ORIGINAL ARTICLE

Effect of Nutritional Rehabilitation on Neurodevelopmental Status of Children With Severe Acute Malnutrition

Dilip Upadhyay, Surendra Singh, Deepak Dwivedi

Department of Pediatrics, Shyam Shah Medical College, Rewa, Madhya Pradesh, India

ABSTRACT

Objective: To evaluate the change in the neurodevelopmental status of children (1-30-months-old) with severe acute malnutrition (SAM) following nutritional rehabilitation.

Methods: A prospective study was conducted in the Severe Malnutrition Therapeutic Unit (SMTU) of a tertiary hospital in Central India, between April 2021 and October 2022. Children with primary neurological conditions like cerebral palsy and epilepsy were excluded. Neurodevelopment was assessed using the Developmental Assessment Scale of Indian Infants (DASII) at admission and following nutritional rehabilitation as per the National Health Mission (NHM) guidelines at the time of discharge, 2 months and 4 months follow-up. Developmental quotient (DQ) ≤ 70 was considered delayed.

Results: 114 children with SAM were included; 4 were lost to follow-up. There was an increase in Motor Developmental Quotient (MoDQ) and Mental Developmental Quotient (MeDQ) at discharge, 2 months, and 4 months. The improvement in MoDQ and MeDQ was greater in children with adequate weight gain. Poor weight gain, higher age of presentation and lower MeDQ and MoDQ at admission were associated with persistent developmental delay at 4 months follow-up.

Conclusions: There was a consistent improvement in DQ with improvement in nutritional status.

Key words: *Development, Early intervention, Malnutrition, Weight gain*

Published online: Jul 23, 2024; ***PII***:S097475591600674

INTRODUCTION

Severe acute malnutrition (SAM) is a significant risk factor for inadequate motor, cognitive, and socioemotional development [1,2]. A high prevalence of developmental delay in seen in children with SAM, with motor milestones affected more than cognitive milestones [1]. With the availability of better nutritional rehabilitation facilities and therapeutic foods, the survival rate of children with SAM has improved [3]. Unfortunately, the care of children with SAM has been focused only on nutritional supple-mentation rather than holistic care and development. It is hypothesized that nutritional rehabilitation should improve the developmental status of these children and the developmental delay, as noted in previous studies, is only transient [4]. However, this hypothesis has not been proven adequately and there are chances that malnutrition leads to permanent neurodevelopmental disabilities [5]. Hence the present study was done to asertain the impact of nutritional rehabilitation on the neurodevelopmental status of children with SAM.

Correspondence to: Dr Deepak Dwivedi,
Department of Pediatrics, Shyam Shah Medical College,
Rewa, Madhya Pradesh, India.
deepakdwi72@gmail.com
Received: Feb 17, 2024; Initial review: Mar 9, 2024;
Accepted: Jul 12, 2024

METHODS

The present prospective cohort study was conducted, between April 2021 and October 2022, in the Severe Malnutrition Therapeutic Unit (SMTU) of a tertiary care center in Central India after obtaining clearance from the Institutional Ethics Committee.

Consecutive children aged 1-30 months admitted to the SMTU were assessed for eligibility. Children with primary neurological conditions like cerebral palsy and Dandy Walker malformation were excluded. Participants were included after obtaining written informed consent from the caregivers/parents. Sample size was not calcu-lated due to lack of data from previous studies and a sample of convenience was taken.

The neurodevelopmental assessment was done by DASII [6]. SAM was defined as per the World Health Organization (WHO) as weight-for-height/length z-score (WHZ/WLZ) below -3 SD of the median WHO child growth standards, or a mid-upper arm circumference (MUAC) < 11.5 cm, or by the presence of bepedal edema for children aged more than 6 months. In children less than 6 months, SAM was defined as WLZ < -3 of the median WHO child

growth standards, or by the presence of nutritional edema [7,8]. Socioeconomic assessment was performed using the modified Kuppuswamy scale [9].

All children underwent a detailed clinical examination including anthropometric assessment. Children less than 10 kg were weighed on an electronic scale, while those weighing > 10 kg were weighed using a beam scale. Length was measured using an infantometer in children aged < 2 years; a stadiometer was used for children aged > 2 years. WHO child growth standards were used as reference [10]. MUAC was measured (in cm) by standard technique using a simple measuring tape [11]; a value less than 11.5 cm in children > 6 months was considered as SAM. Neuro-development was assessed using the Developmental Assessment Scale of Indian Infants (DASII) [12].

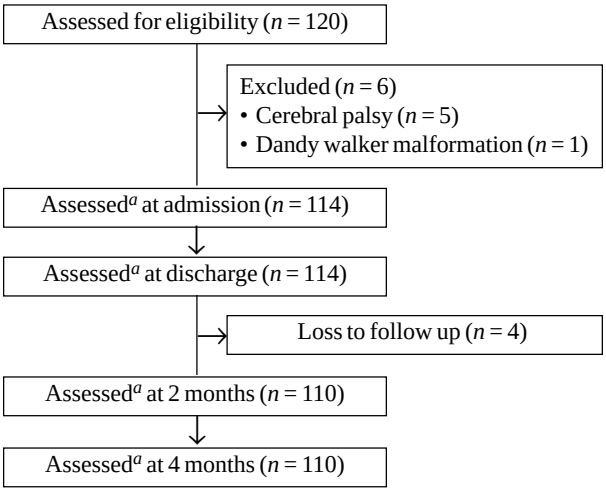
All children in this study were provided standard management for SAM as per National Health Mission (NHM) guidelines [13]. The children were planned for discharge once a weight gain of >15% (of admission) was achieved and/or had satisfactory weight gain for 3 consecutive days (> 5 g/kg/day), with no medical complications [13]. Parents were counselled regarding the dietary management of their children at the time of discharge and were advised to follow-up at 2- and 4 months. At the follow-up visits, dietary counseling and anthropometric assessment was repeated and neuro-development was reassessed. Developmental assessment was done by a single trained examiner. Motor develop-ment quotient (MoDQ) and Mental development quotient (MeDQ) were calculated as per the manual of DASII scale [12]. Developmental delay was defined as development quotient (DQ) ≤ 70 (≤ 2SD) in either the mental or motor scale [1,12]. Developmental delay was classified as mild (DQ 51-70), moderate (DQ 36-50), and severe delay (DQ ≤ 35).

Statistical analysis: Statistical analysis was done using SPSS version 24. Association of DQs (MoDQ and MeDQ) with each variable was done. Continuous variables were presented as mean (SD) and while categorical variables were expressed as numbers and percentages. Proportions and changes in DQ between admission, discharge, and follow-up visits were done using McNemar test and paired t-test, respectively. Risk factors for persistent develop-mental delay at 4 months (place of residence, gender, type of family, age, socioeconomic status, rate of weight gain (weight at 4 months – weight at admission/days since admission), percentage of calorie deficit at admission (calories required – calories consumed/calories required x 100), percentage of protein deficit at admission (protein required – protein consumed / protein required ×100) and DQ (MeDQ and MoDQ) at admission were identified by logistic regression analysis. Univariate logistic regression was initially conducted to identify significant predictors, using a *P* value threshold of < 0.05. Variables meeting this criterion were included in a multivariate logistic regression analysis model and *P* value < 0.05 was considered as significant.

RESULTS

Out of 120 children who were assessed, 114 were finally included as shown in **Fig. 1**; six children were excluded of which 5 had cerebral palsy and 1 had Dandy Walker malformation. Baseline data of the studied cohort is presented in **Table I**. 110 children completed follow-up at 2 months and 4 months. There was no mortality among the children included in the study. There was a significant increase in both MeDQ and MoDQ at discharge, 2 months and 4 months follow-up (**Table II**). Motor delay and mental delay persisted in 27.3% and 16.4% children at 4 months follow-up (**Table II**).

Higher age at presentation, lower rate of weight gain and lower DQ (MeDQ and MoDQ) at admission were significantly associated with persistent developmental delay at 4 months. Mental delay was also found to be associated with a higher percentage of calories and protein deficit at admission (**Table III** and **IV**). Univariate and multivariate Logistic regression analyses revealed that older age, lower weight gain, and lower development quotients at admission were significant predictors of both motor and mental delays at 4 months. For motor delay, children were older (13.9 vs. 10.7 months, adjusted OR 0.852, *P* = 0.009) and had lower weight gain (12.5 vs. 14.4 g/d, adjusted OR 1.143, *P* = 0.076), with significantly lower MoDQ (adjusted OR 1.198, P < 0.001). For mental delay, children were older (14.5 vs. 10.9 months, adjusted OR 0.721, *P* = 0.011), had lower weight gain (12.5 vs. 14.4 g/d, adjusted OR 1.427, *P* =



[a]*Anthropometry, Nutrition (Calorie and protein intake), MoDQ, MeDQ*

Fig. 1 Flow of study participants

Table I Baseline Characteristics of the Sample Studied

Parameter	*Value*
Boys	60 (54.5)
Chronological age at admission (mo)[a]	11.55 (5.7)
Weight at admission (kg)[a]	5.55 (1.4)
Length at admission[a]	67.10 (7.3)
MUAC at admission[a]	10.62 (0.5)
Severe stunting	41 (37.3)
MeDQ[a]	60.91 (25.5)
Mental delay	39 (35.5)
MoDQ[a]	70.71 (23.8)
Motor delay	71 (64.5)
Rural residence	75 (68.2)
Nuclear family	56 (50.9)
Duration of hospital stay[a]	10.52 (1.81)
Socioeconomic status[b]	
Class 2	2 (1.8)
Class 3	77 (70)
Class 4	31 (28.2)

Data presented as n (%) or [a]mean (SD)
[b]As per Modified Kuppuswamy Scales (Class 2: 16-25, Class 3: 11-15, Class 4: 5-10)
MoDQ Motor Developmental Quotient, MeDQ Mental Developmental Quotient, MUAC Mid upper arm circumference

0.024), and higher calorie and protein deficits at admission, with significantly lower MeDQ, (adjusted OR 1.219, P = 0.005). (**Table III** and **IV**).

The improvement in each cluster of motor and mental scale at discharge, 2 months and 4 months, is shown in **Table V**. By 4 months, there was a significant improvement in most clusters of mental scale (except for auditory cognizance) and motor scale (except neck control and locomotion 2).

DISCUSSION

We observed a significant improvement in neuro-development following nutritional rehabilitation, though the persistent delay in a subset of children at 4 months follow-up underlines the complexity of impact of SAM on development. Older age at presentation, slower weight gain, and lower developmental quotients upon admission were the key predictors of these enduring delays, thus emphasizing the need for timely and multifaceted inter-ventions.

Malnutrition reduces the number of neurons and their synapses, increases pruning of dendritic connections, and reduces myelination, all of which are underlying causes of developmental delay [14]. Several studies have shown the association between malnutrition and decreased intelligence, cognitive function, and academic performance [1,2,15-17]. Children who suffered from severe malnutrition in the first three years of life had depressed higher cognitive skills compared to their age-appropriate counterparts [15,16]. The current study provides evidence that MeDQ and MoDQ can improve following nutritional rehabilitation and thus the effect of malnutrition on the nervous system is reversible with appropriate and timely nutritional rehabilitation. Similar findings were reported in a study from Malawi where improvement in stunting and wasting was accompanied with a significant improvement in DQ in all domains at 6-month follow-up [18].

Akin to the results of the current study, poor weight gain has been reported to be significantly associated with persistent delay at 4 months [18,19]. Micronutrient deficiencies, especially vitamin B12, can significantly affect neurological development [20]. Theoretically, improving these vitamin levels should aid in the enhancement of neurodevelopment. All children in the current study were offered micronutrient supplements as per the NHM guidelines, so the impact of a particular nutrient deficiency on development was not specifically looked at. Weight gain may be considered a surrogate marker for overall improvement in nutritional status. In this study, a lower age of presentation was associated with better outcomes which may be because neuroplasticity is more at a younger age and the extent of damage to central nervous system (CNS) due to

Table II Motor and Mental Developmental Quotient at Admission, Discharge, and Follow-up

	Admission (n = 114)	*Discharge (n = 114)*	*P value*	*2 months (n =110)*	*P value* [a]	*4 months (n =110)*	*P value* [b]
MoDQ[c]	61.4 (24.9)	66.8 (24.7)	< 0.001	70.3 (23.5)	< 0.001	73.1 (22.5)	< 0.001
Motor delay	71 (64.5)	52 (47.3)	< 0.001	44 (40)	< 0.001	30 (27.3)	< 0.001
MeDQ[c]	71.8 (21.9)	75.7 (21.5)	< 0.001	77.6 (21.4)	< 0.001	78.9 (20.5)	< 0.001
Mental delay	39 (35.5)	27 (24.5)	< 0.001	18 (16.4)	< 0.001	18 (16.4)	< 0.001

[a]Comparison between admission and 2 months follow-up
[b]Comparison between admission and 4 months follow-up
Data presented as n (%) or [c]mean (SD)
MoDQ Motor Developmental Quotient; MeDQ Mental Developmental Quotient

Table III Risk Factors for Motor Developmental Delay at 4 Months Follow-up

Risk factor	*Motor delay (n = 30, 27.3%)*	*No motor delay (n = 80, 72.7%)*	*P value*	*Univariate logistic regression analysis*		*Multivariate logistic regression analysis[c]*	
				Unadjusted Odds Ratio (95% CI)	*P value*	*Adjusted Odds Ratio (95% CI)*	*P value*
Rural residence[a]	21 (70)	54 (67.5)	0.861	0.890 (0.358, 2.212)	0.802	-	-
Boys[a]	17 (56.3)	43 (51.3)	0.610	1.125 (0.483, 2.620)	0.784	-	-
Nuclear family[a]	16 (53.3)	40 (50.0)	0.954	1.143 (0.493, 2.649)	0.756	-	-
Age (months)[b]	13.9 (5.4)	10.7 (5.6)	0.009	0.904 (0.836, 0.977)	0.010	0.852 (0.756, 0.960)	0.009
Low socioeconomic status[a]	11 (36.7)	20 (25)	0.496	1.818 (0.103, 31.996)	0.683	-	-
Weight gain (g/d)[b]	12.5 (4.2)	14.4 (4.4)	0.044	1.113 (1.000, 1.237)	0.049	1.143 (0.986, 1.325)	0.076
Calorie deficit at admission (%)[b]	40.5 (4.1)	37.6 (4.3)	0.282	0.963 (0.916, 1.011)	0.130	-	-
Protein deficit at admission (%)[b]	40.4 (4.3)	37.5 (3.5)	0.228	0.963 (0.916, 1.011)	0.131	-	-
MoDQ at admission[b]	32.5 (3.9)	71.5 (1.9)	<0.001	1.091(1.056, 1.126)	<0.001	1.198 (1.060, 1.138	< 0.001

Data presented as [a]n (%) or [b]mean (SD), [c]Multivariate analysis done only for those variables which reached significant levels (P<0.05) in univariate analysis
MoDQ Motor Developmental Quotient

Table IV Risk Factor for Mental Developmental Delay at 4 Months Follow-up

Risk factor	*Mental delay (n = 18, 16.4%)*	*No mental delay (n = 92, 83.6%)*	*P value*	*Univariate logistic regression analysis*		*Multivariate logistic regression analysis[c]*	
				Unadjusted Odds Ratio (95% CI)	*P value*	*Adjusted Odds Ratio (95% CI)*	*P value*
Rural residence[a]	12 (66.7)	63 (68.5)	0.880	1.086 (0.371, 3.180)	0.880	-	-
Boys[a]	12 (66.7)	48 (52.2)	0.259	1.883 (0.634, 5.302)	0.263	-	-
Nuclear family[a]	9 (50)	47 (51.1)	0.933	0.957 (0.349, 2.630)	0.993	-	-
Age (months)[b]	14.5 (5.5)	10.9 (5.6)	0.016	0.895 (0.816, 0.983)	0.020	0.721 (0.560, 0.927)	0.011
Low socioeconomic status[a]	7 (38.9)	24 (26.1)	0.201	3.423 (0.189, 62.116)	0.404	-	-
Weight gain (g/d)[b]	12.5 (3.5)	14.4 (4.4)	0.013	1.180 (1.031, 1.350)	0.016	1.427 (1.048, 1.944)	0.024
Calorie deficit at admission (%)[b]	43.7 (4.3)	37.3 (5.3)	0.010	0.915 (0.858, 0.975)	0.060	-	-
Protein deficit at admission (%)[b]	43.5 (4.1)	37.2 (4.6)	0.010	0.915 (0.858, 0.975)	0.060	-	-
MeDQ at admission[b]	36.3 (22.6)	78.7 (13.5)	< 0.001	1.116 (1.061, 1.174)	< 0.001	1.219 (1.061,1.401)	0.005

Data presented as [a]n (%) or [b]mean (SD), [c]Multivariate analysis done only for those variables which reached significant levels (P<0.05) in univariate analysis
MeDQ Mental Developmental Quotient

prolonged malnutrition must be less in these children. However, we could not find studies supporting this presumption and further research is required to find reasons for the same. This study also analyzed the various clusters of development and DQ was assessed in each follow-up. There was significant improvement in all clusters at follow-up. Most children did not reach the age of locomotor 2 so the mean value was very low. There may be other risk factors for persistent developmental delay like multivitamin deficiency especially vitamin B12, minerals deficiency etc. which were not studied and is limitation of present study. Future studies may clear this point further.

Table V Scores in Motor and Mental Clusters at Admission, Discharge, 2 Months and 4 Months Follow-up

Cluster No	*Number of items*	*Admission*	*Discharge*	*P value* [a]	*2 months*	*P value* [b]	*4 months*	*P value* [c]
Motor Cluster								
I	Neck control (7)	6.6 (0.11)	6.7 (0.09)	0.171	6.9 (0.02)	0.001	6.94 (0.02)	0.769
II	Body control (23)	14.6 (0.53)	15.77 (0.50)	< 0.001	17.51 (0.42)	0.000	18.15 (0.42)	< 0.001
III	Locomotion 1 (10) (Basic gross motor skills like crawling, standing, walking etc.)	3.5 (0.28)	3.9 (0.27)	< 0.001	4.8 (0.28)	0.000	6.0 (0.26)	< 0.001
IV	Locomotion 2 (13) (Advanced gross motor skills like tip toe walking, jumping, balancing etc.	0.5 (1.95)	0.4 (1.2)	0.075	0.5 (1.3)	0.828	0.85 (1.7)	0.182
V	Manipulation (14)	8.5 (0.43)	9.3 (0.44)	< 0.001	10.5 (0.35)	0.000	12.03 (0.26)	< 0.001
Mental Cluster								
I	Cognizance (visual) (25)	15.1 (0.72)	17.3 (0.73)	< 0.001	20.1(0.68)	< 0.001	21.1 (0.89)	0.001
II	Cognizance (auditory) (7)	5.69 (0.12)	5.71 (0.21)	0.453	5.81 (0.21)	0.023	6.62	< 0.001
III	Reaching and manipulation (36)	9.3 (1.17)	11.88 (1.12)	< 0.001	16.12 (1.02)	< 0.001	17 (1.14)	< 0.001
IV	Memory (11)	3.78 (0.36)	3.98 (0.36)	< 0.001	5.41(0.33)	< 0.001	6.05 (0.50)	< 0.001
V	Social interaction and imitative behavior	6.65 (0.62)	9.40 (0.67)	< 0.001	12.78 (0.48)	< 0.001	13 (0.56)	< 0.001
VI	Language 1 (vocalization, speech and communication) (11)	3.25 (0.22)	3.89 (0.20)	< 0.001	4.7 (0.17)	< 0.001	5.1 (0.18)	< 0.001
VII	Language 2 (vocabulary and comprehension)	1.6 (2.32)	1.78 (2.62)	< 0.001	2.23 (2.94)	< 0.001	2.4 (2.67)	< 0.001

Data presented as mean (SD)

Comparison between [a] admission and discharge, [b] admission and 2 months, [c] admission and 4 months

WHAT THIS STUDY ADDS?

- Nutritional rehabilitation in children with SAM children improves the motor (MoDQ) and mental developmental quotient (MeDQ).
- Poor weight gain, higher age of presentation and lower MeDQ and MoDQ at admission are associated with persistent developmental delay.

This study conclusively demonstrates that nutritional rehabilitation markedly improves neurodevelopment in children with SAM, while also highlighting poor treatment response as a risk for ongoing developmental delays. It underscores the urgent need for further research on the long-term effects of SAM and strategies for prevention. This work adds a dimension to our understanding of impact of malnutrition on the neurodevelopment and recovery pathways.

Ethics clearance: Institutional Ethics Committee Shyam Shah Medical College No. S.No./IEC/MC/2020:482 dated Jan 08, 2021.

Contributors: DU, SS: Concept, design and data collection. DD: Concept and analysis. All authors were involved in manuscript writing and approved the final version.

Funding: None. *Competing interest*: None stated.

REFERENCES

1. Dwivedi D, Singh S, Singh J, Bajaj N, Singh HP. Neurodevelopmental status of children aged 6-30 months with severe acute malnutrition. Indian Pediatr. 2018;55: 131-3.
2. Grantham-McGregor S. A review of studies of the effect of severe malnutrition on mental development. J Nutr. 1995; 125:2233S-8S.
3. Singh K, Badgaiyan N, Ranjan A, et al. Management of children with severe acute malnutrition: experience of nutrition rehabilitation centers in Uttar Pradesh, India. Indian Pediatr. 2014;51:21-5.
4. Afzal E, Khan S, Ali I, Aftab K, Arshad R, Abbas A. Developmental status in children with severe acute malnutrition. J Islamic Int Med Coll. 2020;15:245-9.
5. Dauncey MJ, Bicknell RJ. Nutrition and neurodevelopment: Mechanisms of developmental dysfunction and disease in later life. Nutr Res Rev. 1999;12:231-53.
6. Phatak P, Misra N. Developmental assessment scales for Indian infants (DASII) 1-30 months - Revision of Baroda Norm with indigenous material. Psychol Stud. 1996; 41:55-6.
7. World Health Organization. WHO Child Growth Standards and the Identification of Severe Acute Malnutrition in Infants and Children. Accessed on Feb 10, 2024. Available from: *https://www.who.int/publications/i/item/9789241 598163*
8. World Health Organization. Identification of severe acute malnutrition in infants under 6 months of age. Accessed on Feb 12, 2024. Available from: *https://www.who.int/tools/elena/interventions/sam-identification-infants*
9. Majumder S. Socioeconomic status scales: Revised Kuppuswamy, BG Prasad, and Udai Pareekh's scale updated for 2021. J Family Med Prim Care. 2021;10:3964-7.
10. World Health Organization. Child growth standards. Accessed on Jan 30, 2024. Available from: *https://www.who.int/tools/child-growth-standards*
11. Sachdeva S, Dewan P, Shah D, Malhotra RK, Gupta P. Mid-upper arm circumference v. weight-for-height Z-score for predicting mortality in hospitalized children under 5 years of age. Public Health Nutr. 2016;19:2513-20.
12. Lata K, Mishra D, Mehta V, Juneja M. Neurodevelopmental status of children aged 6-30 months with congenital heart disease. Indian Pediatr. 2015;52:957-60.
13. National Health Mission. Participant Manual: Facility Based Care for Severe Acute Malnutrition. Accessed on Mar 24, 2024. Available from: *https://www.nhm.gov.in/images/pdf/programmes/child-health/IEC-materials/PARTICIPANT-MANUAL_FBCSA-Malnutrition.pdf*
14. Georgieff MK, Brunette KE, Tran PV. Early life nutrition and neural plasticity. Dev Psychopathol. 2015;27:411-23.
15. Prado EL, Dewey KG. Nutrition and brain development in early life. Nutr Rev. 2014;72:267-84.
16. van den Heuvel M, Voskuijl W, Chidzalo K, et al. Developmental and behavioural problems in children with severe acute malnutrition in Malawi: A cross-sectional study. J Glob Health. 2017;7:020416.
17. Khandelwal N, Mandliya J, Nigam K, Patil V, Mathur A, Pathak A. Determinants of motor, language, cognitive, and global developmental delay in children with complicated severe acute malnutrition at the time of discharge: An observational study from Central India. PLoS One. 2020;15:e0233949.
18. Babikako HM, Bourdon C, E Mbale et al. Neurodevelop-ment and recovery from wasting. Pediatrics. 2022;150: e2021055615.
19. Sudfeld CR, McCoy DC, Danaei G, et. al. Linear growth and child development in low- and middle-income countries: A meta-analysis. Pediatrics. 2015;135:e1266-75.
20. Atiq A, Shah D, Sharma S, Meena RK, Kapoor S, Gupta P. Prevalence and predictors of vitamin B12 deficiency in children with severe acute malnutrition, and its association with development. Indian J Pediatr. Nov 16, 2023. Epub ahead