

## Neuroimaging (MRI) in Children with Microcephaly and Severe Acute Malnutrition

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### Abstract

**Objective:** To study the change in brain by neuroimaging (MRI brain) in children with microcephaly and severe acute malnutrition aged 1 month to 60 months.

**Materials and Methods:** Children attending Bal Chikitsalaya, Maharana Bhupal Government Hospital, RNT Medical College, Udaipur (Rajasthan) were evaluated as per protocol. Microcephaly was defined as head circumference (HC) less than 3 SD or Z score < -3. Nutrition status of microcephaly children was recorded using weight for height criteria. Change in brain was evaluated by neuroimaging (MRI).

**Results:** 65 children with microcephaly and SAM were enrolled in the study. 38(58.46%) were male and 27(41.54%) were female. Male to female ratio was 1.41:1. Most children presented with developmental delay 64(98.46%), abnormal tone 46(70.77%), convulsion 9(16.98%), regression of mile stone 5(7.69%) and tremor 5(7.69%). Anaemia was present in 62(95.38%) children. Among these children, TMBE 4(44.44%) was most common cause of convulsion followed by malaria 2(22.22%), hypocalcemia 2(22.22%) & pyogenic Meningitis 1(11.11%). The most frequent MRI findings were cerebral atrophy in 42(64.62%) cases followed by finding of TBME with diffuse cerebral atrophy in 5(7.69%), diffuse cerebral atrophy with periventricular leucomalacia in 2(3.08%), diffuse cerebral atrophy with delayed myelination in 1(1.54%), hypomyelination/delayed myelination in 1(1.54%), leucomalacia with delayed myelination in 1(1.54%) and periventricular leucomalacia in 1(1.54%).

**Conclusion:** Most children with Microcephaly and SAM had developmental delay, anaemia, abnormal tone, regression of mile stone and convulsion. Cerebral atrophy was most frequent finding on neuroimaging (MRI).

**Keywords:** Cerebral atrophy, Developmental delay, Microcephaly, Neuroimaging, SAM

### Introduction

Microcephaly is a descriptive term that refers to a cranium that is significantly smaller than the standard for the individual's age and sex. It should usually be considered as a neurologic sign and defined as "Occipitofrontal head circumference (OFC) more than 3 SDs below the mean for age and gender due to small brain<sup>[5,9,20]</sup>. Microcephaly may be described as primary and secondary. Primary microcephaly in which the brain fails to grow to the correct size during pregnancy<sup>[4]</sup>. Secondary (also known as acquired) microcephaly is a condition in which a child's head circumference is within the normal range at birth and for an undefined period thereafter, but then does not increase as fast as normal and result in small head(microcephaly)<sup>[6]</sup>.

Malnutrition is a worldwide health problem, exists in many forms, affects the developing and mature nervous system, and has acute and chronic health implications. The rapidly developing brain is more vulnerable to nutrient insufficiency yet also demonstrates its greatest degree of plasticity. Certain nutrients have greater effects on brain development than do others. These include protein, energy, certain fats, iron, zinc, copper, iodine, selenium, vitamin A, choline, and folate. Nutrients and growth factors regulate brain development during fetal and early postnatal life. The developing brain between 24 and 42 wk of gestation is particularly vulnerable to nutritional insults because of

the rapid trajectory of several neurologic processes, including synapse formation and myelination<sup>[12]</sup>. Nutrients are necessary not only for neurons but also for supporting glial cells. For any given region, early nutritional insults have a greater effect on cell proliferation, thereby affecting cell number<sup>[16,19]</sup>. Later nutritional insults affect differentiation, including size, complexity, and in the case of neurons, synaptogenesis and dendritic arborization. Nutrients can affect not only neuroanatomy, but also neurochemistry and neurophysiology. Neurochemical alterations include changes in neurotransmitter synthesis, receptor synthesis, and neurotransmitter reuptake mechanisms<sup>[7,15]</sup>.

Malnutrition is one of the causes of microcephaly<sup>[4]</sup>. Comprehensive study on change in brain of children with microcephaly and SAM is not available in the literature. Hence the present study has been planned with aims to study the change in brain by neuroimaging (MRI brain) in children with microcephaly and severe acute malnutrition.

### Materials and Methods

65 children with microcephaly and SAM were enrolled in the study. The study was conducted on all the children aged 1 month to 60 months with microcephaly (HC < -3SD) and SAM admitted in Bal Chikitsalaya, Maharana Bhupal Government Hospital, RNT medical college, Udaipur, Rajasthan, India during a period of 12 months from January 2015 to December

2015. Approval was taken from the hospital ethical committee. A written informed consent was taken from the parents. The head circumference was measured by placing a non-stretchable tape around the cranial vault to include the widest part of the forehead and the most prominent part of the occipital area to arrive at the largest possible measurement<sup>[4]</sup>. Microcephaly was defined as head circumference (HC) less than 3 SD or Z score < - 3. WHO growth charts were used for assessing anthropometric parameters<sup>[11]</sup>. Detailed history (antenatal, natal, postnatal, developmental and family), general and systemic examination was carried out. Screening of developmental delay by Denver developmental screening-II<sup>[18]</sup>.

**Investigation:** Neuroimaging (MRI Brain) was done in all children included in the study. The head coil was used for the scan. It was performed on 1.5 Tesla unit (Philips achiva machine) using a head coil. Cerebral atrophy was defined by bifrontal index<sup>[17]</sup>, bicaudate index<sup>[10]</sup> and width of sylvian fissure<sup>[18]</sup>. All the collected data was managed and analysed with standard software of Biostatics (SPSS Version 20).

## Results

65 children with microcephaly and SAM were enrolled in the study. 38(58.46%) were male and 27(41.54%) were female. Male to female ratio was 1.41:1. Most of the children 60(92.31%) were admitted because of not growing well/ loss of weight/ not eating well Primary SAM was present in 50(76.92%) children and 15(23.08%) children had secondary SAM. Among these children, TBME 4(26.67%) and cerebral palsy 4(26.67%) were two most common cause of secondary SAM followed by Tubercular pneumonia 2(13.33%), VACTERL Association 1(6.67%), Down syndrome 1(6.67%), Goldenhar Syndrome 1(6.67%), Tracheoesophageal fistula 1(6.67%) and Celiac disease 1(6.67%). Most of SAM children 59(90.77%) were from lower (Class IV & V) socioeconomic class followed by middle (Class II & III) 6(9.23%) socioeconomic class. Most of mother 44(67.69%) of children were found undernourished (BMI < 18.5kg/m<sup>2</sup>). Among children, intra uterine growth retardation (IUGR) 14(21.54%) and preterm 6(9.23%) were two most adverse perinatal events. Respiratory illnesses were most common (43.07%) associated disease in children with microcephaly and SAM followed by UTI (9.23%), diarrhea (7.69%), TBME (7.69%), malaria (6.15%) & Septicemia (3.07%).

Table (1) demonstrates the clinical profile of the children with microcephaly and SAM. Most children with microcephaly and SAM presented with developmental delay 64(98.46%), abnormal tone 46(70.77%), convulsion 9(16.98%), regression of mile stone 5(7.69%) and tremor 5(7.69%). Anaemia was present in 62(95.38%) children. Among these children, TMBE 4(44.44%) was most common cause of

convulsion followed by malaria 2(22.22%), hypocalcemia 2(22.22%) & pyogenic Meningitis 1(11.11%).

Table (2) demonstrates the change in brain by neuroimaging (MRI brain) in children with microcephaly and SAM. Neuroimaging (MRI) was found abnormal in 53(81.54%) children. Normal brain MRI was seen in 12(18.46%) children. Among the children with microcephaly and SAM, cerebral atrophy (dilated ventricle, prominent sylvian fissures) was seen in 42(64.62%) – 41 children with diffuse cerebral atrophy & 1 child with focal (frontal) cerebral atrophy. Finding of TBME with diffuse cerebral atrophy (dilatation of ventricle, periventricular CSF oozing, tuberculomas, increased vascularity & post contrast meningeal enhancement) was seen in 5(7.69%) children. Diffuse cerebral atrophy with periventricular leucomalacia was seen in 2(3.08%) children. Diffuse cerebral atrophy with delayed myelination was seen in 1(1.54%) child. Hypomyelination/delayed myelination was seen in 1(1.54%) child. Leucomalacia with delay myelination was seen in 1(1.54%) child. Periventricular leucomalacia was seen in 1(1.54%) child.

Table (3) demonstrates the change in brain by neuroimaging (MRI brain) in children with primary SAM. Neuroimaging (MRI) was found abnormal in 40(80%) children. Among the children with microcephaly and primary SAM, diffuse cerebral atrophy was seen in 38(76%) children. Diffuse cerebral atrophy with delayed myelination was seen in 1(2%) child. Hypomyelination/delayed myelination was seen in 1(2%) child.

**Table 1: Clinical profile of the children with microcephaly and SAM**

S. No.	Clinical feature		No. of children (%)
1	Developmental delay		64(98.46%)
2	Anaemia		62(95.38%)
3	Abnormal tone	i. Hypertonia	41(63.08%)
		ii. Hypotonia	5(7.69%)
4	Convulsion	i. Generalised	8(12.31%)
		ii. Focal	1(1.54%)
5	Regression of mile stone		5(7.69%)
6	Tremor		5(7.69%)

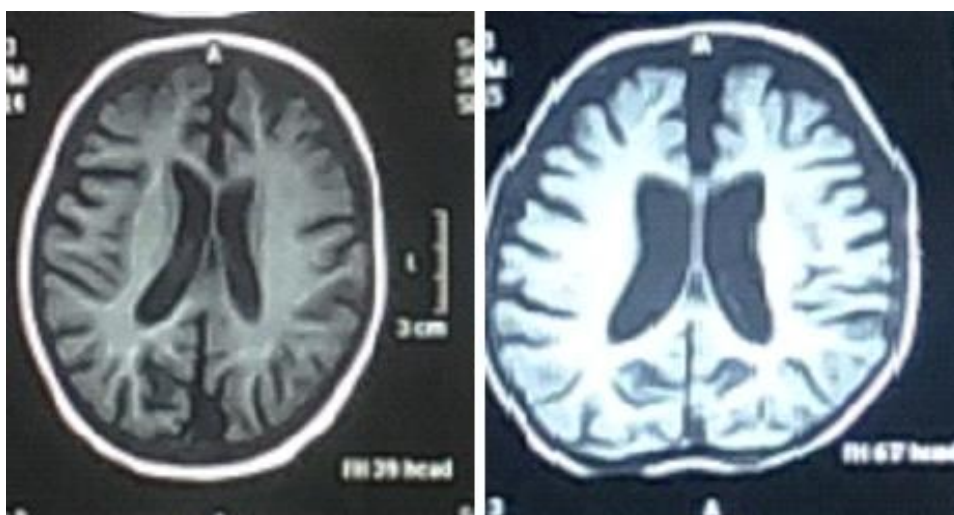
**Table 2: Neuroimaging (MRI brain) in children with microcephaly and SAM**

S. No.	Neuroimaging finding		No. of children (%)
1	Cerebral atrophy	Diffuse	41(63.08%)
		Focal	1(1.54%)
2	TBME with diffuse cerebral atrophy		5(7.69%)
3	Diffuse cerebral atrophy with periventricular leucomalacia		2(3.08%)
4	Diffuse cerebral atrophy with delayed myelination		1(1.54%)
5	Hypomyelination/delayed myelination		1(1.54%)
6	Leukomalacia with delay myelination		1(1.54%)
7	Periventricular leucomalacia		1(1.54%)
8	Normal		12(18.46%)

**Table 3: Neuroimaging (MRI brain) in children with primary SAM**

S. No.	Neuroimaging finding		No. of children (%)
1	Diffuse cerebral atrophy		38(76%)
2	Diffuse cerebral atrophy with delayed myelination		1(2%)
3	Hypomyelination/delayed myelination		1(2%)
4	Normal		10(20%)

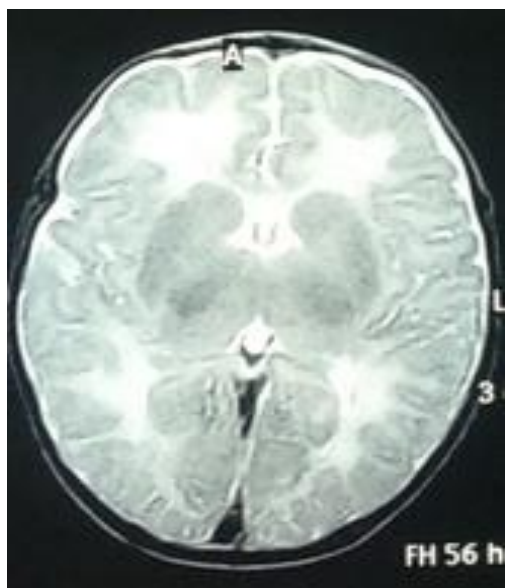
### Some Important Neuroimaging of Children with Microcephaly and SAM

**Fig. 1****Fig. 2**

**Fig. 1 & 2: T1 weighted MRI images shows diffuse cerebral atrophy in the form of dilatation of ventricular system and prominence of cortical sulci & fissures with loss of volume of white matter.**



**Fig. 3: T2 weighted MRI image shows diffuse cerebral atrophy in the form of dilatation of ventricular system and prominence of cortical sulci & fissures with delayed myelination**



**Fig. 4: T2 weighed MRI image shows symmetrical abnormal signals in the periventricular white matter of frontal & parietal lobes appears hyperintense, suggestive of periventricular leukomalacia.**

### Discussion

65 children with microcephaly and SAM were enrolled in the study. Higher prevalence of severe degree of malnutrition in children with microcephaly has been reported in other study<sup>[14]</sup>. 38(58.46%) were male and 27(41.54%) were female. Male to female ratio was 1.41:1. Higher prevalence of microcephaly among male children have been observed in other studies<sup>[2,11,14]</sup>. Most of SAM children 59(90.77%) were from lower (Class IV & V) socioeconomic class

followed by middle (Class II & III) 6(9.23%) socioeconomic class. Most of mother 44(67.69%) of children were found undernourished (BMI < 18.5kg/m<sup>2</sup>).

The lower socioeconomic strata, illiteracy - specially of mothers, determine the microenvironmental factors such as the quality of care during prenatal, perinatal and postnatal periods, nutrition, sanitation etc., in which the child develops. These, in turn, predispose the children to recurrent infections and malnutrition. The child's own apathy or inactivity due to these factors and/or due to the deficits resulting from microcephaly with mental retardation, and, perhaps the deformity in more severe forms, may lead to neglect and under stimulation of these children.

In the present study most children with microcephaly and SAM presented with developmental delay 64(98.46%), abnormal tone 46(70.77%), convulsion 9(16.98%), regression of mile stone 5(7.69%) and tremor 5(7.69%). Anaemia was present in 62(95.38%) children. Among children, TMBE 4(44.44%) was most common cause of convulsion followed by malaria 2(22.22%), hypocalcemia 2(22.22%) & pyogenic Meningitis 1(11.11%).

In the present study neuroimaging (MRI) was found abnormal in 53(81.54%) children. Normal brain MRI was seen in 12(18.46%) children. Among the children with microcephaly and SAM, cerebral atrophy (dilated ventricle, prominent sylvian fissures) was seen in 42(64.62%) – 41 children with diffuse cerebral atrophy & 1 child with focal (frontal) cerebral atrophy. Finding of TBME with diffuse cerebral atrophy (dilatation of ventricle, periventricular CSF oozing, tuberculomas, increased vascularity & post contrast meningeal enhancement) was seen in 5(7.69%) children. Hypomyelination and/or delayed myelination were seen in 2(3.08%) children. Diffuse cerebral atrophy with periventricular leukomalacia was seen in 2(3.08%) children. Leukomalacia with delay myelination was seen in 1(1.54%) child. Periventricular leukomalacia was seen in 1(1.54%) child.

Househam et al.<sup>[13]</sup> conducted study on computed tomography in severe protein energy malnutrition from South Africa, in the year 1987, performed Computed tomography of the brain on eight children aged 1 to 4 years with severe protein energy malnutrition all having clinical features typical of kwashiorkor. They found that severe cerebral atrophy or brain shrinkage according to standard radiological criteria was present in every case. Akinyinka et al.<sup>[3]</sup> conducted study on the computed axial tomography of the brain in protein energy malnutrition from Nigeria, in the year 1995 evaluated forty consecutive cases of protein energy malnutrition, the brain morphology was assessed by computed tomography within 24 hours of admission. Cerebral shrinkage was shown in six of 14 (42.9%) cases of marasmus, ten of 14 (71.4%) cases of kwashiorkor, and 11 of 12 (91.7%) cases of marasmic-

kwashiorkor. Ventricular dilatation was demonstrated in 57.1% of marasmus cases, 71.4% of kwashiorkor cases and 91.7% of patients suffering from marasmic-kwashiorkor.

Elham et al.<sup>[11]</sup> conducted study on magnetic resonance imaging of the brain in the diagnostic evaluation of microcephaly has been reported the most frequent MRI finding is brain atrophy in 11(20%) cases followed by demyelination 10(18.18%) cases, leukomalecia & atrophy 7(12.7%) cases, demyelination & atrophy 6(10.9%) cases, basal ganglia lesion 5(9%) cases, congenital brain malformations in 4(7.3%) cases, microcephalic changes 3(5.5%). Aggarwal A et al.<sup>[2]</sup> studied clinical profile of children with developmental delay and microcephaly and reported hypoxic ischemic encephalopathy change as most common MRI brain finding. In present study was different from Elham et al.<sup>[11]</sup> and Aggarwal A et al.<sup>[2]</sup> because in both the studies nutrition status of children with microcephaly was not assessed.

### Conclusion

Most children with Microcephaly and SAM had developmental delay, anaemia, abnormal tone, regression of mile stone and convulsion. Cerebral atrophy was most frequent finding on neuroimaging (MRI).

### Abbreviations

CBC – Complete Blood Count  
 CP – Cerebral Palsy  
 EEG - Electroencephalography  
 HC - Head Circumference  
 HIE - Hypoxic Ischemic Encephalopathy  
 IUGR - Intra Uterine Growth Retardation  
 LFT – Liver Function Test  
 SAM – Severe Acute Malnutrition  
 TBME - Tuberculo Bacterial Meningoencephalitis  
 WHO – World Health Organization

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