Indian Journal of Pediatrics
https://doi.org/10.1007/s12098-023-04909-x

ORIGINAL ARTICLE

Prevalence and Predictors of Vitamin B12 Deficiency in Children with Severe Acute Malnutrition, and its Association with Development

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Received: 12 June 2023 / Accepted: 16 October 2023

Abstract

Objectives To determine the proportion of children with severe acute malnutrition (SAM) having vitamin B12 deficiency, its clinical predictors, and its association with development.

Methods In this cross-sectional study, 100 children between 1 mo to 59 mo [mean (SD) age 17 (12.75) mo; 55 males], with diagnosis of SAM as per WHO criteria, were included. Serum vitamin B12, serum folate, and serum ferritin levels were measured by chemiluminescence immunometric assay method, while serum Homocysteine (Hcy) level was measured by enzymatic cycling method. Development assessment was done by Denver Development Screening Tool (DDST-II).

Results The mean (SD) serum vitamin B12 (cobalamin) levels were 296.52 (246.95) pg/mL; 45% children were vitamin B12 deficient (<203 pg/mL). Hyperhomocysteinemia (>14 µmol/L) was present in 39 (39%), and among these 69% (27/39) children had concomitant low serum vitamin B12 levels. Severe anemia and hypoproteinemia were significantly and independently associated with vitamin B12 deficiency [aOR (95% CI) 3.22 (1.13, 10) and 10 (1.66, 58.82), respectively]. Out of 45 children who were vitamin B12 deficient, 93%, 87%, 62% and 80% had gross motor, fine-motor, language and adaptive-cognitive delay, respectively. Vitamin B12 level was significantly associated (P <0.001) with developmental delay.

Conclusions There is a high prevalence of vitamin B12 deficiency in children with SAM, which is also associated with development delay across all domains (except language) in these children.

Keywords Vitamin B12 · Deficiency · Developmental delay · Predictors · Severe acute malnutrition · Children

Introduction

Childhood malnutrition, including severe acute malnutrition (SAM), is an important public health problem in low- and middle-income countries (LMICs). In India, as per the fifth National Family Health Survey (NFHS-5), 19.3% of under-five children were wasted and 7.7% had severe wasting [1]. Apart from increasing mortality risk, malnutrition also increases the risk of deficiency of various micronutrients due to lack of quality foods, inadequate intake and poor absorption.

Micronutrient deficiencies constitute important comorbidities in SAM, especially in infants and pre-school children. Iron, vitamin A, iodine, zinc, folate, vitamin B12 and vitamin D are micronutrients of public health importance in childhood and adolescence. According to Comprehensive National Nutrition Survey (CNNS)-2019, the prevalence of vitamin B12 deficiency (<203 pg/mL) was 14%, 17% and 31% among pre-school children, school- age children and adolescents, respectively [2]. Studies have documented high prevalence of vitamin B12 deficiency ranging from 29-57% in under-five children [3–5]. Apart from the hematological effects, vitamin B12 deficiency also results in restricted myelination and, depending on the area of the nervous system affected, the child can present with varied cognitive and intellectual problems, and delayed

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Published online: 16 November 2023

development [6–8]. Thus, it becomes imperative to assess the B12 levels for early diagnosis to avert serious hematological and non-hematological manifestations.

Limited literature is available regarding vitamin B12 deficiency in children with SAM, and majority of them have assessed the hematological effects only [9, 10]. To rationalize the treatment, there is also a need to determine clinical predictors associated with vitamin B12 deficiency in children with SAM. Therefore, current study was planned to evaluate the prevalence of vitamin B12 deficiency in children with SAM, its clinical predictors, and its association with child development.

Material and Methods

This was a cross-sectional study conducted in the Department of Pediatrics at a teaching hospital in Delhi, primarily catering to the children belonging to urban low-income families. An approval from the Institutional Ethics Committee–Human Research (IEC–HR) was obtained before the commencement of the study and written informed consent was taken from the caregiver(s) of children before enrolment. All children aged between 1-59 mo presenting to the outpatient department or emergency room of the hospital for any complaint between January, 2021 to April, 2022 were screened for presence of SAM as per WHO criteria [11]. Children with critical illness, cranio-vertebral malformations or known chronic systemic illnesses, those with a history of neonatal hypoxic-ischemic encephalopathy /intra-cranial hemorrhage/ meningitis/ head injury or any other acute event that could have influenced development status, and those who received vitamin B12 supplements or blood transfusion in preceding 3 wk were excluded.

Detailed relevant demographic and clinical history was documented in a predesigned performa. Socio-economic status was determined by using Modified Kuppuswamy scale [12]. Clinical examination findings and baseline anthropometric parameters (weight, length, mid-upper arm circumference and head circumference) were recorded as per standard techniques [13]. Z-scores were calculated using age- and sex- appropriate WHO standards using the WHO Anthro software [14, 15].

Besides the routine laboratory work-up, serum B12, serum folate, serum ferritin and homocysteine (Hcy) levels were also estimated. Serum B12, folate and ferritin levels were measured on fully automated analyser based upon chemiluminescence immunometric assay method (Access-2 Beckman Coulter analyser). Serum homocysteine was analysed by enzymatic cycling method on fully automated chemistry analyser (Beckman Coulter AU-680). Serum B12 <203 pg/mL, serum ferritin <12 ng/mL (for <5 y of age) and <15 ng/mL (for >5 y of age), and serum folate <4 ng/mL were considered deficient [2]. The normal range for serum homocysteine was considered as 6–14 µmol/L.

Developmental assessment was done using the Denver Developmental Screening Tool-II (DDST-II; Denver Developmental Materials, Inc.) which screens children's development based on performance and parent report items in four areas of functioning: fine motor, gross motor, personal-social, and language. DDST-II tool was administered by Postgraduate trainee who was trained for administering the tool under the guidance of a Child Development Specialist for one month before the commencement of enrolment. The tool was administered by the same investigator in all the participants.

All enrolled children were managed and discharged according to the facility-based guidelines for the management of children with SAM prescribed by the National Rural Health Mission, Ministry of Health and Family Welfare (India) 2013 [16]. In infants under 6 mo of age, frequent breastfeeding or expressed breast milk was given as early as possible for feeding. For non-breastfed infants, milk-based starter diet (75 kcal per 100 mL) was started. Therapeutic diets (starter and catch-up diets) were prepared as per the standard guidelines under supervision of trained dieticians in the hospital kitchen. F-75 starter diet (130 mL/kg/d) was fed every two hourly; and once child was stabilized, catch-up diet (100 kcal per 100 mL) was started at 150 mL/kg/d fed every four hourly. Children diagnosed with vitamin B12 deficiency were treated with intramuscular or intravenous methylcobalamin, 100 µg (50 µg in infants) daily for one week followed by alternate day for one week and then 500 µg weekly for one month.

In the study by Goyal et al., the prevalence of vitamin B12 deficiency in children with SAM was 37.5% [17]. To estimate this proportion with relative precision of 25% and 95% confidence level, a sample size of 91 children with SAM was calculated to be sufficient. Hundred children were enrolled to compensate for any losses of blood sample during processing and analysis.

Data was analyzed with IBM SPSS Statistics Ver.25. Continuous data were summarized as mean ± SD while categorical in number and percentage. For predictors of vitamin B12 deficiency, proportion (for categorical variable) and mean (SD) or median (IQR) were compared between children having B12 deficiency and those not having it, by univariate analysis using Chi-square test and odds ratios. Multiple logistic regression was performed using vitamin B12 deficiency as a dependent variable and factors with $P < 0.20$ on univariate analysis and factors which had a direct biological plausibility as independent variables. Development categories (Normal/ Suspect) were compared between B12-deficient and non-deficient children by chi-square tests/ fisher's exact test. P value <0.05 was considered statistically significant.

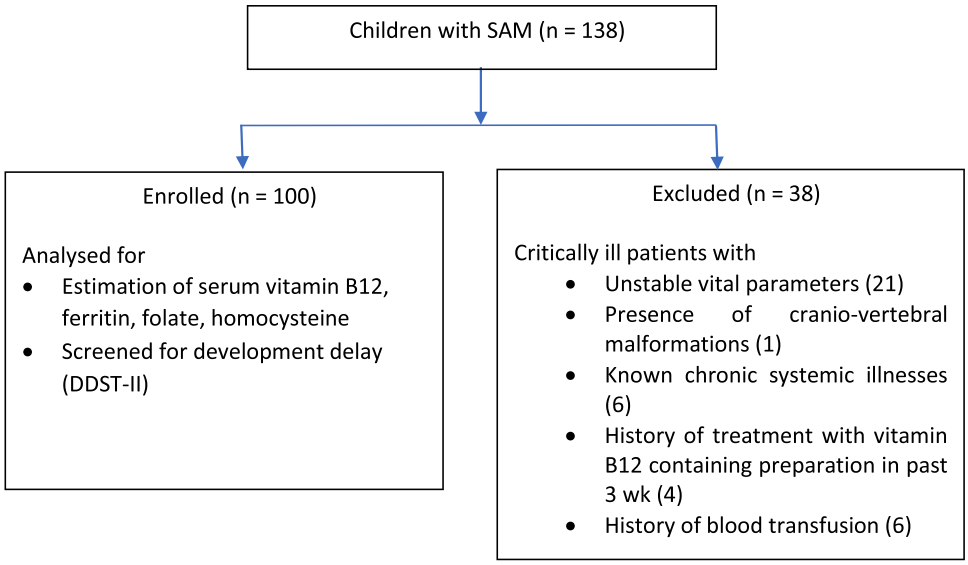

Fig. 1 Flow of the participants in the study. *DDST-II* Denver Developmental Screening Tool-II, *SAM* Severe acute malnutrition

Results

A total of 100 children (55 males, 45 females) aged 1 mo to 59 mo, presenting with SAM were included in the study (Fig. 1). The mean (SD) age of children was 17 (12.75) mo; nearly two-thirds of the participants were under the age of two years, including 41 (57%) infants. Table 1 presents the socio-demographic and anthropometric parameters of children with SAM. A large majority (87%) of the children had weight-for-height Z score (WHZ) <-3SD, whereas only about 52% met the criteria of a low mid upper arm circumference (MUAC <11.5 cm). Seventy-three children were stunted [height-for-age Z score (HAZ) <-2SD] and 36% had severe stunting. Five of the participants presented with bipedal edema (three had WHZ <- 3SD and two had MUAC <11.5 cm). Almost all of the participants were from

Table 1 Comparison of socio-demographic and anthropometric parameters between B12 deficient and non-deficient children with SAM (N = 100)

Parameter	B12 deficient (n = 45)	B12 non-deficient (n = 55)	*P*-value
Age (mo)	16.21 (12.9)	17.80 (12.8)	0.536
Age (<6 mo)[a]	7 (15.5)	11 (20)	0.565
Preterm (<37 wk)[a]	25 (55.5)	27 (49)	0.520
LBW (<2500 g)[a]	23 (51.5)	38 (69)	0.119
Low SES (Lower/ upper-lower)[a]	20 (44.4)	16 (29)	0.112
Mother diet (non-vegetarian)[a]	13 (28.8)	21 (38.1)	0.329
Calorie deficit (kcal/d)	40.06 (9.62)	44.51 (7.67)	0.012
Protein deficit (g/d)	7.93 (11.24)	12.18 (9.36)	0.498
Duration of EBF (mo)	4.45 (2.61)	4.45 (2.91)	0.998
Appropriate feeding practices[a, b]	9 (20)	10 (18.1)	0.818
WAZ	-4.00 (0.79)	-4.05 (0.98)	0.776
HAZ	-2.55 (1.03)	-2.64 (1.44)	0.718
WHZ	-3.71 (0.65)	-3.76 (0.70)	0.732
Head circumference (cm)	43.02 (3.27)	42.89 (3.19)	0.837
HCZ	-1.94 (1.11)	-2.39 (1.12)	0.050
MUAC (cm)	11.38 (0.78)	11.34 (0.68)	0.764

EBF Exclusive breastfeeding, *HAZ* Height-for-age Z score, *HC* Head circumference, *HCZ* Head circumference Z score, *LBW* Low birth weight, *MUAC* Mid upper arm circumference, *SES* Socio-economic status, *WAZ* Weight-for-age Z score, *WHZ* Weight-for-height Z score

All values in mean (SD) except:

[a]no. (%)

[b]Exclusive breastfeeding till 6 mo of age and optimal complementary feeding started at 6 mo of age

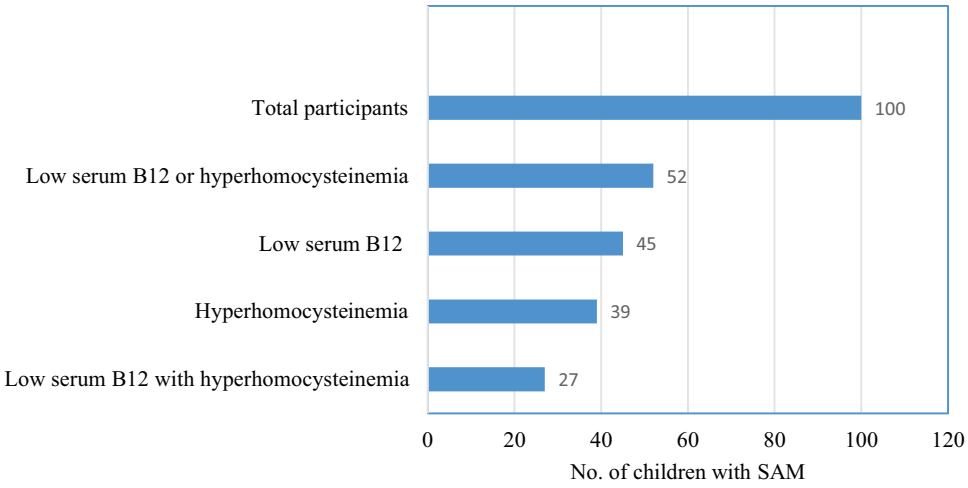

Fig. 2 Status of low serum B12 levels and hyperhomocysteinemia in enrolled children. *SAM* Severe acute malnutrition

lower or upper-lower socioeconomic background according to Modified Kuppuswamy scale. Approximately half of the participants were born at full-term (gestational age 37–41 wk), and 61% had low birth weight. Mean (SD) duration of exclusive breastfeeding was 4.4 (2.76) mo, exclusive breastfeeding till 6 mo of age and initiation of optimal complementary feeds were present only in 19% of the participants. Diarrhea was the most common presenting complaint in 49% followed by cough/ fast breathing in 38%.

Pallor was noticed in 81% children, among which 20 required blood transfusion. Clinical features of vitamin B12 deficiency, namely, hyperpigmentation, glossitis, angular cheilitis were present in 35%, 29%, and 37% children, respectively. Ninety-three children with SAM had anemia with mean (SD) hemoglobin level of 7.7 (2.14) g/dL. As defined by recommended WHO cut-offs of hemoglobin for age group 6–59 mo [18], 42%, 43% and 8% children had severe, moderate and mild anemia, respectively.

The serum cobalamin levels ranged from 31.5-1500 pg/mL with mean (SD) of vitamin B12 level was 296.52 (246.95) pg/mL. Of the 100 enrolled study participants, 45% had low serum vitamin B12 levels. Hyperhomocysteinemia (>14 µmol/L) was present in 39% children, among these 27 (69.2%) children had concomitant low serum B12 levels (Fig. 2). Five participants had isolated folate deficiency with hyperhomocysteinemia. The mean (SD) of serum folate levels was 11.72 (6.51) ng/mL. The mean (SD) of serum ferritin were 32.62 (41.78) µg/L. Out of 100 enrolled participants, 44% had low ferritin levels and 18% had concomitant B12 deficiency.

Analysis of clinical predictors of vitamin B12 deficiency in children with SAM is presented in Table 2. On univariate analysis, stunting, severe anemia, folate deficiency, hyperhomocysteinemia and hypoproteinemia had odds ratio >1 for vitamin B12 deficiency, but only severe anemia, hyperhomocysteinemia and hypoproteinemia were statistically significant (P <0.05). On multivariable logistic regression, the adjusted odds for vitamin B12 deficiency were significantly higher for severe anemia and hypoproteinemia.

On developmental assessment using DDST-II screening tool, out of 45 vitamin B12 deficient children with SAM,

Table 2 Assessment of clinical predictors of vitamin B12 deficiency in children with SAM (N = 100)

	B12 deficient (n = 45)	B12 non-deficient (n = 55)	OR (95% CI)	*P*-value	aOR (95% CI)
LBW (<2500 g)	23 (51)	38 (69)	0.48 (0.19, 1.21)	0.119	0.34 (0.1, 1.06)
Low SES	20 (44)	16 (29)	1.95 (0.85, 4.46)	0.112	2.85 (0.97, 8.33)
Microcephaly	8 (17.7)	17 (30.9)	0.48 (0.18, 1.25)	0.131	0.59 (0.17, 2.0)
Stunting	33 (73.3)	40 (72.7)	1.03 (0.42, 2.50)	0.305	
Severe anemia (Hb <7 g/dL)	26 (57.7)	15 (27.2)	3.64 (1.57, 8.43)	0.002	3.22 (1.13, 10)
Iron deficiency	18 (40.1)	26 (47.2)	0.67 (0.30, 1.51)	0.340	
Folate deficiency	5 (8.8)	5 (9.1)	1.25 (0.33, 4.62)	0.738	
Hyperhomocysteinemia	27 (60)	12 (21.8)	5.37 (2.24, 12.89)	<0.001	
Hypoproteinemia	10 (22.2)	2 (3.6)	7.57 (1.56, 36.6)	0.004	10 (1.66, 58.82)

All values in no. (%)

LBW Low birth weight, *SAM* Severe acute malnutrition, *SES* Socio-economic status

Table 3 Comparison of development status of B12 deficient and non-deficient children with SAM (N = 100)

Risk of development delay	B12 deficient (n = 45)	B12 non-deficient (n = 55)	*P*-value
Gross-motor	42 (93.3)	33 (60)	<0.001
Fine-motor	39 (86.6)	34 (61.8)	0.001
Language	28 (62.2)	31 (56.3)	0.764
Adaptive-cognitive	36 (80)	34 (61.8)	0.003
Overall (global developmental delay)	18 (40)	11 (20)	<0.001

All values in no. (%)

SAM Severe acute malnutrition

42 (93.3%), 39 (86.6%), 28 (62.2%) and 36 (80%) had gross motor, fine motor, language and adaptive-cognitive delay, respectively. Vitamin B12 level was significantly associated with suspect development delay in all domains, except language. A total of 29 children exhibited delay in all four domains with 18 (40%) children belonging to B12 deficient group ($P < 0.001$) (Table 3).

Discussion

In the present study involving 100 children with SAM (1–59 mo), approximately half of the children had low serum vitamin B12 levels, whereas over one-third had hyperhomocysteinemia. Severe anemia and hypoproteinemia were significantly associated with vitamin B12 deficiency. This data suggests that there is high prevalence of vitamin B12 deficiency in children with SAM, which is also significantly associated with developmental delay in all domains.

Previous studies have also documented a high prevalence (16.3% to 58%) of vitamin B12 deficiency in children with SAM [9, 10, 17, 19–22]. These differences in magnitude of vitamin B12 deficiency may be related to a different cut-off for diagnosis of deficiency [17, 21], differences in feeding practices and the differing proportion of infants who are at lower risk of deficiency due to intake of B12 from breast milk.

Myelination is an important step during the early brain development, and vitamin B12 plays an important role in the development, growth and maturation of the nervous system during early years of life. Its deficiency has been associated with restriction of myelination or demyelination of nerves, altered S-adenosyl methionine: S-adenosyl homocysteine ratio, imbalance of neurotrophic and neurotoxic cytokines in the brain cells [23]. Apart from the hematological manifestations, clinically, vitamin B12 deficiency manifests as hypotonia, involuntary movements, developmental delay or regression of milestones, convulsions and cerebral atrophy, even in children without any significant co-morbidities [7, 8, 24]. Studies have also documented a significant improvement in the developmental milestones and reversal of the changes with the increase in the vitamin B12 levels [8, 25, 26].

In the present study, severe anemia and hypoprotenemia were the factors significantly associated with vitamin B12 deficiency in children with SAM. The association of severe anemia is easily explained as vitamin B12 is a major nutritional factor for hemoglobin synthesis. Association of vitamin B12 deficiency and hypoalbuminemia could be related to common dietary sources. Dietary vitamin B12 in humans is exclusively sourced from animal-origin foods, which are also rich sources of proteins. Thus, lack of consumption of animal-origin foods may predispose children to both hypoalbuminemia and vitamin B12 deficiency. Also, there is some evidence to suggest that lower B12 status is related to increased pro-oxidant and decreased antioxidant status compared to those with normal B12 status [27]. As dysadaptation related to free-radical-mediated oxidative stress is one of the main mechanisms for children with SAM to develop edema and hypoproteinemia [28], it is plausible that vitamin B12 deficiency may precipitate oxidative stress induced dysadaptation leading to hypoproteinemia in children with SAM. Another less important reason could be the presence of defects in gut and proximal tubular transport proteins which are associated with albuminuria (leading to hypoproteinemia) and B12 deficiency [29].

The authors documented an association of developmental delay in all domains (except language) with B12 deficiency in children with SAM. In an earlier study on 177 children with uncomplicated SAM (6–59 mo), 61% had global developmental delay on screening using DDST-II and statistically significant association was found between age <2 y and mixed breastfeeding practices [30]; vitamin B12 status was not evaluated. In a study by Adhaulia et al. [6] developmental delay using Vineland Social Maturity Scale was observed in 55.5% of children, and was significantly associated with age <2 y. They did not observe any significant association between vitamin B12 levels and delayed development. The mean levels of vitamin B12 levels in their study were higher as compared to present study. In a study by Goyal et al. among the B12 deficient children, seven (23.3%) had borderline Developmental quotient (DQ), and 23 (76.7%) had delayed development [17]. None of these studies reported domain-wise information of developmental delay, and only mean (SD) of total DQ scores

were mentioned. Risk of delay in the language domain, though present in more than half of children with SAM, was not significantly different between vitamin B12-deficient and non-deficient groups in the present study. Previous studies have also documented cognitive dysfunction, hypotonia, motor dysfunction and abnormal movements to be the main features of vitamin B12 deficiency, which could be related to specific sites of patchy delayed myelination or demyelination.

The main strengths of present study were that it was conducted in a geographic area catering to low-income urban population with high prevalence of malnutrition in children, where malnutrition and micronutrient deficiencies are likely to be a significant health problem, and the authors also assessed functionally important outcomes in the form of developmental delay as this could impact the practices and policy regarding supplementation and rehabilitation practices in SAM. The main limitation was that it was a hospital-based enrolment, with majority of enrolled children having complicated SAM, especially with concomitant infections such as diarrhea. As acute infections are known to adversely affect the micronutrient nutriture, this could have led to overestimation of vitamin B12 deficiency in the present study. Thus, these results may not be generalizable to uncomplicated SAM in the community. Also, authors could not perform assay for serum and urine methyl-malonic acid and holotranscobalamin (HoloTC) levels, which are regarded as more accurate markers of functional deficiency of vitamin B12. They did not follow the recruited patients for hematological and neurological recovery after correction of vitamin B12 deficiency, and thus are unable to comment on cause-and-effect relationship between the deficiency and these outcomes.

Conclusions

The authors conclude that there is a high prevalence of vitamin B12 deficiency in children with SAM as more than half have low serum vitamin B12 levels and/or high Hcy levels. Also, vitamin B12 deficiency is significantly associated with developmental delay in these children. As B12 deficiency in early childhood may have long term consequences on neurodevelopment, children with SAM may be screened for vitamin B12 deficiency and receive appropriate treatment. This may have potential to prevent the long-term consequences on their neurodevelopment. Current WHO and IAP guidelines on management of children with SAM need a relook to include diagnosis and management of vitamin B12 deficiency in the algorithm.

Authors' Contributions DS, PG: Study conceptualization; AA: Data collection & writing the initial draft of manuscript; SS, SK: Laboratory assessment, data analysis and its interpretation; DS: Supervised data collection, statistical analysis and interpretation; RKM: Statistical analysis and interpretation, manuscript writing, review and editing; SK, PG: Critical inputs to manuscript writing. All authors approved the final version of the manuscript. DS will act as guarantor for this manuscript.

Funding This study was supported by Intra-Mural Research Grant of University College of Medical Sciences.

Declarations

Conflict of Interest None.

References

1. Ministry of Health and Family Welfare., Govt. of India. National family Health Survey (NFHS-5). Compendium of fact sheets – key indicators. Available at: https://main.mohfw.gov.in/sites/default/files/NFHS-5_Phase-II_0.pdf. Accessed on 10th March 2023.
2. Ministry of Health and Family Welfare (MoHFW), Government of India, UNICEF and Population Council. Comprehensive National Nutrition Survey (CNNS) National Report. New Delhi. 2019. Available at: https://nhm.gov.in/WriteReadData/l892s/1405796031571201348.pdf. Accessed on 4th May 2020.
3. Kalyan GB, Mittal M, Jain R. Compromised vitamin B12 status of Indian infants and toddlers. Food Nutr Bull. 2020;41:430–7.
4. Jali S, Gajjar R, Kamate M. Study of serum vitamin B12 levels in pregnant mothers and their newborns and its relation to growth of the infants. Indian J Child Health. 2022;4:203–6.
5. Mittal M, Bansal V, Jain R, et al. Perturbing status of vitamin B12 in Indian infants and their mothers. Food Nutr Bull. 2017;38:209–15.
6. Adhaulia A, Maurya M, Tiwari AD. Developmental delay in children with severe acute Malnutrition and its association with vitamin B12 deficiency. Int J Contemp Pediatr. 2019;6:548–51.
7. Azad C, Jat KR, Kaur J, et al. Vitamin B_{12} status and neurodevelopmental delay in Indian infants: a hospital-based cross-sectional study. Paediatr Int Child Health. 2020;40:78–84.
8. Goraya JS, Kaur S, Mehra B. Neurology of nutritional vitamin B12 deficiency in infants: case series from India and literature review. J Child Neurol. 2015;30:1831–7.
9. Khanna S, Kumar P, Sharma S, Chandra J, Sinha R. Nutritional and hematological profile of children with severe acute Malnutrition rehabilitated with or without vitamin B12. Int J Community Med Public Health. 2022;9:882–6.
10. Verma D, Singh SK, Ziauddin M, Kumari R. 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. Int J Contemp Pediatr. 2021;8:1366–73.
11. World Health Organization. WHO Child Growth Standards and the Identification of Severe Acute Malnutrition in Infants and Children: A Joint Statement. Available at: https://www.who.int/nutrition/publications/severemalnutrition/9789241598163/en/. Accessed on 11th November 2022.
12. Saleem SM, Jan SS. Modified kuppuswamy socioeconomic scale updated for the year 2021. Indian J Forensic Community Med. 2021;8:1–3.
13. Gupta P. Anthropometry: assessment of growth. In: Gupta P, editor. Clinical methods in Pediatrics. New Delhi: CBS Publishers; 2021. p. 58–110.
14. World Health Organization. The WHO Child Growth Standards., 2006. Available at: http//www.who.int/tools/child-growth-standards. Accessed on 29th November 2022.
15. WHO. Anthro for Personal, Computers. Version 3.2.2, 2016: Software for Assessing Growth and Development of the World's

Children. Geneva: WHO; 2010. Available at: http://www.who.int/childgrowth/software/en/. Accessed on 29th November 2022.
16. Ministry of Health Family Welfare, Govt of India. Participant Manual for Facility-Based Care of Severe Acute Malnutrition. New Delhi: Ministry of Health and Family Welfare, Government of India. 2013. Available at: https://nhm.gov.in/images/pdf/programmes/child-health/IEC-materials/PARTICIPANT-MANUAL_FBCSA-Malnutrition.pdf. Accessed on 30th November 2022.
17. Goyal S, Tiwari K, Meena P, Malviya S, Asif M. Cobalamin and folate status in malnourished children. Int J Contemp Pediatr. 2017;4:1480–4.
18. McLean E, Cogswell M, Egli I, Wojdyla D, De Benoist B. Worldwide prevalence of anaemia, WHO vitamin and mineral nutrition information system, 1993–2005. Public Health Nutr. 2009;12:444–54.
19. Yaikhomba T, Poswal L, Goyal S. Assessment of iron, folate and vitamin B12 status in severe acute Malnutrition. Indian J Pediatr. 2015;82:511–4.
20. Kamath L, Ratageri VH, Kanthi AS, Fattepur SR, Desai RH. Status of vitamin B12, zinc, copper, selenium, manganese, molybdenum and cobalt in severe acute Malnutrition. Indian J Pediatr. 2023;90:988–93.
21. Murthy KA, Malladad A, Kariyappa M. Estimation of serum folate and vitamin B12 levels in children with severe acute Malnutrition. Int J Contemp Pediatr. 2020;7:1013–6.
22. Vaid A, Sharma M, Jamunashree B, Gautam P. Serum vitamin B12 levels in severe acute Malnutrition hospitalized children between age group 6 months to 59 months in Kangra, India. Int J Contemp Pediatr. 2018;5:1997–2001.
23. Dror DK, Allen LH. Effect of vitamin B12 deficiency on neurodevelopment in infants: current knowledge and possible mechanisms. Nutr Rev. 2008;66:250–5.
24. Umasanker S, Bhakat R, Mehta S, et al. Vitamin B12 deficiency in children from Northern India: time to reconsider nutritional handicaps. J Family Med Prim Care. 2020;9:4985–91.
25. Torsvik I, Ueland PM, Markestad T, Bjørke-Monsen AL. Cobalamin supplementation improves motor development and regurgitations in infants: results from a randomized intervention study. Am J Clin Nutr. 2013;98:1233–40.
26. Strand TA, Taneja S, Ueland PM, et al. Cobalamin and folate status predicts mental development scores in north Indian children 12–18 mo of age. Am J Clin Nutr. 2013;97:310–7.
27. van de Lagemaat EE, de Groot LCPGM, van den Heuvel EGHM. Vitamin B12 in relation to oxidative stress: a systematic review. Nutrients. 2019;11:482.
28. Golden MH, Ramdath D. Free radicals in the pathogenesis of kwashiorkor. Proc Nutr Soc. 1987;46:53–68.
29. Pollock CA, Poronnik P. Albumin transport and processing by the proximal tubule: physiology and pathophysiology. Curr Opin Nephrol Hypertens. 2007;16:359–64.
30. Saleem J, Zakar R, Bukhari GMJ, et al. Developmental delay and its predictors among children under five years of age with uncomplicated severe acute Malnutrition: a cross-sectional study in rural Pakistan. BMC Public Health. 2021;21:1397.