2]
Upper	8	0 [0.0]	8 [10.0]		
Upper middle	63	2 [11.7]	61 [82.4]		
Lower middle	13	11 [64.7]	2 [2.7]		
Lower upper	7	4 [23.5]	3 [4]		
Lower lower					
Dietary history of baby					
Exclusive breast feeding	44	14 [82.3]	30 [40.5]	6.84 [1.63-33.06]	0.004
Exclusive breast feeding after 6 months of age	20	9/12 [75.0]	11/44 [25.0]	9.0 [1.75-52.2]	0.002
Diluted cow milk	3	0 [0.0]	3 [4.0]	-	
Undiluted cow milk	2	0 [0.0]	2 [2.7]	-	
Buffalo milk	5	0 [0.0]	5 [6.7]	-	
Formula feeding	18	3 [17.6]	15 [20.2]	0.84 [0.17-3.75]	
Complimentary feeding started and adequate	19	0 [0.0]	19 [25.6]	-	
Vegetarian mother	61	16 [94.1]	45 [60.8]	10.3 [1.2- 82.0]	0.008[2]
Mean weight for height ± SD		7.03 ± 2.4	6.66 ± 2.44	-	0.416[1]
Wasting	23	5 [29.4]	18 [24]	0.67 [0.22-2.5]	0.437[2]
Mean height for age + SD		67.77 ± 7.3	66.11 ± 7.2	-	0.175[1]
Stunting	16	3 [17.6]	13 [17]	1.0 [0.25 – 4.0]	0.617[FE][2]
DQ less than 70	25	11 [64.7]	14 [18.9]	7.8 [2.4-24.8]	0.000 [FE][2]
Mean DQ ± SD		64 ± 24.89	81.21 ± 25.83	-	0.018[1]

Table 2: Comparison of demographic and anthropometric features of vitamin B12 deficient and non deficient group. (*Fischer Exact test; 1-student 't' test; 2-χ^2 test; wasting- weight for height<3 SD; Stunting- height for age<3 SD).

Hematologic/ Biochemical parameter	Vitamin B12 status		P *
	Deficient	Sufficient	

[mean values]	[N=17]	[N=74]	
Hemoglobin [gm/dl]	8.62 ± 3.38	9.03 ± 2.59	0.588*

Total Leukocyte Count [per cubic mm] :	11123 ± 8890	13494 ± 6333	0.202*
Differential neutrophil count [%]:	52.29 ± 16.82	49.41 ± 16.93	0.528*
Platelets [per cubic mm]:	233000 ± 184330	369648 ± 195662	0.010*
Mean corpuscular volume [MCV in cubic micron]	92.41 ± 15.13	74.73 ± 8.20	0.000**
Mean corpuscular haemoglobin [MCH] in pg	27.76 ± 3.45	25.21 ± 4..06	0.018*
Mean corpuscular haemoglobin concentration	31.11 ± 3.71	28.58 ± 3.74	0.010*
Mean level of Folic acid in ng/ml	16.11 ± 4.41	14.33 ± 5.09	0.187

Table 3: Comparison of hematological parameters among Vitamin B_{12} deficient and sufficient (* student t test; **Kruskal-Wallis test).

References

1. Stabler SP (2013) Vitamin B12 deficiency. New England J Med 368: 2.
2. Smith J, Coman D (2014) Vitamin B12 defiency: an update for the general physician. Pediatrics and Therapeutics 4: 1.
3. Smith AD, Refsum H (2009) Vitamin B-12 and cognition in the elderly. Am J Clin Nutr 89: 707S-11S.
4. Black MM (2003) Micronutrient deficiencies and cognitive functioning. J Nutr 133: 3927S-3931S.
5. Dror DK, Allen LH (2008) Effect of vitamin B12 deficiency on neurodevelopment in infants: current knowledge and possible mechanisms. Nutr Rev 66: 250-255.
6. Jadhav M, Webb JK, Vaishnava S, Baker SJ (1962) Vitamin B12 deficiency in Indian infants. A clinical syndrome. Lancet 2: 903-907.
7. Sklar R (1986) Nutritional vitamin B12 deficiency in a breast-fed infant of a vegan-diet mother. Clin Pediatr (Phila) 25: 219-221.
8. Gambon RC, Lentze MJ, Rossi E (1986) Megaloblastic anaemia in one of monozygous twins breast fed by their vegetarian mother. Eur J Pediatr 145: 570-571.
9. Cheron G, Girot R, Zittoun J, Mouy R, Schmitz J, et al. (1989) [Severe megaloblastic anemia in 6-month-old girl breast-fed by a vegetarian mother]. Arch Fr Pediatr 46: 205-207.
10. Bar-Sella P, Rakover Y, Ratner D (1990) Vitamin B12 and folate levels in long-term vegans. Isr J Med Sci 26: 309-312.
11. Kühne T, Bubl R, Baumgartner R (1991) Maternal vegan diet causing a serious infantile neurological disorder due to vitamin B12 deficiency. Eur J Pediatr 150: 205-208.
12. Grattan-Smith PJ, Wilcken B, Procopis PG, Wise GA (1997) The neurological syndrome of infantile cobalamin deficiency: developmental regression and involuntary movements. Mov Disord 12: 39-46.
13. Lövblad K, Ramelli G, Remonda L, Nirkko AC, Ozdoba C, et al. (1997) Retardation of myelination due to dietary vitamin B12 deficiency: cranial MRI findings. Pediatr Radiol 27: 155-158.
14. Guez S, Chiarelli G, Menni F, Salera S, Principi N, et al. (2012) Severe vitamin B12 deficiency in an exclusively breastfed 5-month-old Italian infant born to a mother receiving multivitamin supplementation during pregnancy. BMC Pediatr 12: 85.
15. Renault F, Verstichel P, Ploussard JP, Costil J (1999) Neuropathy in two cobalamin-deficient breast-fed infants of vegetarian mothers. Muscle Nerve 22: 252-254.
16. Erol I, Alehan F, Gümüs A (2007) West syndrome in an infant with vitamin B12 deficiency in the absence of macrocytic anaemia. Dev Med Child Neurol 49: 774-776.
17. Incecik F, HergÃ¼ner MO, AltunbaÅŸak S, Leblebisatan G (2010) Neurologic findings of nutritional vitamin B12 deficiency in children. Turk J Pediatr 52: 17-21.
18. Taskasen M, Yaramis A, Katar S, Pirinccioglu G, Soker M (2011) Neurological presentations of nutritional vitamin B12 deficiency in 42 breastfed infants in southeast Turkey. Turk J Med Sci 41: 1091-96.
19. Antony AC (2003) Vegetarianism and vitamin B-12 (cobalamin) deficiency. Am J Clin Nutr 78: 3-6.
20. Strand TA, Taneja S, Ueland PM, Refsum H, Bahl R, et al. (2013) Cobalamin and folate status predicts mental development scores in North Indian children 12-18 mo of age. Am J Clin Nutr 97: 310-317.
21. Jones KM, Ramirez-Zea M, Zuleta C, Allen LH (2007) Prevalent vitamin B-12 deficiency in twelve-month-old Guatemalan infants is predicted by maternal B-12 deficiency and infant diet. J Nutr 137: 1307-1313.
22. Mohan Bairwa, Meena Rajput, Sandeep Sachdeva (2013) Modified Kuppuswamy's Socioeconomic Scale: Social Researcher Should Include Updated Income Criteria, 2012. Indian J Community Med. 38: 185–186.
23. http://www.who.int/childgrowth/standards/height_for_age/en
24. Malin AJ (1971) Indian Adaptation of the Vineland Social Maturity Scale. Lucknow, India: Indian Psychological Corp.
25. Oberley MJ, Yang DT (2013) Laboratory testing for cobalamin deficiency in megaloblastic anemia. Am J Hematol 88: 522-526.
26. Kapil U, Sareen N (2014) Prevalence of ferritin, folate and vitamin B12 deficiencies amongst children in 5-18 years of age in Delhi. Indian J Pediatr 81: 312.
27. Bhate V, Deshpande S, Bhat D, Joshi N, Ladkat R, et al. (2008) Vitamin B12 status of pregnant Indian women and cognitive function in their 9-year-old children. Food Nutr Bull 29: 249-254.
28. McLean ED, Allen LH, Neumann CG, Peerson JM, Siekmann JH, et al. (2007) Low plasma vitamin B-12 in Kenyan school children is highly prevalent and improved by supplemental animal source foods. J Nutr 137: 676-682.
29. Strand TA, Taneja S, Kumar T, Manger MS, Refsum H, et al. (2015) Vitamin B-12, folic acid, and growth in 6- to 30-month-old children: a randomized controlled trial. Pediatrics 135: e918-926.
30. Taneja S, Bhandari N, Strand TA, Sommerfelt H, Refsum H, et al. (2007) Cobalamin and folate status in infants and young children in a low-to-middle income community in India. Am J Clin Nutr 86: 1302-1309.