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A cross-sectional study of severe acute malnutrition impact on auditory evoked potentials in children age 6–59 months

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ABSTRACT

Background: Malnutrition is a public health concern in India. According to NFHS-5, the number of children under 5 years who are stunted (less height-for-age) and underweight (less weight-for-age) in India, are 35.5% and 32.1%, respectively. Many researchers reported that malnutrition affects myelination and neural maturation of the auditory brainstem pathway. **Aims and Objectives:** In this study, auditory evoked potential (AEP) parameters were studied in severly acute malnutrition (SAM) children of 6 months to <5 years of age. **Materials and Methods:** Fifty children, with severely malnourished (Their weighted age was 51–60% of the expected weight, and height for age <85% of the expected height) and 50 healthy children (with weight >80% of expected with normal height for their age), aged 6–59 months were included in the study. The parameters of AEPs were recorded using RMS-EMG EP MARK II, a 4-channel machine. **Results:** In our study, 30 (60%) males and 20 (40%) females had severe acute malnutrition. There were significant differences in the mean latencies of the waves I to V and the mean interpeak latencies (IPLs) of the waves I-III and I-V on the right and left ears between the study and control groups (P<0.05). The mean IPLs of I-III and I-V on the right side were found to be longer in the SAM group than in the control group (P<0.05. While the mean absolute peak latencies of wave, I found prolonged on both ears in the children with SAM (P<0.05). **Conclusion:** In the present study, severely acute malnourished children showed changes in AEPs characterized by absolute wave prolonged latencies and interpeak intervals compared with normally nourished children.

Key words: Auditory evoked potentials; Severe acute malnutrition; Children under 5 years; Interpeak latencies

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INTRODUCTION

Children are the world's most valuable resource and its great hope for the future. They are the foundation of the country. Severe acute malnourishment (SAM) is a significant public health problem in India and many developing countries. The World Health Organization (WHO) defines "severe acute malnutrition (SAM) as very low weight for height or a mid-arm circumference of <115 mm, or by the presence of nutritional edema."[1] The literature has shown that adequate nutrition, especially protein, iron, choline, and polyunsaturated long fatty acids, contributes to proper neuronal structure. A lack of in one or more of these elements in the critical period of brain development due to malnutrition can lead to impaired myelination, weak synaptic junctions, and neural arborization limitation.[2] Malnutrition affects early organizational processes such as neurogenesis, cell migration, and differentiation during the brain growth spurt period.[3]

The auditory evoked potentials (AEPs) are very sensitive measures related to brain function and have been used by many researchers with the diverse objective in humans, as in the pioneering studies by Hecox and Galambos (1974); and

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in experimental studies in animals young et al.,[4] Bellia et al.,[5] reported that Brainstem Auditory evoked potential (BAEP) is of great importance in evaluating the malnutrition of auditory pathways, especially for at-risk children.[5]

It appears that the long duration of continuous protein energy malnutrition (PEM) arrests the process of myelination thereby preventing the increase in the caliber of myelinated nerve fibers. Perinatal undernutrition in rats produces severe retardation of fiber growth in caliber in the sciatic nerve, spinal roots, and optic nerve. Since the early waves form the peripheral part of the auditory pathway, nerve conduction velocity is related more to diameter than the internodal length of nerve fibers.[6] The conventional view, supported by pioneering work using DNA as an indicator of brain growth, was that the brain is most vulnerable to malnutrition during the critical period of brain growth and development.

Thus, this study aimed to characterize and compare AEP responses among undernourished and normal under 5 year age children. This study will increase the knowledge base of this subject, which will enable necessary corrective and/or preventive measures, as there is a shortage of this type of research in the literature.

Aims and objectives

The aim of the study was to assess the electrophysiological parameters of AEP in malnourished and normally nourished children aged 6–59 months.

MATERIALS AND METHODS

This study was conducted in the Post Graduate Laboratory, Department of Physiology, Gajra Raja Medical College Gwalior, Madhya Pradesh. The case–control study was conducted from January 2021 to December 2021. The children were recruited from the severe malnutrition treatment unit, at Kamla Raja Hospital, Gwalior. The study group consisted of 50 SAM children, (32 males and 18 females) who had severe malnutrition according to IAP and WHO classification.[7] They had Weight for age, 51–60% of expected weight and height for age <85% of the expected height. The control group consisted of 50 normal children (30 males and 20 females) with weight >80% of expected with normal height for their age.

Ethical committee approval (Vide no. 955/IEC-GRMC2021) was obtained from the institution before commencing the study.

The study's aim and nature were explained to the parents/guardians. Informed written consent was obtained from the parent/guardian of the child before the test. A detailed clinical, anthropometry, and neurological examination were done. BAEP was measured using a four-channel RMS EMG-EP MARK II machine.

Inclusion criteria

Severely malnourished children in the age group of 6–59 months based on anthropometric measurements like weight for age and height for age according to the WHO criteria for SAM were included in this study.

Exclusion criteria

Genetic, metabolic, and endocrine causes for short stature and ear pathology were excluded from the study.

Statistical analysis

It was done using SPSS version 20. The result was analyzed using an unpaired student "t"-test. Values were expressed as mean with standard deviation. The control group was compared with severely malnourished children. $P<0.05$ was considered statistically significant.

Procedure

The aim and procedure of the test were explained to the subject and parents/guardians. A complete examination of the external ears was done. To achieve complete relaxation hypnotic chloral hydrate, 50 mg/kg was used in children above 18 months. The subject was asked to avoid applying hair oil after the last head bath. Skin preparation was done by gently abrading and degreasing before applying electrodes. Electrodes were placed according to the 10–20 international system of EEG electrode placement. Channel 1: Ai -Cz (active electrodes over ipsilateral ear); channel 2: Ac-Cz (Contralateral ear). The ground electrode was placed 20% from the nasion (Fz). A headphone was placed over the ear, delivering stimulus at a rate of 10–15/s. The intensity of the stimulus is set at 60 dB. An average of 2000 sweeps were recorded using click stimulus. Absolute latency of waves I, II, III, IV, and V and interpeak latencies (IPLs) of I-III, III-V, and I-V were recorded. Peak latencies were measured from the stimulus's onset to the wave's peak.

RESULTS

The age and sex distribution of the children studied is shown in Table 1. The children were divided into four age groups. The maximum number of patients involved in our study belonged to 1.5–3.5 years of age, that is, 1.6 (32%). The mean age was 2.73±1.30 years. There was no statistically significant difference ($P>0.05$) in age and gender distribution between the two groups (Table 1).

Out of 50 SAM children, 30 males (60%) and 20 females (40%), aged 6–59 months (mean age 2.73±1.30 years) with severe acute malnutrition and 50 normal healthy children (30 males (60%) and 20 females (40%), aged 6–59 months (mean age 2.83±1.23 years) were included in the study. In our study, there was a preponderance of males in SAM patients accounting for 60%. Although the prevalence of the disease is more in males, there was not a statistically significant difference between the groups for gender (P>0.05). We compared the anthropometric parameters between the two groups as shown in (Table 2), the readings of the mean height, weight, and Mid upper arm circumference exhibited significant statistical differences among the SAM patients and controls.

The mean and the standard deviations of absolute peak latency and interpeak latency in milliseconds of AEPs in the study and control groups are shown in (Table 3). One example of the auditory evoked auditory potential of a 2.5-year-old female child of SAM was depicted in Figure 1. A significant prolongation of absolute peak latencies in I, II, and IV, and I, III, and IV were seen in the left and right ears, respectively. There were significant differences in the mean of IPLs of the waves I-III and I-V on the right ear between the study and control groups (P<0.05). There was no statistically significant difference in IPLs of the left ear.

DISCUSSION

Malnutrition is widely prevalent in all developing countries and children are the worst sufferers. The different works of the literature showed abnormal AEPs in children with different degrees of malnutrition. AEPs have been applied widely to the examination of the

Table 1: Distribution of participants according to age and gender

Age group (In years)	Severely acute malnourished (SAM) (n=50)		Normal (n=50) n (%)		χ^2(P-value)
	Male (30) n (%)	Female (20) n (%)	Male (32) n (%)	Female (18) n (%)	
<1.5	7 (14.0)	5 (10.0)	7 (14.0)	4 (8.0)	0.53 (df=9) (0.99) Not Significant
1.5-3	10 (20.0)	6 (12.0)	11 (22.0)	6 (12.0)	
3-4	7 (14.0)	5 (10.0)	9 (18.0)	5 (10.0)	
>4	6 (12.0)	4 (8.0)	5 (10.0)	3 (6.0)	
Mean age (SD)	2.73±1.30		2.83±1.23		

Table 2: Anthropometric comparison in SAM cases and controls

Anthropometry	Severely acute malnourished Mean±SD	Normal Mean±SD	t-value	P-value
Height (cm)	76.76±9.76	90.06±10.97	6.40	0.01*
Weight (kg)	7.33±1.38	12.28±2.00	14.40	0.01*
MUAC (cm)	10.04±0.98	12.62±0.53	16.30	0.01*
Age (years)	2.73±1.30	2.83±1.23	0.39	0.701

*Significant Statistically, MUAC: Mid upper arm circumference

Table 3: Comparison of auditory evoked potentials and mean latencies in severely acute malnourished (Case) and normal (Control)

AEP in ms	Site of Ear	Severely acute malnourished (Case-SAM) Mean±SD	Normal (control) Mean±SD	t-test value (P)
Wave I	L	1.68±0.35	1.52±0.39	2.1 (0.036*)
	R	1.79±0.22	1.582±0.401	3.2 (0.002*)
Wave II	L	2.78±0.47	2.56±0.42	2.40 (0.018*)
	R	2.74±0.42	2.70±0.20	0.54 (0.58)
Wave III	L	3.47±0.54	3.44±0.42	0.27 (0.79)
	R	3.84±0.52	3.59±0.22	3.10 (0.003*)
Wave IV	L	4.97±0.59	4.73±0.62	1.98 (0.05*)
	R	5.03±0.64	4.79±0.34	2.28 (0.02*)
Wave V	L	5.71±0.54	5.59±0.52	1.18 (0.24)
	R	5.73±0.54	5.72±0.32	0.15 (0.88)
IPL I-III	L	1.79±0.70	1.93±0.45	−1.069 (0.29)
	R	1.99±0.57	1.77±0.43	2.13 (0.03*)
IPL III-V	L	2.24±0.76	2.14±0.64	0.72 (0.47)
	R	2.16±0.73	2.156±0.51	0.04 (0.96)
IPL I-V	L	4.04±0.57	4.07±0.55	−0.28 (0.78)
	R	4.15±0.62	3.93±0.41	2.096 (0.03*)

*Significant Statistically, I–V, numbers of the waves for, AEP: Auditory evoked potentials; R: Right, L: Left, IPL: Inter peak latency, SAM: Severely acute malnourished

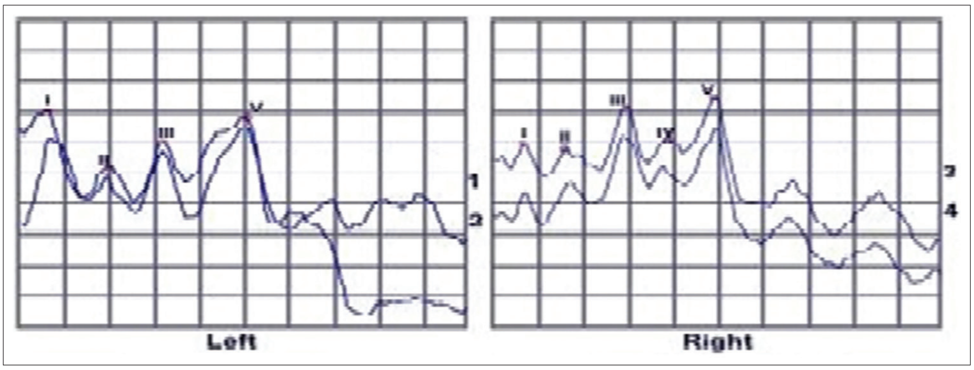

Figure 1: Brainstem Auditory evoked potential (BAEP) in a 2.5-year-old SAM child. Recording on the left and right ear

integrity of brainstem nuclei and peripheral auditory pathways.[8] Conduction through the neural pathways has also been seen to be affected by nutritional status as shown by Soury et al.[9]

The present study observed prolongation of Wave I, II, III, IV, and Prolonged inter-peak latency I–III, I–V with $P<0.05$ in the SAM group. This may be due to imperfect growth and development of myelin-producing initial abnormalities in an increase in interpeak latency particularly I–III. Vandana and Tandon[10] measured AEP responses in 20 chronic malnourished children of 3–6 years of age and found that there is significant prolongation in peak latencies of waves I, II, III, and IV. IPLs of I–III and III–V were also prolonged as malnutrition affects the peripheral developmental process of auditory pathways in the brainstem. Significantly prolonged absolute latencies of waves I, II, III, IV, and V were observed when compared to children with normal levels. The reason suggested was severe low weight for age may have subtle effects on the sensory–neural auditory brainstem system that are manifested as altered BAEP latencies. This result of our study is consistent with this result. Penido et al.,[11] studied the auditory brainstem potentials in children with PEM to determine the effects of PEM on the developing brain in children. Significant differences were recorded in the mean latencies of waves I, II, III, IV, and V on both ears and in the mean IPLs of waves I–III and I–V on the right ear between the study and control group, suggesting the defect in myelination of auditory brainstem pathways in children with moderate/severe PEM. Penido et al.,[11] found an increase in the absolute latencies of wave I-V and interpeak latency I-V and III-V indicating the involvement of peripheral as well as central pathways in malnourished children. In some studies Wiggins and Odabaş et al.,[12,13] the decrease in the number of neurons, synthesis of structural proteins, and myelination due to nutritional deficiencies can be related to the delayed central responses of BAER. Similarly, Sharma et al.,[14] studied ABEP in PEM versus normal children and observed the mean wave V latency and mean IPL waves I–V and III–V were significantly different. The kwashiorkor group had significantly longer mean wave V latency than the right ear marasmus group and the bilateral control group. The kwashiorkor group had significantly longer mean IPL waves I–V than the right ear marasmus group and then the left ear control group. The kwashiorkor group also had significantly longer mean IPL waves III–V than the left ear of the control group. In the study of Ampar et al.,[15] abnormalities were evenly distributed between the I–III, III–V, and I–V IPLs in severely malnourished children, and in another study, the ABPs of malnourished infants differed from the controls at admission but not at discharge. Similarly, Sharma et al.,[14] revealed that the malnourished infants had smaller ABP amplitudes at discharge, whereas controls did not.

In the present study, absolute peak latencies of waves in left ear I, II, and IV were significantly prolonged in SAM with $P<0.05$. Waves I, III, and IV were prolonged in the right ear. Wave V latency was prolonged but could not be significant statistically. IPLs of I–III and I-V in the right ear of SAM patients were delayed statistically significant in the SAM group when compared to the normal nourished group but could not establish statistically significant results in the left ear. This may be due to imperfect growth and development of myelin-producing initial abnormalities which increases interpeak latency. Similar findings have also been reported earlier in various studies by De Almeida and Matas,[16] Rubha and Vinodha,[17] De Almeida and Matas.[18] These findings showed that AEPs were markedly impaired bilaterally in children with SAM. Recently, Choudhury and Benasich[18] have reported an increased cortical threshold and prolongation of the central motor conduction time in children with malnutrition. Counter et al.,[19] have shown the association of malnourishment with abnormal brainstem auditory evoked responses in children 2–15 years of age. Significantly prolonged absolute latencies of waves I, II, III, IV, and V were observed when compared to malnourished children with normal children. The reason suggested was that malnourishment with low hemoglobin levels may have subtle effects on the sensory–neural auditory brainstem system that are manifested as altered BAEP latencies. Severe acute malnutrition leads to functional changes in the auditory system detectable by delayed BAEP. AEP is an easy, non-invasive, and feasible method of detecting auditory impairment in children. These changes could be attributed to myelination defects in the auditory pathway's neural tissue. Similarly, Zuanetti et al., and Vandana and Tandon[8,10] revealed that conduction through the neural pathways has also been seen to be affected by nutritional status.

Limitations of the study

The limitation of the study includes its small size. The AEP was done only at a single point in time. Only the severely acute malnourished children were taken as subjects. Cortical AEP were not used to assess the auditory pathways. Follow-up studies should be conducted to assess children who have recovered from malnutrition.

CONCLUSION

The present study shows significant alteration in BAEP responses in children with severe malnutrition (SAM) which may be due to nutritional deficiency affecting myelination of auditory brainstem pathways. These abnormalities depend on the duration and severity of malnutrition. Severe and chronic malnutrition affects BAEP–I, II, III, IV, and IPL I–III, I–V findings. Thus, there is a strong association between the duration and severity of malnutrition with BAEP abnormalities. Hence, this electrophysiological test can be used to detect malnutrition at its early stage.

FUTURE PROSPECTS

Further studies are required with large sample sizes and stratification of various severity of malnutrition. Long latency potentials can also be included in the analysis of BAEP to get more knowledge about the cortical pathway.

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Authors' Contributions:
AA, NS- Concept and design of the study prepared the first draft of the manuscript; **AA, NS, VV**- Interpreted the results; reviewed the literature and manuscript preparation**; AA, NS, VV, PA, ASR**- Concept, coordination, statistical analysis and interpretation, preparation of manuscript and revision of the manuscript.

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