

Original Research Article

Cranial imaging in children with malnutrition aged 6 to 60 months

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ABSTRACT

Background: India has 57 million or more than a third of the world's 146 million undernourished children. Protein energy malnutrition is associated with cerebral atrophy which may be detrimental to intellectual development. The aim and objective of this study was to study the changes in the brain by cranial imaging in children with malnutrition aged 6 months to 5 years and to correlate these changes with severity of malnutrition.

Methods: It was a hospital based prospective study done in Bal Chikitsalay, Maharana Bhupal government hospital, Udaipur during the study period July 2015 to July 2016. Total 120 children were enrolled, out of which 80 were severely malnourished, 20 were moderately malnourished and 20 normally nourished children undergoing neuroimaging for some other reason taken as controls. All the cases were subjected to CT scan and the following parameters were noted. Central atrophy was evaluated by bifrontal index (BFR) and bicaudate index (BCR). Cortical atrophy was evaluated by width of sylvian fissure (SFW) and widening of interhemispheric fissure (IHD). These parameters were then compared with the severity of malnutrition and among controls. Data was analysed with standard software of biostatistics using parametric tests, Pearson's correlation analysis, ANOVA test and student's t test.

Results: On an average 80% of SAM and 10% of MAM had various degree of cerebral atrophy while none of the controls showed significant degree of cerebral atrophy.

Conclusions: Effect of malnutrition on brain can be objectively assessed by CT indices, BFR, BCR, SFW and IHD to define the degree of cerebral atrophy in the malnourished population.

Keywords: Malnutrition, Neuroimaging, Cerebral atrophy

INTRODUCTION

Malnutrition is one of the most common global health problem, involving hundreds of millions of children in the world, contributing to childhood morbidity, mortality, impaired intellectual development, suboptimal adult work capacity and increased risk of diseases in adulthood.^{4,5} Protein-energy malnutrition produces notable morphological changes in the brains of children suffering from malnutrition and leads to cerebral atrophy. In brain tissue, atrophy describes a loss of neurons and the connections between them. These changes damage the

intellectual potential of those who survive and limit their capacity to become part of the competitive world.^{6,7} Nutritional inadequacy remains one of the major non genetic factors affecting development of brain leading to permanent deficits in learning and behaviour.⁸ There is evidence that the earlier the dietary insult, the more severe and permanent are its effects.⁸ The studies in experimental animals in the west and children in developing countries have revealed the adverse effects of PEM on the biochemistry of developing brain which have been described in children in clinical data, biochemical studies, reduction in brain size, neuro-CT scan, magnetic

resonance imaging (MRI).^{9,10} Brain size is reduced as the result of changes in structural proteins, growth factor concentrations and neurotransmitter production.⁷ The cortex and hippocampus appear to be particularly vulnerable to protein-energy malnutrition.¹¹ Hence the present study was planned with the objective to study the changes in the brain by cranial imaging in children with malnutrition aged 6 months to 5 years and to correlate these changes with severity of malnutrition so that early recognition can save the intellectual potential of these children before becoming irreversible.

METHODS

This was a hospital based prospective study on children aged 6 months to 5 years with moderate to severe malnutrition, admitted in nutritional rehabilitation centre of a tertiary care centre in north India (Bal Chikitsalay, Maharana Bhupal government hospital, Udaipur) during the study period July 2015 to July 2016. The sample size was calculated by WHO anthropo calculator. Children having history of perinatal insult, NICU admissions, any evolving central nervous system disease or secondary malnutrition were excluded from the study. The controls were taken as children of similar age group with normal nutritional status undergoing CT scan for some other reason like simple head trauma or sporadic convulsions whose CT scans were reported as normal by radiologist.

The anthropometric measurements (weight, height, weight for height, MUAC) were taken as per standard protocol and were classified in to moderate and severe SAM as per WHO child growth standards Z score charts multicentre growth reference study (MGRS). All the cases qualifying inclusion criteria were subjected to CT scan using Philips brilliance 16 slice MDCT scan and the following parameters were noted (Figure 1). Central atrophy (dilatation of the ventricles) was evaluated by bifrontal index and bicaudate index (Table 1).¹² Cortical atrophy was evaluated by SFW and widening of interhemispheric fissure (6-11mm) (Table 2).¹²

All the collected data was managed and analysed with standard software of biostatics (SPSS version 20). Results are expressed as mean±standard deviation for continuous variables and as number (%) for categorical data. Parametric tests were used for statistical analysis. Differences between CT variables of malnourished children and the controls with same age were determined by student’s t test (independent group t test). Pearson’s correlation analysis were used to determine correlations between different variables. Multiple groups were compared using the ANOVA test. For all tests, the difference was considered significant if the probability p<0.05. Ethical clearance was taken from the ethical committee of the institution before starting the study. Patients were enrolled after written and informed consent from their parents.

Table 1: Evaluation of central atrophy (dilatation of the ventricles) by the bifrontal index*.¹²

Degree of atrophy	Range (in mm)	Mean (in mm)	Standard deviation (in mm)
Normal	<0.28	0.26	0.054
Mild	0.28-0.32	0.30	0.013
Moderate	0.33-0.37	0.35	0.017
Severe	>0.38	0.41	0.034

*Bifrontal index (BFR) is bifrontal diameter (FH) divided by the distance between the inner table of the skull at the same level (ITfh); where bifrontal diameter is the distance between the widest extent of the two frontal horns; (BFR=FH/ITfh) (all measurements determined in mm on the photograph).

Table 2: Evaluation of cortical atrophy by the width of sylvian fissure*.^{12,14}

Degree of atrophy	Range (in mm)	Mean (in mm)	Standard deviation (in mm)
Normal	0-6	4.7	1.16
Mild	6-9	7.8	0.68
Moderate	9-11	10.4	0.96
Severe	>11	14.7	2.40

*Width of sylvian fissure was taken as the average of the maximum width of two sylvian fissure at its anterior-posterior diameter on the section showing them at their widest

Bicaudate index (BCR)

It is bicaudate diameter(CC) divided by the distance between the inner table of the skull at the same level (ITcc). Where bicaudate diameter is the minimum

distance between the lateral ventricles where the caudate nuclei produces the maximum indentation.¹³

$$BCR = \frac{CC}{ITcc}$$

Cut off for defining cerebral atrophy in the study was taken as 0.14.¹²

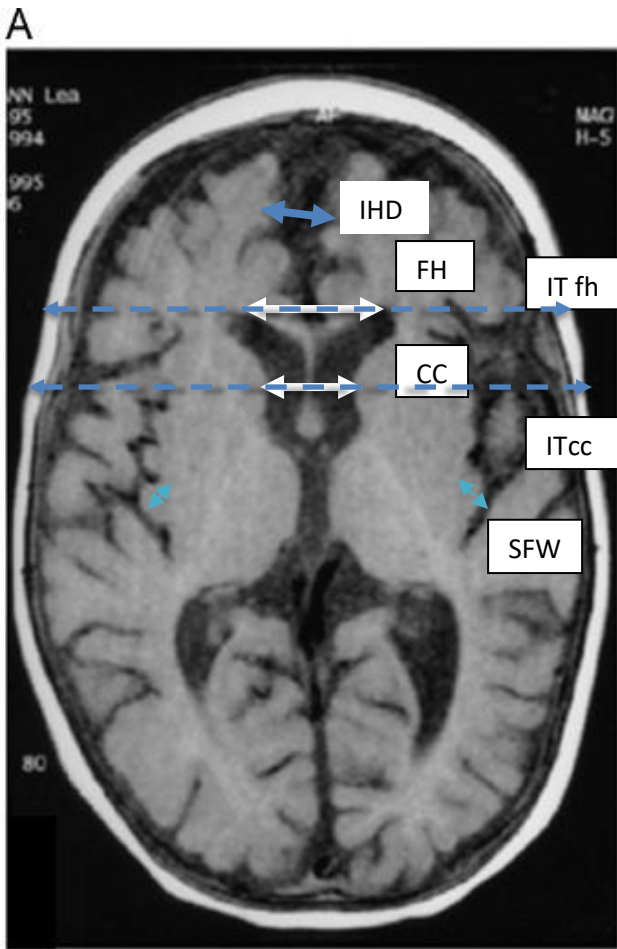


Figure 1: CT brain of a severely malnourished child with cerebral atrophy showing the measurements taken for study.

*IHD=interhemispheric distance, FH=bifrontal diameter, CC=bicaudate diameter, SFW=sylvian fissure width, ITfh=distance between the inner table of the skull at the level of bifrontal diameter, ITcc=distance between the inner table of the skull at the level of bicaudate diameter.

The interhemispheric fissure, also known as the medial longitudinal fissure, is a deep groove located in the midline between both cerebral hemispheres and contains the falx cerebri.^{15,16} All the CT variables were measured by one person only after taking training from the radiologist.

RESULTS

In this study 120 children were enrolled, out of which 80 were severely malnourished (WHZ score <-3 SD), 20 were moderately malnourished (WHZ score <-2 SD) and 20 normally nourished children undergoing neuroimaging for some other reason taken as controls. Most of the children (57.5%) were in the age group of 12-36 months followed by 6-11 months (34.16%).

Bifrontal index was taken as a measure of central atrophy. Majority of SAM (80%) population had some degree of central atrophy, mild (BFR 0.28-0.32, 43.75%), moderate (BFR 0.33-0.37, 31.25%) followed by severe (BFR >0.38, 21.25%) while only 21.25% had normal (BFR <0.28) scan. 10% of MAM population showed only mild atrophy. None of the control population had central atrophy (p<0.001) (Table 3).

Bicaudate index is also taken as a measure of central atrophy. 77.5% of SAM population had abnormal bicaudate index (BCR >0.14) and only 22.5% had normal bicaudate index (BCR <0.14) while only 15% in MAM and none in control showed abnormal bicaudate index (p<0.001) (Table 4).

Table 3: Evaluation of cerebral atrophy by BFR.

BFR	SAM		MAM		Control	
	Number	%	Number	%	Number	%
<0.28 (normal)	16	21.25	18	90	20	100
0.28-0.32 (mild cerebral atrophy)	28	43.75	2	10	0	0
0.33-0.37 (moderate cerebral atrophy)	33	31.25	0	0	0	0
>=0.38 (severe cerebral atrophy)	3	21.25	0	0	0	0
<0.001 (HS)						

*BFR (bifrontal index), SAM (severe acute malnutrition), MAM (moderate acute malnutrition).

Table 4: Evaluation of central atrophy by BCR.

BCR	SAM		MAM		Control	
	Number	%	Number	%	Number	%
<=0.14 (normal)	18	22.5	17	85	20	100
>0.14 (abnormal)	62	77.5	3	15	0	0
<0.001 (HS)						

*BCR (bicaudate index), SAM (severe acute malnutrition), MAM (moderate acute malnutrition).

Table 5: Evaluation of cortical atrophy by SFW.

SFW (in mm)	SAM		MAM		Control	
	Number	%	Number	%	Number	%
0-6 (normal)	29	36.25	18	90	20	100
>6-9 (mild cerebral atrophy)	24	30	2	10	0	0
>9-11 (moderate cerebral atrophy)	25	31.25	0	0	0	0
>11 (severe cerebral atrophy)	2	2.4	0	0	0	0
	<0.001 (HS)					

*SFW (sylvian fissure width), SAM (severe acute malnutrition), MAM (moderate acute malnutrition).

Table 6: Evaluation of cerebral atrophy by the width of the interhemispheric fissure distance (IHD).

IHD (in cm)	SAM		MAM		Control	
	Number	%	Number	%	Number	%
0-3 (normal)	3	3.75	16	80	19	95
3-6 (mild cerebral atrophy)	36	45	4	20	1	5
6-9 (moderate cerebral atrophy)	27	33.75	0	0	0	0
>9 (severe cerebral atrophy)	14	22.5	0	0	0	0
	<0.001 (HS)					

*IHD (interhemispheric distance), SAM (severe acute malnutrition), MAM (moderate acute malnutrition).

Table 7: CT scan variables in study groups (BFR/BCR/SFW/IHD).

Age	CT variables	SAM (mean±SD)		MAM (mean±SD)		Control (mean±SD)	
6 months to <1 year	BFR	0.32	0.05	0.27	0.00	0.25	0.03
	BCR	0.16	0.03	0.12	0.02	0.12	0.01
	SFW	6.50	2.35	3.34	1.36	2.77	1.42
	IHD	7.93	2.21	3.97	2.02	3.53	1.80
1-3 years	BFR	0.32	0.04	0.27	0.02	0.24	0.03
	BCR	0.17	0.04	0.13	0.02	0.12	0.02
	SFW	7.17	2.62	4.55	1.46	2.31	0.55
	IHD	8.54	2.63	3.36	1.97	2.53	0.68
>3 – 5 years	BFR	0.31	0.04	0.26	0.01	0.24	0.01
	BCR	0.16	0.04	0.13	0.02	0.11	0.05
	SFW	6.27	3.14	5.20	0.14	2.58	0.88
	IHD	7.73	2.95	5.80	4.10	2.40	0.85

* BFR (bifrontal index), BCR (bicaudate index), SFW (sylvian fissure width), IHD (interhemispheric distance), SAM (severe acute malnutrition), MAM (moderate acute malnutrition).

SFW taken as a measure of cortical atrophy. Majority (63.75%) of the SAM population had some degree of atrophy mild (SFW >6-9 mm) in 30%, moderate degree (SFW >9-11 mm) in 31.25% and severe (SFW >11 mm) in 2.4% while only 36.25% had normal SFW (SFW 0-6 mm). 10% of MAM population also showed mild atrophy and no atrophy was seen in control group (p<0.001) (Table 5).

Interhemispheric distance (IHD) was taken as the second measure of cortical atrophy on CT scan. Majority (96.25%) of SAM children had some degree of cerebral atrophy, with mild atrophy (IHD >6-9 mm) seen in 36 children (45%), moderate atrophy (IHD >9-11 mm) seen

in 27 (33.75%) children and severe atrophy (IHD >11 mm) seen in 14 children (22.5%). Only 3 children (3.75%) had normal IHD (SFW 0-6 mm). Mild degree of atrophy was also seen in 20% of MAM children and 5% of controls (p<0.001) (Table 6).

We saw that mean values of all the CT measurements of cerebral atrophy increases with severity of malnutrition indicating increasing degree of cerebral atrophy and are significantly higher than the controls (p<0.001). In controls mean values of CT measurements (BFR/BCR/SFW/IHD) further decreases with age but not significantly while very less difference was noted in CT measurements of children upto 3 years of age (Table 7).

DISCUSSION

Malnutrition in children is one of the most common health problem affecting almost 45% of children in developing country like India.¹⁷ As already stated effects of malnutrition on the body are protean involving almost all the organ systems in the body. Protein-energy malnutrition produces notable morphological changes in the brains of children suffering from malnutrition.

Many studies have now proved that malnutrition has a detrimental and long lasting effect on brain and may leads to cerebral atrophy but only very few studies have given objective measurements to quantify these changes while no study till now has correlated these changes on brain with severity of malnutrition.

CT provides us with a convenient and noninvasive method of examining the morphology of the human brain in vivo. In our study, we evaluated the effect of malnutrition on brain in terms of various linear measurements of brain (BFR/BCR/SFW/IHD) through CT scan and correlated these changes with severity of malnutrition.

We found that for cortical atrophy on evaluating BFR, 80% of SAM population had various degrees of atrophy while in MAM group 10% had mild degree of atrophy. On evaluating BCR, we found that 77.5% of SAM and 15% of MAM population had abnormal BCR. On evaluating cerebral atrophy by FWS, 63.75% of SAM population showed various degrees of atrophy while in MAM population 10% showed mild degree of atrophy. On evaluating IHD, we found that 96.25% of SAM population had various degrees of atrophy, 4% in MAM population had mild atrophy while one patient in control group also had mild degree of atrophy. None of controls showed any degree of atrophy in respect of BFR, BCR and SFW while only one case showed mild degree of atrophy on IHD evaluation. In all the CT indices we found that severity of atrophy increases with severity of malnutrition which was found to be significant ($p < 0.05$).

In a similar study by Tatawy et al on 40 infants aged 12-30 months with protein energy malnutrition, he found that central and cortical atrophy of various degrees was found in 100% of cases, the severity correlating with the duration of protein deficiency where central atrophy (dilatation of the ventricles) was evaluated by the bifrontal index and cortical atrophy was evaluated by the SFW. He also found that the BCR had a mean value of 0.2 (range, $0.150.27 \pm 0.03$), substantially higher than that of the normal controls (0.14), however, it did not show significant correlation with the duration of the disease.¹² In a study by Househam et al on computed tomography of the brain in children aged 1 to 4 years with severe protein energy malnutrition, he found that there was pronounced enlargement of the ventricles and cerebral sulci, indicating a severe degree of cerebral atrophy. The cerebellum was relatively spared and did not show the

severe degree of volume loss seen in the cerebral hemispheres.¹⁸ In a study by Odabas et al in 2004 on cranial MRI findings in children with moderate and severe protein energy malnutrition to determine cerebral abnormalities in malnutrition in childhood, 75% children showed abnormal MRI findings, all of them had cerebral atrophy and 75% had cerebral atrophy plus ventricular dilatation. They concluded that most (75%) children with moderate/severe PEM had abnormal MRI findings and therefore they suggested that children with PEM should be evaluated for cerebral atrophy.¹⁹

Limitations

The results of our study should be considered within its strengths and limitations. Better results could have been interpreted with a larger sample size to understand the prevalence of effects of malnutrition on brain. CT scan though is an easy and good technique to evaluate the morphological changes in brain but MRI could have been even better and radiation free method to evaluate the same. A follow-up repeat neuroimaging after treating malnourished children could have better attributed these changes to malnutrition and tell the nature of reversibility of these changes on treatment.

CONCLUSION

Thus we concluded that malnutrition has a significant adverse effect on the brain as evidenced in our study by the presence of various degree of cerebral atrophy observed in around 80% of children suffering from severe acute malnutrition and around 10% of children suffering from moderate acute malnutrition. We found CT scan indices of cerebral atrophy, BFR and BCR, SFW and IHD as convenient imaging tool to label and grade cerebral atrophy in such children. This could help in determining the prognosis and future cognitive and intellectual potential in children suffering with malnutrition and the urgency of early intervention to stop further damage to their brain.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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