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TO STUDY THE STATUS OF VITAMIN B12 DEFICIENCY IN CHILDREN WITH SAM ATTENDING NMCTH

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ABSTRACT

Background: Vitamin B12 deficiency is one of the most common micronutrient deficiencies, which is associated with poor cognitive development and growth. **Objectives:** To study the status of vitamin B12 deficiency in children with SAM attending NMCTH pediatrics department. **Results:** Among 95 children enrolled in this study, 54 (56.85%) were vitamin B12 deficient. Among vitamin B12 deficient children, 38(70.37%) were male, and 16(29.62%) were female. The mean age of vitamin B12 deficient children was 18.91 months, and the mean vitamin B12 level of the overall patient was 299.7 pg/ml. Out of 54 vitamins B12 deficient children, the majority, 51.57%, had severe anemia, 72.63% belong to upper lower socioeconomic status. The overall majority were boys, about 55.89%, and 42.10% were female. **Conclusions:** Micronutrients play a central part in the metabolism and maintenance of tissue function. The present study concludes a relatively high prevalence of vitamin B12 deficiency in severely malnourished children. Efforts should be directed to prevent its deficiency in pregnant and breastfeeding women and their infants with special attention in malnourished children. Deficiency of vitamin B12 should be considered in all cases with SAM children regardless of blood indices.

Keywords: Anemia, Severe acute malnutrition (SAM), Vitamin B12 deficiency

INTRODUCTION

Malnutrition among children is a major global health problem that contributes to the mortality of children, morbidity, altered intellectual development, suboptimal working capacity of adults, and increase risk of disease in adulthood.[1] Globally, one-third of deaths under 5 years age are attributed to under nutrition, of 10% are severely undernourished. [2, 3]According to the World Health Organization, severe acute malnutrition (SAM) is defined as weight for height < -3SD, visible severe wasting and/or Edema of both feet (excluding other cause of Edema), mid-upper arm circumference(MUAC) less than 11.5 cm in children age 6 months to 59 months.[4]SAM remains the bigger threat to children because mortality rates among children with SAM are nine times higher than well-fed children, and estimate death directly attributable to SAM vary from 0.5-2 million annually. [5,6]

In Nepal, about half of all death among under 5 years of age (54/1000 live births) are associated with malnutrition, and the prevalence of SAM in under-5s increase between 2001 (1.1%) and 2006 (2.6%) but remained constant between 2006 and 2011 [7,8] and avoidable SAM mortality is approximately 1500 annually.[9] In Nepal, the incidence of SAM in children under 5 years of age was 4.14%.[10] One of the main causes of pediatric morbidity, hospitalization, and mortality in severe anemia and very significant comorbidity in cases of SAM.[11]

It has been demonstrated that SAM with anemia is at greater risk of mortality than SAM without anemia. [12, 13] The prevalence of nutritional anemia in children under five years of age is 58.5% (80 million) and nutritional anemia is primarily caused by an iron deficiency of 66% (52.8 million) [11.] While iron deficiency dominates the spectrum of nutritional anemia, many micronutrient deficiencies, particularly vitamin B12 are significant contributors to the etiopathogenesis of anemia .[11] SAM is often linked to micronutrient deficiencies such as iron, vitamin B12, and folate during early childhood and infancy. [14] Vitamin B12 is a vital micronutrient needed in early childhood and during infancy for rapid growth, development, and increase demand and deficiency can lead to megaloblastic anemia, poor growth, and increased infection. Vitamin B12 deficiency can lead to irreversible neurological damage to brain development.[15,16]

Infants and young children with vitamin B12 deficiency are also susceptible to movement disorders. Symptoms of infants include irritability, abnormal reflexes, difficulty feeding, brain growth failure, and permanent disability.[17-19] Also, measuring serum vitamin B12 level may be helpful in its supplementation with the appropriate dose and form. The aims of the study was to find out the status of vitamin B12 deficiency in children with SAM and their possible association between them attending NMCTH pediatrics department. The study was also conducted to determine the socio-demographic characteristics of the participants.

RESEARCH DESIGN AND METHODOLOGY

Type of study

This is a cross sectional hospital-based study

Study site: -

General pediatric ward and Intensive Care Unit at National Medical College and Teaching Hospital, Birgunj, Nepal

Study Duration: - 12 Months (November 2021 to October 2022)

Target Population: All the children age 6 months to 59 months presenting to Pediatrics department with diagnosis fitting to severe acute malnutrition criteria.

Study Variables : Sociodemographic variables- Age, Sex, Weight, Height, MUAC, Socioeconomic status ,Illness Variables- Hemoglobin level, Serum Vitamin B12 Level (pg/ml),

SELECTION CRITERIA

Inclusion criteria

i. Children diagnosed as primary SAM as per WHO guidelines concerning growth parameters
- Weight for height less than -3SD.
- Visible severe wasting.
- Edema of both feet (excluding other causes of Edema).
- Mid arm circumference less than 11.5 cm (in infant more than 6 months of age)

ii. The age group of 6- 59 months.

iii. Parents / Guardians willing to give written informed consent.

Exclusion criteria

i. Anemia due to acute blood loss.

ii. All children with non-nutritional anemia (malignancies, Hemolytic anemia, Aplastic anemia, liver disease, gastrointestinal disorders (inflammatory bowel disorder, celiac disease, and malabsorption), myeloproliferative disorder, diabetes, heart disease, pancreatic insufficiency, and AIDS

iii. Children diagnosed to have secondary SAM.

iv. Children with a history of oral or parenteral supplementation of vitamin B12 in the previous 6 months, folic acid supplementation, proton pump inhibitors, and H2 (antihistaminic receptor 2) blockers

Tools and Techniques for Data collection

Ethical Committee clearance was obtained from the institution (Ref- F-NMC/572/078-079) before starting the study. Informed written consent from the caregivers of children was taken.

Complete anthropometric evaluation (Height, Weight, MUAC), along with the demographic profile and relevant information of the individual patient (including participant name, age, and gender, date of birth, parents name, occupation, income, caste, religion, family size, type of family, food habit, present major illness and address with their phone number) was collected using structured proforma.

The socioeconomic status of participants was noted according to Kuppuswamy's Socioeconomic Status Scale, which is Upper class, Upper middle class, Lower middle class, Upper lower class, and Lower class. [20] determine the socio-demographic characteristics of the participants.

According to WHO, an indicator of children's nutritional status is the height for weight, weight for height, and clinical signs.The anemia of the participant was classified as severe, moderate, and mild as per WHO criteria. i.e., mild anemia (hemoglobin 9.0–10.9 gm/dL), moderate anemia (hemoglobin 7.0–8.9 gm/dL), and severe anemia (hemoglobin less than 7.0 gm/dL). [21]

Clinical examination was done for a clinical sign of malnutrition. The clinical sign looked for in this age-group were Edema, anemia, hepato-splenomegaly, tropical ulcer, and any sign of infection. A blood sample was sent for further laboratory for investigations. CBC was done by Beckman Coulter, DxH500 automated hematology analyzer. Vitamin B12 levels were estimated by chemiluminescence Immunoassay (CLIA) using Beckman coulter, Access 2 automated Immunoassay analyzer in the department of Biochemistry. The sample was collected in plain and EDTA vial, and if any delay in transportation to the lab, then storage of vial was done at -20 degree Celsius. All the procedures were done by the standard recommended protocol as per the IFCC guideline. Vitamin B12 level <100 pg/ml was considered deficient, and levels between 100-200pg/ml were considered as borderline deficiency and >200pg/ml considered as normal. [22]

The statistical analysis was carried out using Statistical Package for Social Sciences (SPSS version 20.0).

OBSERVATIONS AND RESULT

A total of 95 children suffering from SAM were included in this study, and they are included according to the inclusion criteria enlisted above.

Table 1: Distribution of vitamin B12

Investigation		**Frequency**	**Percentage**
Vitamin B12 Level	<100	54	56.85%
	100-200	18	18.94%
	>200	23	24.21%
Total		95	100%

Table 1 represents the distribution of vitamin B12 deficiency among SAM children. Out of 95 children, 54(56.85%) were having vitamin B12 deficiency, i.e., serum vitamin B12 level <100pg/ml, 18(18.94%) children were having borderline vitamin B12 level (100-200pg/ml), and the rest 23(24.21%) children were not having vitamin B12 deficiency. The result of the present study suggests a high prevalence of vitamin B12 deficiency among severely malnourished children.

Table 2: The mean age of vitamin B12 deficient children

Vitamin B12 <100	**Minimum Age in months**	**Maximum Age in months**	**Mean**	**SD**
54	6	56	18.91	14.607

Similarly, Table 2 shows, the mean age of vitamin B12 deficient children is 18.91 months with an SD of 14.6. The child's minimum age was 6 months, and the oldest child was of 56 months of age.

Table 3: The mean of vitamin B12 of the study population

	N	**Minimum**	**Maximum**	**Mean**	**Std. Deviation**
Vitamin B12 level	95	32.12	1210	299.7	361.65

Table 3 represents, the mean of vitamin B12 of the study population was 299.7 with a standard deviation of 361.65. The minimum level of vitamin B12 observed was 32.12 pg/ml, and the maximum level of vitamin B12 noted was 1210 pg/ml.

Table 4: Distribution of vitamin B12 level among gender

Investigation		Male	Female	P-value
Vitamin B12 Level	<100	38 (70.37%)	16(29.63%)	0.011
	100-200	9 (50%)	9(50%)	
	>200	8(34.78%)	15(65.22%)	
Total		55(57.90%)	40(42.10%)	95(100%)

Table 4 shows that among 95 children enrolled in the present study, 55 (57.90%) were male, and 40 (42.10%) were female with a Male: female ratio of 1.3:1. Out of 55 males, 38(70.37%) were vitamin B12 deficient, and out of 40 females, 16 (29.63%) were vitamin B12 deficient. The result is statistically significant, with a p-value of 0.011.

Table 5: Distribution of vitamin B12 level according to immunization status

Investigation		UP TO DATE	Incomplete	P-value
Vitamin B12 Level	<100	41 (75.93%)	13 (24.07%)	.811
	100-200	14 (77.78%)	4 (22.22%)	
	>200	19 (82.61%)	4 (17.39%)	
Total		74 (77.90%)	21 (22.10%)	95(100%)

Table 5 represents, out of 95 SAM children, immunization status up to date was achieved by 74(77.90%) children, and the rest 18(21.10%) children had incomplete immunization.

Among 54 children who were vitamin B12 deficient, 13(24.07%) children were incompletely immunized, and the remaining 41 (75.93%) children have completed their immunization up to date. The result was not statistically insignificant, with a p-value of .811.

Table 6 shows, Out of 95 children, 69 (72.63%) children belong to upper lower socioeconomic background, 8 (8.42%) belong to upper-middle and rest 18 (18.95%) belong to lower socioeconomic status. Out of 54 vitamin B12 deficient children, 39 (72.22%) children belong to upper lower socioeconomic status, and 14(25.93%) belong to lower socioeconomic status, and only 1 (1.85%) belonged to upper-middle socioeconomic background. This result shows that there is a high prevalence of vitamin B12 deficiency among children belonging to upper lower socioeconomic backgrounds.

Table 6: Distribution of vitamin B12 level according to socio-economics status

Investigation		Lower	Upper lower	Upper middle	P-value
Vitamin B12 Level	<100	14 (25.93%)	39 (72.22%)	1(1.85%)	0.007
	100-200	3 (16.67%)	14 (77.77%)	1 (5.5%)	
	>200	2 (8.69%)	15(65.21%)	6 (26.10%)	
Total		18(18.95%)	69(72.63%)	8(8.42%)	95(100%)

DISTRIBUTION OF VITAMIN B12 LEVEL BASED ON ANTHROPOMETRY

Table 7: For stunting, i.e., weight for height (WH)

Investigation		<-3SD	>-3 SD	P-value
Vitamin B12 Level	<100	38 (70.38%)	16 (29.62%)	0.037
	100-200	11(61.1%)	7 (38.9%)	
	>200	9 (39.13%)	14 (60.87%)	
Total		58(61.05%)	37(38.95%)	95(100%)

Table 7 shows that 54 children were vitamin B12 deficient, out of which 38 (70.38%) were severely stunted, i.e., <-3 SD, and the rest were moderately stunted.

Table 8: For MUAC (Mid-upper arm circumference)

Investigation		<11.5 cm	>11.5 cm	P-value
Vitamin B12 Level	<100	40 (74.08%)	14(25.92%)	0.011
	100-200	16(88.89%)	2 (11.11%)	
	>200	11(47.83%)	12(52.17%)	
Total		67(70.53%)	28(29.47%)	95(100%)

Above table 8 represents, 40 (74.08%) were having MUAC <11.5 cm and 14 (25.92%) were having >11.5 cm among the vitamin B12 deficient children which is statistically significantly (p value=0.011).

Table 9: Distribution of vitamin B12 level according to feeding practices

Investigation		EBF before or after 6 months	EBF up to 6 months	P-value
Vitamin B12 Level	<100	32 (59.26%)	22(40.74%)	0.037
	100-200	11(61.11%)	7(38.89%)	
	>200	8(34.78%)	15(65.22%)	
Total		51 (53.68%)	44(46.32%)	95(100%)

Table 9 represents 44(46.32%) children were on exclusive breastfeeding up to 6 months, while 51 (53.68%) were exclusively breastfed either before or after 6 months. Out of 54 children who are vitamin B12 deficient, 22(40.74%) were on EBF up to 6 months, and the majority 32 (59.26%) were exclusive breastfeeding infant either before or continue after 6 months of age. The result is statistically significant, with a p-value of 0.037.

Table 10: Association of SAM children with vitaminB12 deficient with the severity of anemia

Investigation		Severe	Moderate	Mild	p-value
Vitamin B12 Level	<100	39 (72.22%)	8(14.82%)	7(12.96%)	0.000
	100-200	6(33.33%)	10(55.55%)	2(11.11%)	
	>200	4(17.40%)	14(60.87%)	5(21.73%)	
Total		49 (51.58%)	34(35.79%)	12(12.63%)	95(100%)

Table 10 explains the correlation of severity of anemia among the severely malnourished child. Out of 95 children, 49(51.58%) children were severely anemic, 34(35.79%) children had moderate anemia, and the rest 12 (12.63%) had mild anemia.

Out of 54 vitamin B12 deficient, 39(72.22%) children were affected by severe anemia, 8 (14.82%) suffered from moderate anemia, and the rest 5(12.96%) had mild anemia. The result of the present study is statistically significant with a p-value of 0.000

DISCUSSION

Malnutrition is a serious global issue. Among children under five years of age in the developing world, 206 million are stunted, 50 million are wasted, and 167 million are underweight due to lack of food and the presence of disease.[23]

Geographically, 70–80% of undernourished children worldwide live in lower and middle-income countries, including Nepal.[24]

It is estimated that there are nearly 16.6 million severe acute malnourished. In Africa, approximately 4.1 million under five years of children are estimated to suffering from severe acute malnourished.[25]

It is estimated at 8.1 million (7.5%) under-five children in India suffering from SAM. Nearly 0.6 million deaths occur annually.[26] In Nepal, the prevalence of SAM among children under 5 increased between 2001 (1.1%) and 2006 (2.6%) but remained constant from 2006 to 20(11.10 11). It is estimated that the number of preventable deaths of children due to SAM is around 1500 each year. Prevalence of SAM was about 4.14%.[10]

One of the main causes of pediatric morbidity, hospitalization, and mortality in severe anemia and very significant comorbidity in cases of SAM.[11] It has been demonstrated the SAM children with anemia are at greater risk of mortality than SAM without anemia.[12, 13]

The prevalence of nutritional anemia in children <5 years of age is 58.5% (80 million). Nutritional anemia is chiefly contributed by iron deficiency anemia 66% (52.8 million).[23]

While iron deficiency dominates the spectrum of nutritional anemia, many micronutrient deficiencies, particularly vitamin B12, are significant contributors to the etiopathogenesis of anemia.[11]

SAM is often linked to micronutrient deficiencies such as iron, vitamin B12, and folate during early childhood and infancy. Vitamin B12 is a vital micronutrient needed in early childhood and during infancy for rapid growth, development, and increase demand .and deficiency can lead to megaloblastic anemia, poor growth, and increased infection, as well as vitamin B12 deficiency can lead to irreversible neurological damage to brain development.[16, 27]

The objective of our study was to estimate the burden of Vitamin B12 deficiency in children with SAM. This study focuses on the burden of Vitamin B12 deficiency in SAM children, thereby addressing the need to institute appropriate therapeutic supplementation measures.

A total of 95 children with SAM were included in this study. Out of which, 55(57.90%) were male, and 40(42.10%) were female. Similar results were also obtained in another hospital-based study by Yadav SS et al. [28] Also can be explained by differential health-seeking behaviors of patients where a male child is still preferred in Nepal. Another reason could be that boy was more influenced by environmental stress than girls.

The present study shows that 54(56.85%) children were vitamin B12 deficient, and 18(18.94%) had borderline vitamin B12 levels. Among vitamin B12 deficient, 38(70.37%) were male, and 16(29.63%) were female. 64(67.36%) children were between the age of 6-20 months. A similar result has been obtained in another study conducted by Vaid A et al.[23] Also, this result was supported by Yahikhomba T et al. on the assessment of iron, folate, and vitamin B12 status children with SAM children aged 6-60 months concluded that prevalence of cobalamin deficiency in SAM children is much more than folate deficiency.[29]

In this study, the mean value of vitamin B12 of study children was 299.7, and this finding is following a study done by Goyal S et al.., which conclude the mean vitamin B12 value was 353.8.[30]

In our study, the mean age of the study population was 18.91 months, and a study by Chhabra A et al., concluded that nutritional megaloblastic anemia occurs commonly in malnourished children; the commonest age is 3-18 months.[31] Both studies show a similarity in their result.

The present study shows; 49(51.58%) children have been affected by severe anemia, moderate anemia was seen in 34(35.79%) children, and mild anemia in 12.63% of children. There was a significant correlation between weight for height <-3SD and vitamin B12 deficiency (p=0.037) and MUAC <11.5 cm and vitamin B12 deficiency (p=0.011) in this study. A similar result was obtained in another study. Yahikhomba T et al.[29]

In the present study, among vitamin B12 deficient children, 72.22% had severe anemia with a significant p-value of 0.00. This shows that there is a higher chance of developing severe anemia in severely malnourished children with vitamin B12, and severe anemia increases the risk of mortality and morbidity as well as hospitalization. This result is consistent with a study done by Goyal S et al.[30]

The present study shows a significant relationship between feeding practices and vitamin B12 deficiency in SAM children. Out of 95 SAM children, only 44(46.3%) infants were exclusively breastfed up to 6 months, and the rest 51(53.68%) were under improper feeding practices, i.e., these children were exclusively breastfed either before or after 6 months age. Those children who are under improper breast feeding practices suffers more from SAM than others. A similar result was obtained in Nepal's study by Pravana NK et al., which shows the 2/3rd of SAM children had improper breastfeeding practices[10]. Among 54 vitaminB12 deficient children, 32(59.26%) children exclusively breastfed before or after 6 months, and they tend to suffer more than others. Only 40.7%% exclusively breast up to 6 months developed SAM with vitamin B12. This result is per a study done in India by Murthy KA et al.[11] The result also supported by; Vitamin B12 deficiency is well recognize in exclusively breastfed infants of vitamin B12 deficient mother and also concentration of vitamin B12 in breast milk reflect maternal vitamin B12 stores. A study in in rural Karnataka by Pasricha et al. found that concentration ferritin and vitamin B12 were decrease in toddlers who continue to receive breast milk.[29] Maternal vitamin B12 stores often depleted among women in low income countries, including up to one- third of women in rural Nepal.[32, 33]

Maternal pre-pregnancy nutritional status plays an important role in a child's health. This was seen in a randomized, placebo-controlled clinical trial done in pregnant women <14 weeks of gestation in Bangalore, India.[14] This study showed that pretreatment with 50μg of oral vitamin B12 in antenatal period plus routine iron and folic acid supplementation to all pregnant women had a higher level of serum vitamin B12 at third trimester and 6 weeks postnatal as compared to the placebo group. Infants born to B12 supplemented mothers also had a higher concentration of vitamin B12 at 6 weeks postnatal. Hence, maternal vitamin B12 levels reflect the stores in infancy, and improvement in mothers' pre-pregnancy nutritional status is essential. Evaluation of maternal hemoglobin or vitamin B12 levels has not been performed as a part of our study. However, as the burden of vitamin B12 deficiency was higher (60.4%) in the age group 6-20 months, maternal malnutrition could have contributed to the. Maternal health programs must be strengthened as birth.

CONCLUSION

The present study concludes that there is a high prevalence of vitamin B12 deficiency in severely malnourished children. We observed a large proportion (56.47%) of patients to be deficient. The younger age (<2 years) is the most vulnerable age for vitamin B12 deficiency. Efforts should be directed to prevent its deficiency in pregnant and breastfeeding women and their infants, with special attention to malnourished children. Anemia is one of the determining factors that increase the risk of morbidity and mortality when associated with SAM and this study conclude that among SAM children with vitamin B12 72.23% children were affected by severe anemia. The deficiency was more common in young children, lower socioeconomic status class, exclusively breast before or after 6 months, and/or having delayed initiation of complementary feeding. It has a clear association with adverse developmental outcomes. Maternal malnutrition contributes to poor stores of Vitamin B12 in infancy. Improving the status of vitamin B12 deficiency might reduce the burden of childhood anemia and improve these children's neuronal development.

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