Original Article

Developmental delay in children with severe acute malnutrition and its association with Vitamin B_{12} deficiency

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ABSTRACT

Background: There are high rates of developmental delay (DD) in children with severe acute malnutrition (SAM). Vitamin B_{12} is mandatory for the myelination of brain during the early childhood period. **Objective:** The objective of the study was to find out the percentage of DD in SAM and its association with Vitamin B_{12} deficiency. **Materials and Methods:** A prospective, observational study was done in SAM children aged 0–60 months who were admitted in Nutritional Rehabilitation Centre. Developmental assessment was done by Vineland Social Maturity Scale and developmental quotient <70 was considered as DD. **Results:** DD was found in 55.3% of children. Vitamin B_{12} deficiency, insufficiency, and sufficiency were found in 14.6%, 24.3%, and 50.5% of children, respectively, and Vitamin B_{12} level was not significantly associated with DD in children with SAM (p=0.290). **Conclusion:** More than half of SAM children had DD and it was not significantly associated with Vitamin B_{12} levels.

Key words: *Developmental delay, Severe acute malnutrition, Vitamin B_{12} deficiency*

In India, 43.5% of children under 5 years of age are underweight including 43% moderate-to-severe cases and 16% severe malnutrition [1]. A study done by van den Heuvel *et al.* showed around 80% delay in the development of children with severe acute malnutrition (SAM) [2]. Studies have shown that malnutrition can lead to developmental delay (DD) [3-7]. The various causes of DD in children with SAM are either deficiency of Vitamin B_{12}, iron, calorie, and selenium or psychological deprivation. Vitamin B_{12} deficiency results in restricted myelination and, depending on the area of the nervous system affected, the child can present with varied cognitive and intellectual problems.

A study done by Dubal found that the prevalence of Vitamin B_{12} deficiency among children 1–6 years of age was 9.5% [8]. Another study done by Jain *et al.* revealed the correlation between Vitamin B_{12} deficiency and DD [9]. Agarwal *et al.* also found a clear association between Vitamin B_{12} deficiency and impaired neurodevelopmental status [10]. The objective of the study was to find out the prevalence of DD in SAM and its association with Vitamin B_{12} deficiency.

MATERIALS AND METHODS

This prospective observational study was done in SAM children admitted in Nutritional Rehabilitation Centre (NRC) of a tertiary care center of Eastern Uttar Pradesh. The children with SAM aged 0–59 months admitted in NRC from September 2016 to August 2017 were included in the study. SAM was defined as weight for height below 3 standard deviation (SD or Z scores) of the median World Health Organization growth reference and/or the presence of bipedal edema and/or mid-upper arm circumference (MUAC) below 11.5 cm. In a child below 6 months of age, all the criteria were same except that MUAC was not included in the study. The ethical clearance was taken by the Institutional Ethical Committee.

The exclusion criteria were underlying neurological disease such as perinatal asphyxia/hypoxic-ischemic encephalopathy, cerebral palsy with mental retardation, meningitis or congenital central nervous system malformations, heart disease, inborn errors of metabolism, children born preterm, patients on proton-pump inhibitors or histamine-2 receptor antagonists before hospital admission, and unstable vital parameters (shock, severe respiratory distress, and coma).

Complete history was taken and examination was done according to the predefined pro forma. Infant and Young Child Feeding (IYCF) indicators, namely, early initiation of breastfeeding (BF) within 1-h, exclusive BF (EBF) up to 6 months of age, timely introduction of complementary feeding between 6 and 8 months, minimum meal frequency (MMF), and minimum dietary diversity (MDD), i.e., consuming at least four food groups were calculated.

Developmental assessment was done by trained personnel (investigator) using Vineland Social Maturity Scale (VSMS). Developmental age (DA) was calculated by VSMS and then developmental quotient (DQ) was calculated using the formula: DQ = 100 × (DA/Chronological age). DQ <70 was considered as DD.

Complete blood count was done by the automated cell counter. Serum Vitamin B_{12} level was measured by the standard chemiluminescence assay (ARCHITECT Plus Analyzer by Abbott Diagnostics). Megaloblastic anemia was defined as mean corpuscular volume (MCV) (femtoliter [fL]): >108 at birth and >78 for age 0.5–5 years. Depending on the level of Vitamin B_{12}, the patients are categorized under Group A: Vitamin B_{12} <200 pg/ml (deficiency), Group B: Vitamin B_{12} 200–350 pg/ml (insufficiency), and Group C: Vitamin B_{12} >350 pg/ml (adequate).

Continuous data were summarized as mean±SD while discrete (categorical) in number and percentage. Continuous groups were compared by one-factor analysis of variance and the significance of mean difference between the groups was done by Newman–Keuls *post hoc* test after ascertaining normality by Shapiro–Wilk test and homogeneity of variance between groups by Levene's test. Categorical groups were compared by Chi-square test.

RESULTS

A total of 103 children were included in our study. The mean age of children was 14.15±10.26 months with male-to-female ratio of 1.2:1. Most of the children belonged to the district of Allahabad (53.4%) followed by Pratapgarh (12.6%) and Kaushambi (8.7%). Out of 103 children, 41 (39.8%) were in lower middle class, 37 (35.9%) in upper lower, 18 (17.5%) in upper middle, and 7 (6.8%) belonged to lower class of socioeconomic status according to Kuppuswamy scale. Sepsis (39.8%) was the most common complication, followed by pneumonia (13.6%), acute diarrhea (10.7%), chronic diarrhea (6.8%), persistent diarrhea (1%), anemia (7.8%), and infantile tremor syndrome (4.9%). Sixty-eight (66.0%) children were completely immunized and 34 (32.0%) were incompletely immunized.

The VSMS score, DA, and DQ of children ranged from 1 to 48, 1 to 44 months, and 4 to 97%, respectively, with mean of11.70±11.08, 8.48±8.94 months, and 58.14±25.49%, respectively, as shown in Table 1. Fifty-five (55.3%) children had DD with DQ <70.

Early initiation of BF, EBF, timely introduction of complementary feeds, MMF, and MDD was seen in 71 (68.9%), 58 (56.3%), 69 (67.0%), 75 (72.8%), and 48 (46.6%) cases, respectively. Pallor was found in 74 (71.8%) children, edema in 17 (16.5%) children, and signs of Vitamin B_{12} deficiency, namely, hyperpigmentation, glossitis, or both were present in 20 (19.4%), 31 (30.1%), and 10 (9.7%) children, respectively. There were 67 children (65.0%) who were anemic (hemoglobin [Hb] <10 gm/dL). Among them, 50 (48.5%) children had mild-to-moderate anemia while 17 (16.5%) were severely anemic (Hb <7 gm/dL). Pancytopenia was found in 3 (2.9%) children. Macrocytosis and microcytosis (MCV <72 fL) were found in 25 (24.3%) and 52 (50.5%) children, respectively.

Vitamin B_{12} levels were assessed only in 92 children due to some technical problem. Vitamin B_{12} was deficient, insufficient, and normal in 15 (16.3%), 25 (27.5%), and 52 (56.5%) children, respectively. Socioeconomic status was not associated with Vitamin B_{12} levels (p=0.97) and Vitamin B_{12} level was not associated (p=0.29) with DD (Table 2).

Among the other risk factors, children with age <2 years (p=0.047) with SAM had significant DD. However, there was no association of DD with sex, pallor or edema, Hb, socioeconomic status, and IYCF indicators. However, MDD after 6 months was significantly associated with DD (Table 3).

Table 1: Developmental assessment of severe acute malnutrition children (n=103)

Developmental profile	Mean±standard deviation/number (%)
Vineland Social Maturity Scale (score)	11.70±11.08
Developmental age (months)	8.48±8.94
DQ (%)	58.14±25.49
Developmental delay (DQ <70)	57 (55.3)

DQ: Developmental quotient

DISCUSSION

DD was found in 55.5% of children and was significantly present in children below 2 years of age. The mean Vitamin B_{12} levels in SAM children were 629.46±551.43 pg/ml. There was no association between Vitamin B_{12} levels and DD. IYCF practices were not associated with DD except MDD.

The study had 68 (66%) children who were completely immunized. According to the National Family Health Survey (NFHS)-4, children with fully immunized status in India were 62% while in Uttar Pradesh, its only 51.1% [11]. The most common complication in the study was sepsis (39.8%) followed by pneumonia (13.6%) and diarrhea (10.7%). These results were in accordance with the study done by Choudhary *et al.* [12]. However, Kumar *et al.* and Dhanalakshmi and Devi found diarrhea as the most common complication followed by acute respiratory tract infections [13,14]. Another study done by Meena *et al.* revealed loss of appetite followed by anemia as the most common complication [15]. The results of IYCF indicators in the study were higher than those reported in the NFHS-4 data.

In our study, Vitamin B_{12} deficiency was present in 16.3% of patients while insufficiency was present in 27.2% of children; therefore, a total of 43.5% of children had low Vitamin B_{12} levels. The socioeconomic status was not associated with Vitamin B_{12} deficiency in this study which was in accordance with the results

Table 2: Association of Vitamin B_{12} deficiency and developmental delay

Developmental delay	Group A (n=15)	Group B (n=25)	Group C (n=52)	p value
Present	11 (73.3)	12 (48.0)	29 (55.8)	0.29
Absent	4 (26.7)	13 (52)	23 (41.2)	
Vineland Social Maturity Scale (score)	8.13±13.8	10.68±7.22	12.26±12.32	
Developmental quotient	53.21±27.89	59.23±23.88	56.38±26.79	

Table 3: Risk factors of developmental delay in severe acute malnutrition children (n=103)

Infant and Young Child Feeding indicators and drug intake	Developmental delay (n=57)	Normal development (n=46)	p value (Chi-square test)
Early initiation of BF	37	34	0.326
Exclusive BF	29	29	0.218
Complementary feeds	34	35	0.071
Minimum dietary diversity	19	29	0.002
Minimum meal frequency	43	32	0.505
Anemia			
No (Hb >12 g/dL)	22	14	0.563
Mild to moderate (Hb <10)	25	25	
Severe (Hb <7 g/dL)	10	7	
Edema	9	5	0.191
Age <24 months	54	38	0.047
Socioeconomic status			
Upper middle	25	16	0.29
Lower middle	22	15	
Upper lower	8	10	
Lower	2	5	

BF: Breastfeeding, Hb: Hemoglobin

obtained by Mittal *et al*. [16]. Dubal (2014), in Gujarat, found the prevalence of Vitamin B_{12} deficiency as 9.5% [8]. Lower prevalence in this study could be because the study group was not SAM. A study done by Goyal *et al.* (2017), in Udaipur, showed Vitamin B_{12} deficiency in 37.5% and insufficiency in 11.25% of children with total prevalence of 48.75% which was similar to our study [17]. However, the mean Vitamin B_{12} level was 353.65±330.76 pg/ml which was lower than in our study. This may be due to the small sample size in their study. Another study done by Kapil and Sareen estimated that the prevalence of cobalamin deficiency was 67.2% for children in the age group of 5–11 years and 68.3% for those in the age group of 12–18 years [18].

In our study, we did not find any association of Vitamin B_{12} deficiency with DD. However, studies done by Biancheri *et al*., Graham *et al*., Jain *et al.,* and Agarwal *et al*. showed an association of Vitamin B_{12} levels with DD [10,19-21]. The difference in the results could be because our study was done in SAM children where DD is multifactorial. Gottschling-Lang *et al*. did not find any association of DD with socioeconomic status similar to our study [22].

The strengths of our study were that it was done in an NRC where strict protocols were followed. Developmental assessment was appropriately done by trained personnel (investigator) who has been trained for using VSMS. The advantage of using VSMS for developmental assessment is that it is relatively easy to administer and can be used to calculate DQ even in the neonatal age group. Besides this, the subject is not required to perform formal tasks, so some estimate of the level of functioning can be obtained even in most severely handicapped children. There were few limitations of the study. The sample size was small and we could not estimate urinary methylmalonic acid which is a better marker of Vitamin B_{12} levels due to non-availability of this facility in our area.

CONCLUSION

We found that one out of two of severe malnourished children has DD which is one of the major morbidities; however, Vitamin B_{12} deficiency was not significantly associated with DD. It becomes important that IYCF practices should be communicated and taught to every mother to reduce the incidence of malnutrition.

AUTHORS'CONTRIBUTION

ADT, MM, and AA conceptualized the study design. AA and MM collected the data and drafted the paper. Statistical analysis was done by ADT, MM, and ADT. ADT, MM, and AA revised the draft and final approval was given by all.

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