Cranial Magnetic Resonance Imaging (MRI) Changes in Severely Malnourished Children before and after Treatment.

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Abstract: Protein energy malnutrition is an important problem in developing countries. Neurological changes is associated with sever malnutrition. **Aim of Work**: Our study seeks to document the morphological changes in the brain of infants suffering from severe malnutrition of both edematous and non-edematous types and to follow up these changes and its outcome after nutritional rehabilitation according to the WHO regimen using cerebral MRI imaging. **Patients and Methods:** Seventeen children suffering from severe malnutrition were included in this study. Patients included 7 males and 10 females and their ages ranged from 2 to 24 months who had attended Minia University outpatient clinic. All the children were evaluated and treated in hospital according to WHO standardized protocol for management of severe malnutrition. Patients were referred to Radiology Department for MRI of their brains on admission and again after 90 days of treatment. **Results:** Cerebral atrophy and ventricular dilatation are common findings in the brains of children suffering from moderate and severe PEM. Children with both edematous and non-edematous types of PEM are almost equally affected. However, the changes are reversible in most cases when nutritional rehabilitation is undertaken. Brain myelination process doesn't show significant delay in these patients and the brain stem and cerebellum were normal in all of them. **Conclusion:** Severely malnourished children should be evaluated by Z score and treated by WHO recommendation. Cranial MRI findings in these patients include brain atrophy and ventricular dilatation but these changes are reversible so, early treatment is very important and can help to prevent permanent neurological derangements.

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1. Introduction

Still, up till now in the 21 century, Protein energy malnutrition (PEM) is an important public health problem in the developing countries. (PEM), a natural ramification of poverty, continues to be a perennial source of concern to a large segment of the world population. The developing nervous system of a child is especially vulnerable to deprivations in nurture. Peripheral nerve and muscle derangements are clinically evident by weakness, hypotonia and hyporeflexia in accordance with severity and duration of PEM. [(1)]

The brain of the child is one of the most vulnerable organs affected during growth with potential morphological changes, which can be detectable with neuroimaging technology. [(2)] Several neuropathological studies of the brain have shown that PEM may have adverse impact on the number of neurons and synapses, degree of myelination, and total cerebral lipid content of the developing brain .[(3)]

Previous cranial imaging studies of the brain in patients with protein energy malnutrition (PEM) showed that cerebral atrophy and ventricular dilatation are common findings [(4)] but, fortunately these cranial changes are reversible after achieving nutritional rehabilitation[(5)].

The present study seeks to document the morphological changes in the brain of infants suffering from acute severe malnutrition of both edematous and non edematous types and to follow up these changes and its outcome after nutritional rehabilitation by the standardized WHO regimen using cranial MR imaging.

2.Patients and Methods

This prospective study included seventeen children with age range (2 to 24 months), who had attended Minia University outpatient clinic over the period from May 2010 to May 2011 suffering from severe protein energy malnutrition and failure to thrive. Children were clinically examined and their measurements including weight, height and mid upper arm circumference (MUAC) were taken and plotted using the National Centre for Health Statistics reference values NCHS/WHO. The children were considered to have severe acute malnutrition if they had any of the following:

1- Height for age -2 SD from the median (z-scores) of normal child.

2- MUAC measurement under 11.0 cm.

3- Edema in both feet and legs.

All the children were evaluated and examined for presence of any complications as gastro-enteritis (GE), pneumonia and sepsis. Laboratory investigations including complete blood count, serum creatinine and urea, stool analysis, and electrolytes and serum albumin had been carried out.

Our patients were treated in hospital according to WHO standardized protocol for management of severe malnutrition which includes the following essential ten steps [(6)]:

1- Treat/prevent hypoglycemia
2- Treat /prevent hypothermia
3- Treat/prevent dehydration
4- Correct electrolyte imbalance
5- Treat/prevent infection
6- Correct micronutrient deficiencies
7- Start cautious feeding
8- Achieve catch up growth
9- Provide sensory stimulation and emotional support
10- Prepare for follow up after recovery

Patients were considered for hospital discharge when their weight for height reached 90% of median.[(6)]

All 17 patients were referred to Radiology Department for MR imaging of their brains on admission and again after 90 days of treatment. T1 and T2 weighted sagittal and axial MRI images were acquired as well as fluid attenuation inversion recovery (FLAIR) sequences using General Electric 0.2 T open MRI system.

3. Results

Seventeen children suffering from severe malnutrition were included in this study. Patients included 7 males and 10 females and their age ranged from 2-24 months.

The children were classified clinically on admission into 2 groups according to presence or absence of edema into 9 edematous and 8 non-edematous **(Table 1).** There was no significant correlation between the presence of edema and age, sex, weight, length and /or head circumference. But there was significant correlation between the presence of edema and the child's weight for height Z score number with *P* value 0.01.

Table (2) shows that edema was more common in children presented with gastroenteritis (*P*-value = 0.01) than in children presented with complications other than gastroenteritis like pneumonia, sepsis and/ or convulsion. Results of laboratory investigations showed no significant difference between edematous & non-edematous groups except for the presence of RBCs in the stool analysis of children with gastroenteritis (*P* = 0.002) (**Table 3**).

All children were treated in our hospital according to WHO standardized protocol for management of severe malnutrition.

Table (1) Demographic characteristics of 17 severely malnourished children on admission

	Edematous malnutrition (NO = 9)	Non edematous malnutrition (NO = 8)	*P* -Value
Age (months) mean ± SD	9.2±7.04	6.4±3.7	0.3
Sex:			0.6
Male No (%)	3 (33.3%)	4 (50%)	
Female No (%)	6(66.7%)	4 (50%)	
Weight(kg) mean ±SD	5.2±2.6	3.7±1.01	0.1
length (cm) mean ±SD	57.3±7.5	64.4±11.5	0.1
Head circumference (cm) mean±SD	41.4±3.7	38.8±3.5	0.1
Weight for height Z score No (%)			0.01
<-2 SD	6 (66.7%)	0 (0)	
<-3 SD	3 (33.3%)	6 (75%)	
<-4 SD	0 (0)	2 (25%)	

Table (2) Associated complications in severely malnourished children

	Edematous malnutrition (NO = 9)	Non edematous malnutrition (NO = 8)	*P*- Value
Pneumonia (%)	0	2 (25%)	-
Gastroenteritis (%)	7 (77.8%)	2 (25%)	0.01
Sepsis (%)	1 (11.1%)	2 (25%)	0.2
Convulsions*	1 (11.1%)*	0	-

*Convulsions in this patient was related to hypocalcaemia

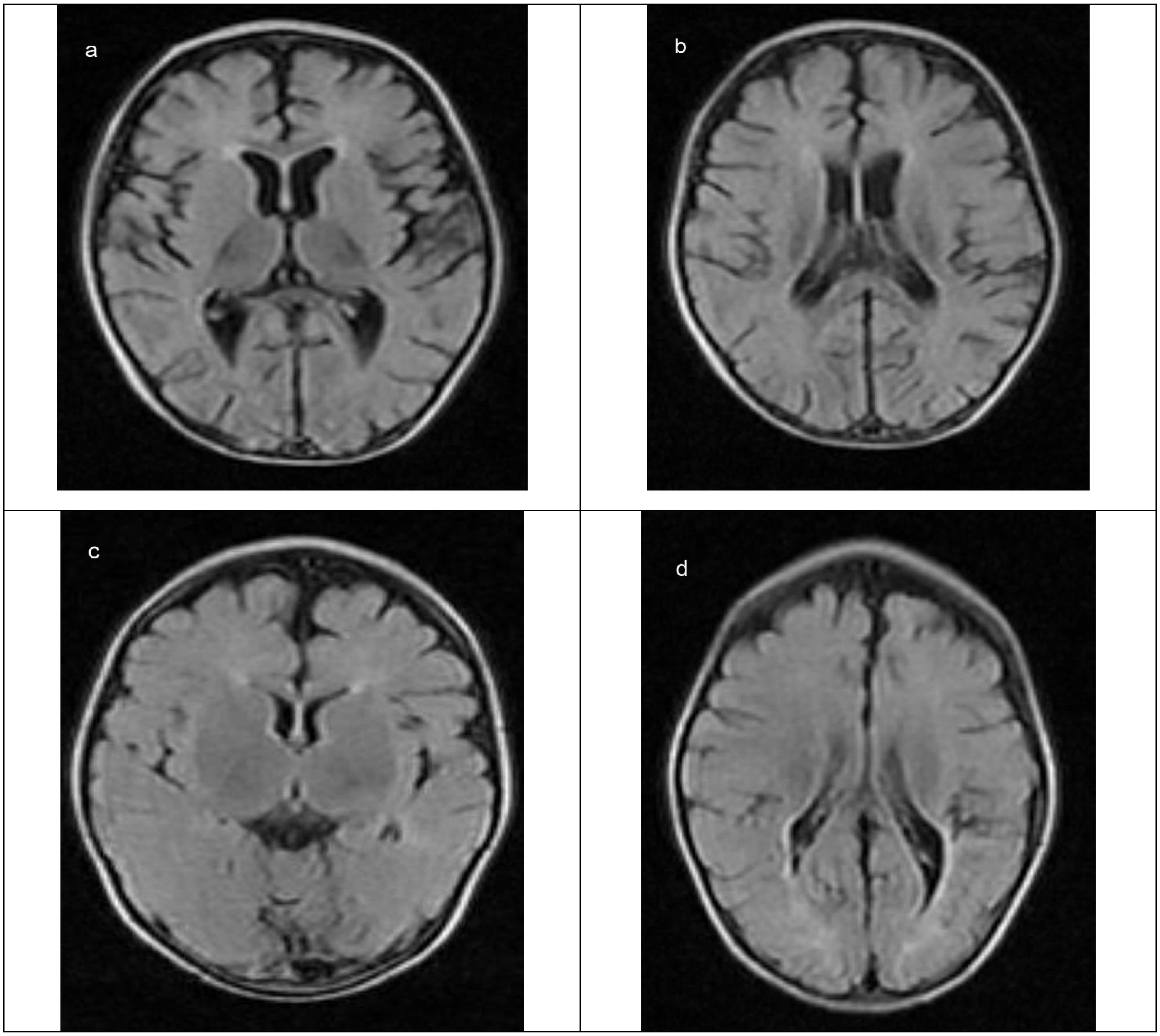

Fig. 1 Axial FLAIR MR images at the level of the basal ganglia. **a** and **b** 10 months old patient on admission showing mild brain atrophy in the form of dilated ventricles and prominent cortical sulci. **c** and **d** follow-up MRI of the same patient at day 90 after treatment showing resolution of the signs of cerebral atrophy with normal ventricular size and cortical sulci.

Table (3): Laboratory findings in severely malnourished children.

	Edematous malnutrition (NO = 9)	**Non edematous malnutrition (NO = 8)**	***P*- Value**
Hb (gm/dl)	9.4±1.5	10.5±1.03	0.4
WBCs ($\times 10^3$)	9.08±3.9	11.8±4.8	0.2
Platelets ($\times 10^3$)	364.8±163.5	502.1±221.2	0.1
Stool: pus cells	2.8±0.7	2±1.6	0.1
RBCs	5.1±4.9	35.6±18.5	0.002
Urine: pus cells	3.2±2.6	3.5±2.01	0.7
RBCs	2.2±1.6	2.2±1.9	0.9

Table (4): Cerebral MRI findings in severely malnourished children.

	Edematous malnutrition (No = 9)	Non edematous malnutrition (No = 8)	*P*- Value
Dilated ventricles	5 (55.6%)	5 (62.5%)	0.3
Cerebral atrophy	7 (77.8%)	7 (87.5%)	0.3
PVWM changes	1 (11.1%)	3 (37.5%)	0.1

Table (5). The distribution of patients according to the degree of cerebral atrophy as seen by MRI on admission and on follow-up

Degree of cerebral atrophy	14 patients with cerebral atrophy		*P*- Value
	On admission	On day 90	
Mild	2 (14.3%)	0	0.2
Mild to Moderate	7(50%)	0	
Moderate	5(35.7%)	2 (14.3%)	

All 17 children included in this study had MRI scans of their brains on admission and on follow-up at 90 days later. Fourteen patients (82%) had positive MR findings on admission consistent with cerebral atrophy while 3 (18%) patients had normal MRI scans. The abnormalities included all or some of the following: widened cortical sulci and sylvian fissures, widened interhemispheric fissures and cerebellar folia, dilated ventricles and enlarged basal cisterns. In addition, 4 patients (28%) had periventricular white matter (PVWM) changes (**Table 4**). There was no significant difference between both edematous and non edematous groups regarding the MRI findings. The degree of cerebral atrophy was determined as mild, mild to moderate or moderate. In two children the changes were mild, in seven they were mild to moderate and in five they were moderate (**Table-5**). Ventricular dilatation, particularly the frontal horns of the lateral ventricles was found in 10 (71%) of 14 patients with cerebral atrophy. On follow-up MRI scans performed 90 days later, the degree of cerebral atrophy had improved in 2 patients and completely resolved in 12 (86%) patients (Figure 1). Grey and white matters of the cerebral hemispheres were equally affected while the brain stem and the cerebellum did not show any abnormality in any of our patients. The myelination distribution appeared to be appropriate for age with no myelination delay detected in any of the examined children.

4. Discussion

In our study we demonstrated that there was significant correlation between the presence of edema and the child's weight for height Z score number with P value 0.01, that was coming in harmony with the results of Bhoomika et al., 2008 that concluded that using Z score system is the best way to determine degree of malnutrition(7).

Also we found that, edema was more common in children presented with gastroenteritis ($P = 0.01$) than in children presented with other complications .The results of laboratory investigations showed no significant difference between edematous and non-edematous groups except for the presence of RBCs in the stool analysis of children with gastroenteritis ($P = 0.002$) and that come in agreement with the results got by Pawellek et al., 2008,who found that PEM is most frequently associated with acute infections, especially gastroenteritis and chronic diarrhea (8) .

Several neuropathological studies of the brain have shown that PEM may have adverse impact on the number of neurons and synapses, degree of myelination, and total cerebral lipid content of the developing brain(3).

In the present study we found that cerebral atrophy and dilated ventricles were the commonest MRI findings seen in the children suffering from severe malnutrition and that comes in concordance with the study carried by Atalabi et al., 2010 (2).

The majority of children with acute protein energy malnutrition in this study (82%) showed MRI features of cerebral atrophy. Researchers in earlier studies demonstrated similar results using computed tomography (CT) (5) and MRI (2). In order to investigate whether these cerebral atrophic changes are reversible or not, researchers have monitored these changes during nutritional rehabilitation and reported complete resolution by day 90 in the majority of their patients (7). Likewise, in this study the results on follow-up brain scans came to confirm significant improvement after nutritional rehabilitation and documented complete resolution of the findings in 12 of 14 patients with initial cerebral atrophy of different degrees. The pathophysiologic changes leading to cerebral atrophy in children with protein energy malnutrition, however, remained a subject of research and postulations. Gunston et al., suggested that loss of myelin lipid accounts for the cerebral shrinkage seen in their patients and restoration of lipid to the myelin membrane with refeeding accounts for the reversal of cerebral shrinkage (7). However, in their study as well as in our study there was no significant nutritional impact on the myelination process and it was regarded as normal for the patient's age. In another patient population with anorexia nervosa, Heinz et al have reported reversible cerebral atrophy and proposed that fluid moves out of intravascular spaces as a result of decreased colloid osmotic pressure and floods the subarachnoid spaces, dilates the ventricles, and widens the cisternal spaces and sulci. When nutrition is improved the plasma proteins rise, and the extracellular fluid moves back into the intravascular space (9,10). Although it was once postulated that loss of myelin lipid accounts for the cerebral shrinkage (7), our study demonstrated that the myelination process was determined as appropriate for age. Likewise, Hazin et al., (11) reported myelination delay in only 2 of their series of 20 children with severe PEM

Conclusion

Cerebral atrophy and ventricular dilatation are common findings in the brains of children suffering from moderate and severe PEM. Children with both edematous and non-edematous types of PEM are almost equally affected. However, the changes are reversible in most cases when nutritional rehabilitation is undertaken. Brain myelination process doesn't show significant delay in these patients and the brain stem and cerebellum are normal in all of them.

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