ORIGINAL RESEARCH ARTICLE

Discriminative Ability of Electrophysiological Tests Such as Nerve Conduction Velocities for The Classification of Malnourished Children from Normal Children

Anju Agarwal[1], Nikhil Agrawal[2], Neetu Sharma[3], Durgesh Shukla[4*], Ajit Singh Rajput[5]

[1,3,4,5]G.R. Medical College Gwalior, M.P., India
[2]AIIMS Jodhpur, Rajasthan, India

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ABSTRACT

Background: Nerve Conduction Velocities (NCVs) measures electrical changes and speed in the nerve. Objectives of this study were: to compare mean velocities, to find rank of importance of different velocities and to frame equation to classify severely acute malnourished (SAM) children with normal children.

Material & Methods: Present case- control study was conducted on 50 SAM children and 50 normal children aged 6 months to 59 months. Independent t test and Discriminant analysis was performed. Standardized discriminant coefficient, canonical correlation and Wilks' Lambda was calculated and p value was judges at 5% level of significance.

Results: NCVs were observed significantly lower among the cases as compared with the controls. Sural Sensory Nerve Velocity holds first position followed by Sensory Nerve Velocity. So, in final discriminant model 3 variables i.e., Sural Sensory Nerve Velocity; Median Sensory Nerve Velocity; Tibial Motor Nerve Velocity were used and 42.1 % of the total variance in the discriminant scores not explained by differences among the groups by the three-variable model. Model is able to classify 82.5% cases correctly.

Conclusion: Sural Sensory Nerve Velocity; Median Sensory Nerve Velocity; Tibial Motor Nerve Velocity were found as most important nerve conduction velocities with a good classification ability.

Key Words: Discriminant; Median Sensory Nerve Velocity; Sural Sensory Nerve Velocity; Tibial Motor Nerve Velocity

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***Correspondence:** Dr. Durgesh Shukla (Email: durgeshstatsgrmc2019@gmail.com)

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INTRODUCTION

Children are the world's most valuable resource and its best hope for the future foundation for a country. Severe acute malnourishment (SAM) is a significant public health problem in India and many developing countries.[1] Children suffering from SAM have weak immune system thus they are more prone to mortality and morbidity. According to National Family Health Survey (NFHS- 5), the number of children under 5 years who are stunted (less height-for-age) in India has 35.5% and the number of underweight children (less weight-for-age) has 32.1%.[2]

Malnutrition causes structural and functional pathology of the brain. Effect of chronic Protein Energy Malnutrition causes stunting and wasting in children. It can also affect higher cognitive processes during childhood (>5 yrs of age).[3] Malnutrition leads to permanent suboptimal physical and mental development resulting in mental retardation.[4] The behaviours and cognitive functions are impaired by malnutrition which is related to an altered emotional response to a stressful event.[5] Today the availability of more sensitive and non-invasive methods like the Nerve conduction study, Brain stem auditory and visual evoked potential to evaluate subtle alteration in central nervous system (CNS) function allows us to better correlate SAM with possible early brain alteration.

Present study was conducted keeping concept in mind that severely malnourished neonates and infants are most susceptible to the phase of exponential brain growth. So, there is a need for early recognition and intervention to prevent permanent neurological sequelae. Present study was conducted considering the Median Motor Nerve Conduction Velocity; Median Sensory Nerve Conduction Velocity; Ulnar Motor Nerve Conduction Velocity; Ulnar Sensory Nerve Conduction Velocity; Tibial Motor Nerve Conduction Velocity; Deep Peroneal Nerve Conduction Velocity; Sural Sensory Nerve Conduction Velocity together. These parameters have not been studied together in a single group of protein energy malnutrition subjects. Even at a global level study on severely acute malnourished with the above parameters not available to evaluate the function of the peripheral and central neural pathways. Electrophysiologic tests i.e., NCVs can provide valuable objective and accurate information that complements the diagnosis of malnutrition based on World Health Organization (WHO) criteria for children. Electrophysiological tests can detect functional abnormalities in various organ systems before they manifest as overt clinical symptoms. So, we designed this study over SAM patients to determine the central as well as peripheral neuropathy and compare the same with the control healthy group.

The present study was conducted with the objectives to compare mean nerve conduction velocities and to find the rank of importance of different velocities for the discrimination of SAM children with the normal children. The study also conducted to predict most effective classifier velocity and to frame classification equation for SAM Children and normal children.

METHODOLOGY

Present case- control study was conducted in the Department of Physiology and severe malnutrition treatment unit (SMTU)- Kamla Raja Hospital (KRH), Gajra Raja (G.R.) Medical College and J.A. Group of Hospitals, Gwalior. (M.P.) on 50 SAM patient's cases (Group-1) with age-sex matched 50 normal nourished healthy controls (Group-2). Sample size was calculated considering average Motor Nerve Conduction Velocity (MVCV) among malnourished children as 33.81 m/sec±17.93 m/sec and average Motor Nerve Conduction Velocity (MVCV) among normally nourished children as 46.58 m/sec± 17.03 m/sec, [6] at 5% level of Significance and 95% Power of test sample size calculated by using this formula sample size $(n) = \frac{2(s)^2(z_{\alpha/2}+Z_{1-\beta})^2}{(\mu_1-\mu_2)^2}$; where $Z_{\alpha/2}$ =1.96 at 5% level of significance ; $Z_{1-\beta}$ =1.64 at 95% power of test; $(s)^2$ is pooled variance = 311.18; mean MVCV among SAM group (μ_1) = 33.81 m/sec ; mean MVCV among normal group (μ_2)=46.58 m/sec, calculated sample size (n) =50 in each group.

The duration of the study was one year i.e., November 2020– November 2021. In the present study severely acute malnourished children and normal children between age 6 months to 59 months of age and whose parents were given written informed consent to participate in the study and children having normal hearing and vision were included for the present study. SAM children were selected as per World Health Organization (WHO) classification. The WHO defines 'severe acute malnutrition (SAM) as very low weight-for-height or a mid-upper arm circumference less than 115 mm, or by the presence of nutritional edema'.[7] Children with any history of genetic, renal, liver, cardiac, endocrine disease, and metabolic disorders caused by short stature, having any history of birth injury or hypoxic brain injury, Subjects with any external ear, middle ear, or cochlear disease or Subjects with pathology in the eye, in which Visual Evoked Potential (VEP) is known to be affected or uncorrected refractive error were excluded from the present study.

Cases were SAM children while controls were normal children. Cases were recruited from the SMTU –KRH and Controls were recruited from the same community from where the cases were belonged as per inclusion criteria. The cases were selected by using systematic random sampling i.e., first child selected randomly and their after at interval of third admission of SAM child at SMTU-KRH were selected and each case was matched with one control in term of place of residence, age and sex. For the selection of normal child as control, preference will be given to the eligible child of the same household of case but for unavailability of

the eligible child in same household, the eligible children of neighbours were recruited as control. Informed consent was taken from the parents of every subject and control. The consent form was written in both (Hindi/English) languages, so the participants can understand it properly. The aim and nature of the study were explained to the subjects and parents/Guardians. Ethical clearance of the present study was obtained from Institutional Ethical committee of G.R. Medical College Gwalior (D.No.: 955/IEC-GRMC/2021 Gwalior Dated: 02-05-2021).

Median Motor Nerve Conduction Velocity; Median Sensory Nerve Conduction Velocity; Ulnar Motor Nerve Conduction Velocity; Ulnar Sensory Nerve Conduction Velocity; Tibial Motor Nerve Conduction Velocity; Deep Peroneal Nerve Conduction Velocity; Sural Sensory Nerve Conduction Velocity in both upper and lower limbs with their mean observed for the both cases and controls measured with the help of non-invasive tests i.e., a computerized RMS EMG EP Mark –II machine was used in the study. Filters were set at 2 Hz and 5 kHz for motor studies and at 20 Hz and 3 kHz for sensory studies. The sweep speed was set at 5 ms/division for MNCS and 2 ms/division for SNCS. 1-cm disc recording electrodes were used for motor studies and ring recording electrodes were used for sensory studies. Supramaximal stimuli were delivered in order to get adequate responses. Data was collected for the following parameters: onset distal latency, conduction velocity and action potential amplitude measured from the peak of the negative potential to the peak of the positive potential (peak to peak). Basic components of recording equipment: Electrodiagnostic equipment consist of both stimulating and recording systems, amplifiers, filters, microprocessor and video and audio monitors in addition to computers.[8-11] Data were coded and entered in Microsoft excel software. Statistical analyses were done using Statistical Package for the Social Sciences (SPSS-20) software. Mean and standard deviation was used to describe various average velocities. The significance of the difference in Mean velocities in cases and controls were compared using the independent t-test. Differences were considered statistically significant at $p<0.05$. Discriminant analysis was performed to classify SAM children with normal children. Standardized discriminant coefficient, canonical correlation and Wilks' Lambda was calculated. Step wise discriminate analysis method was adopted to predict most effective classifier velocity of the nerve. This method ensured that only important velocities were selected while redundant velocities i.e., those contributing very less in the presence of other velocities were discarded from the model with low error rate. The procedure adopted was backward step wise elimination which discarded the variables with smallest F and largest Wilk's lambda step by step. These eliminated variables were used in the model as they are most important and worthy of inclusion into discriminate function. Equation for Discriminant Function of SAM Children (F1) and Normal children were developed using the 30 -30 sample and classification accuracy validation was assessed on 20-20 samples. Predictive Classification ability for SAM and normal children were shown using the graphical representation.

RESULTS

In the present study 50 SAM and 50 controls were observed. In both the groups, 20 (40.0%) females and 30 (60.0%) males were taken. The average age of the SAM children was 2.73 ± 1.30 years while among the control average age was 2.83 ± 1.23 years. The mean age and gender were found to be statistically same in both the groups ($p>0.05$). The **Median Motor Nerve Conduction** velocity **was observed** in SAM and controls were 34.35 ± 10.67 m/s and 44.90 ± 12.68 m/s respectively. **Median Sensory Nerve Conduction Velocity** recorded for SAM and controls were 37.45±13.81 m/s and 46.38±11.53 m/s respectively. There were statistically significant differences in recorded velocities of SAM and controls at a p-value <0.05. (Table 1)

Table 1: Mean comparison of determinants in two groups

Variables	SAM (n=50) (Mean ± SD)	Control (n=50) (Mean ± SD)	t value	P value
Median Motor Nerve Conduction Velocity	34.35±10.67	44.90±12.68	-4.501	0.000
Median Sensory Nerve Conduction Velocity	37.45±13.81	46.38±11.53	-3.508	0.001
Ulnar Motor Nerve Conduction Velocity	37.73±6.86	42.25±4.37	-3.937	0.000
Ulnar Sensory Nerve Conduction Velocity	34.28±4.12	36.71±2.49	-3.569	0.001
Tibial Motor Nerve Conduction Velocity	32.63±3.41	34.99±2.56	-3.932	0.000
Deep Peroneal Nerve Conduction Velocity	34.09±4.46	40.57±5.12	-6.759	0.000
Sural Sensory Nerve Conduction Velocity	34.90±4.25	43.34±6.79	-7.453	0.000

Table 2: Standardized Canonical Discriminant Function Coefficients for determinants

Variables	Standardized Canonical Discriminant Function	Rank of Importance
Motor Nerve Velocity	0.319	5
Sensory Nerve Velocity	0.709	2
Ulnar Motor Nerve Velocity	-0.124	6
Ulnar Sensory Nerve Velocity	-0.030	7
Tibial Motor Nerve Velocity	0.551	3
Deep Peroneal Motor Nerve Velocity	-0.412	4
Sural Sensory Nerve Velocity	1.156	1

Table 3(A): Step wise discriminate analysis method to predict most effective classifier variables

Steps	Variables Not in the Analysis	Tolerance	Min. Tolerance	F to Enter	Wilks' Lambda
0	Median Motor Nerve Velocity	1.000	1.000	7.706	0.883
	Median Sensory Nerve Velocity	1.000	1.000	11.704	0.832
	Ulnar Motor Nerve Velocity	1.000	1.000	11.875	0.830
	Ulnar Sensory Nerve Velocity	1.000	1.000	8.416	0.873
	Tibial Motor Nerve Velocity	1.000	1.000	10.040	0.852
	Deep Peroneal Motor Nerve Velocity	1.000	1.000	18.381	0.759
	Sural Sensory Nerve Velocity	1.000	1.000	34.801	0.625
1	Median Motor Nerve Velocity	0.968	0.968	1.884	0.605
	Median Sensory Nerve Velocity	0.889	0.889	20.024	0.463
	Ulnar Motor Nerve Velocity	1.000	1.000	6.868	0.558
	Ulnar Sensory Nerve Velocity	0.996	0.996	3.927	0.585
	Tibial Motor Nerve Velocity	0.999	0.999	7.047	0.556
	Deep Peroneal Motor Nerve Velocity	0.327	0.327	0.569	0.619
2	Median Motor Nerve Velocity	0.963	0.871	2.127	0.446
	Ulnar Motor Nerve Velocity	0.895	0.796	1.116	0.453
	Ulnar Sensory Nerve Velocity	0.961	0.858	0.986	0.455
	Tibial Motor Nerve Velocity	0.998	0.888	5.450	0.421
	Deep Peroneal Motor Nerve Velocity	0.327	0.317	0.304	0.460
3	Median Motor Nerve Velocity	0.954	0.870	2.568	0.403
	Ulnar Motor Nerve Velocity	0.454	0.454	0.596	0.417
	Ulnar Sensory Nerve Velocity	0.526	0.526	0.544	0.417
	Deep Peroneal Motor Nerve Velocity	0.310	0.303	1.103	0.413

Table 3(B): Ability of Predicted classifiers through Wilks' Lambda

Step	Number of Variables	Wilks' Lambda	df1	df2	df3	Exact F			
						Statistic	df1	df2	Sig.
1	1	0.625	1	1	58	34.801	1	58.000	0.000
2	2	0.463	2	1	58	33.120	2	57.000	0.000
3	3	0.421	3	1	58	25.620	3	56.000	0.000

Table 4: Summary table of Canonical Discriminant Functions

Eigenvalues					Wilks' Lambda			
Function	Eigenvalue	% of Variance	Cumulative %	Canonical Correlation	Wilks' Lambda	Chi-square	df	Sig.
1	1.373	100.0	100.0	0.761	0.421	48.813	3	<0.01

Table 5: Fisher's linear discriminant functions Coefficients

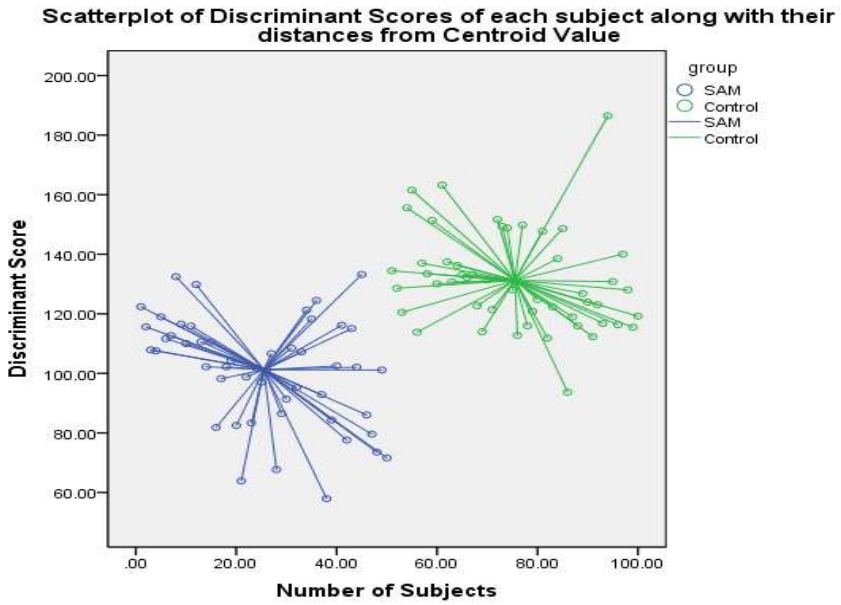
	Group	
	SAM	Controls
Sensory Nerve Velocity	0.453	0.576
Tibial Motor Nerve Velocity	3.995	4.303
Sural Sensory Nerve Velocity	1.670	2.058
Constant	-104.443	-135.442
Equation for Discriminant Function of SAM Children (F1)	0.453* Sensory Nerve Velocity+3.995* Tibial Motor Nerve Velocity+1.670* Sural Sensory Nerve Velocity-104.443	
Equation for Discriminant Function of Control group (F2)	0.453* Sensory Nerve Velocity+3.995* Tibial Motor Nerve Velocity+1.670* Sural Sensory Nerve Velocity-104.443	

If F1 > F2; Allot subject as SAM Children; If F2> F1; Allot subject as Normal Children (control)

Table 6: Percentage of correct classifications in the Developmental and Cross-validated samples

Actual Group Membership	Predicted Group Membership			Overall Classification
	SAM	Control	Total	
Developmental Sample: Classification Count				93.33 %
SAM	30	0	30	
Control	4	26	30	
Developmental Sample: Classification Percentage				
SAM	100.0	0.0	100	
Control	13.3	86.7	100	
Cross-Validation Sample: Classification Count				82.50 %
SAM	16	4	20	
Control	3	17	20	
Cross-Validation Sample: Classification Percentage				
SAM	80.0	20.0	100	
Control	15.0	85.0	100	

Figure 1: Scatter Plot of Discriminant Scores of each subject along with their distances from centroid value



Standardized discriminant coefficient showing that Sural Sensory Nerve Velocity hold first position followed by Sensory Nerve Velocity followed by Tibial Motor Nerve Velocity while Ulner Sensory Velocity stands on last position for discriminating ability to classification of the SAM children with the normal children. (Table 2)

Backward Step wise discriminate analysis method was adopted to predict most effective classifier velocity of the nerve. **In step 1;** Sural Sensory Nerve Velocity was selected (wilks lamda = 0.625; F to enter =34.801). In step 2; Median Sensory Nerve Velocity was selected (wilks lamda = 0.463; F to enter = 20.024). In step 3 Tibial Motor Nerve Velocity was selected (wilks lamda = 0.421; F to enter = 5.450). So, in final discriminant model 3 variables i.e., Sural Sensory Nerve Velocity; Median Sensory Nerve Velocity; Tibial Motor Nerve Velocity were used but 42.1 % of the total variance in the discriminant scores was not explained by this three-variable model. (Table 3 A & Table 3 B)

The canonical correlation was 0.761 showing the good association between the discriminant scores and the groups. In present study significant Wilks' Lambda for three variable model is 0.421 showing that 42.1 % of the total variance in the discriminant scores not explained by differences among the groups by the three-variable model. (Table 4)

Table 5 showing the equation of discriminant model for the classification of SAM children with the normal children which were formed using the Fisher's discriminant score and constant.

Table 6 showing the Developmental Sample model is able to classify correctly 93.33% of SAM children with the normal children. While this model when used on fresh data as validating the model classification ability it was found that this model is able to classify 82.5% cases correctly. Figure 1 showing model classification power in separation of SAM Children with the Normal children.

DISCUSSION

Child growth is internationally recognized as an important public health indicator for monitoring nutritional status in a community. Children who suffer from growth retardation as a result of poor diets or recurrent infections are more susceptible to several infectious diseases, such as severe diarrhoea, malaria, meningitis, and pneumonia.[12,13] Early development of malnutrition during the critical period of brain development has devastating effect on brain growth. This period extends from prenatal to early postnatal life. Active synthesis of myelin occurs in this period. Myelin is composed of protein & phospholipid derived from cell membrane of oligodendrocytes in central nervous system and from Schwann cells in peripheral nervous system. Malnutrition in this period results in physical, chemical, & functional changes in brain. All changes occurring in this period are likely to be irreversible that has a long-lasting effect mainly due to delay in myelination. Malnutrition results in poor learning abilities, impaired cognitive functions and school dropouts.[14-16]

This study has shown significant alteration in the electrophysiological parameters with significant reduction in nerve conduction velocity in children with malnutrition. Abnormal nerve conduction may be caused by various pathological processes, which hamper fast conduction like damage or loss of myelin, focal compression (carpal tunnel syndrome), axonal loss, or generalized peripheral neuropathy, plexopathy and radiculopathy. Similar to our study

some other studies also found that Motor nerve conduction velocity and sensory nerve conduction velocity are significantly lower in children with SAM or of protein energy malnutrition (PEM) as compared with normal children.[10,17-19]

Shanthi Ghosh et al.1979[20] conducted a nerve conduction study on 67 children to assess the effect of malnutrition on the peripheral nervous system. Significant reduction in nerve conduction velocity was observed in children with severe protein energy malnutrition and ongoing long-term malnutrition. The present study results agreed with the results of Nimet kabakus et al. They did a peripheral nerve conduction study in children with iron deficiency anemia. Children with iron deficiency anemia were tested against healthy children. Median motor and sensory nerve conduction velocities were significantly lower than the control group.[21] Study conducted by Md. Zabihullah, et al.[22] shown significant reduction in Sensory Nerve Conduction Velocity (SNCV) in children with severe Protein Energy Malnutrition (PEM) which may be due to nutritional deficiency affecting myelination of peripheral nerves.

Conclusion

In our study Median Sensory Nerve Conduction Velocity; Tibial Motor Nerve Conduction Velocity; Sural Sensory Nerve Conduction Velocity appeared more sensitive and early indicators of malnourishment. Nutritional deficiency during the development of the brain has a long-lasting effect on learning abilities, and psychomotor development. Malnutrion affect the sensory and motor nerve conduction velocity. So, these electrophysiological tests can be used for early detection of malnutrition. It is concluded that further studies are needed to substantiate these changes, especially in a large number of patients with various duration of malnutrition. These changes in our group of subjects support our hypothesis and need further confirmation in patients with a longer duration of disease.

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