EFFECTS OF MALNUTRITION ON MOTOR NERVE CONDUCTION VELOCITY IN CHILDREN UNDER FIVE YEARS OF AGE

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ABSTRACT

BACKGROUND
Protein energy malnutrition is known to be a major health and nutrition problem in Indian paediatric population. The infancy and early childhood period of growths are critical for neurocognitive development and malnutrition during this period can affect maturation of peripheral nerves. Nerve conduction studies can detect conduction changes in peripheral nerves by measuring nerve conduction velocity.
Aim- This study has been carried out to compare and analyse the Motor Nerve Conduction Velocity (MNCV) between healthy controls and malnourished children.

MATERIALS AND METHODS
Study sample consisted of 82 children under five years of age with protein energy malnutrition who were divided into four age groups (Group 1: 06 - 12 months, Group 2: 13 - 24 months, Group 3: 25 - 36 months and Group 4: 37 - 48 months). Within each age group, the patients were further divided into 2 groups on the basis of severity of malnutrition, first as suffering from mild-to-moderate malnutrition (grade 1 and 2 malnutrition) and second as suffering from severe malnutrition (grades 3 and 4 malnutrition). 60 healthy children (n= 15 for each age group) without any nutritional problems served as control subjects. Assessment of nutritional status was done according to the guidelines of the Nutrition Subcommittee of the Indian Academy of Paediatrics. Nerve conduction study was performed on median, ulnar and common peroneal nerves with neuroperfect EMG/NCV/EP System and MNCV was measured. One-Way ANOVA and Tukey-Kramer post-hoc test was applied to analyse the statistical significance of changes in the MNCV.

RESULTS
This study showed significant reduction in MNCV in children with severe malnutrition. No significant difference in MNCV was found in children with mild-to-moderate malnutrition.

CONCLUSION
Malnutrition affects maturation of peripheral nerves as indicated in the present study by significant decrease in MNCV in severely malnourished children. There was no significant decrease in MNCV in children with mild-to-moderate malnutrition. It indicates an association between severity of malnutrition with alteration in MNCV.

KEY WORDS
Malnutrition, Motor Nerve Conduction Velocity (MNCV), Nerve Conduction Study.

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BACKGROUND

Malnutrition is a broad term commonly used as an alternative to undernutrition, but technically it also refers to overnutrition. People are malnourished if their diet does not provide adequate calories and proteins for growth and maintenance or they are unable to fully utilise the food due to illness (undernutrition). They are also malnourished if they consume too many calories (overnutrition).[1] The present study, however, has dealt with the children under five years of age suffering from Protein-Energy Malnutrition (PEM).

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Malnutrition is a silent emergency.[2] It is the underlying cause of child mortality in about 45% of all deaths reported for children under 5 years of age.[3] In 2017, globally 151 million children under 5 years of age had stunted growth and 51 million wasted.[4] The National Family Health Survey 2015-16 (NFHS-4) estimated 35.7% of Indian children under five years to be underweight.[5]

Nutrition plays a key role in physical and mental development of children, especially in the formative years of life.[6] The infancy and childhood period of growths are critical for neurocognitive development.[7,8] Various studies have established an impact of malnutrition on neurochemistry, structure and function of brain.[9-13] Adequate nutrition is considered an aspect of the environment that is expected by the brain for normal development.[14]

During development of the human nervous system, myelination starts in the motor roots of the peripheral nervous system and is followed by myelination of the spinal cord and brain. The majority of myelin is assembled during the first years of postnatal life.[15] Peripheral nerve myelination begins about the 15th week of gestation[16] and continues throughout the first 2 to 5 years of life.[17,18] Malnutrition in under-five children may affect the process of myelination.[19] The loss of myelin may delay or block conduction in the demyelinated axons. Nerve conduction tests can detect slowed conduction in peripheral nerves by measuring nerve conduction velocity. The central idea of this study is related to the predictable responses of the peripheral nerves in children suffering from PEM.

MATERIALS AND METHODS

The present study is a case control study. The study was conducted in Neurophysiology Laboratory, Department of Physiology, Jawaharlal Nehru Medical College and Hospital (JNMCH), Aligarh Muslim University (AMU), Aligarh. Institutional Ethical Committee approval was obtained before commencing the study. Parents/ guardian of 82 children under five years of age with PEM attending the Outpatient Department (OPD) or admitted to the Inpatient Department (IPD) of the concerned Department of Paediatrics, JNMCH, AMU, Aligarh, as well as parents/guardians of 60 healthy children of same age group gave consent for the study during the study period. The sample size estimation was done at convenience. Assessment of nutritional status was done according to the guidelines of the Nutrition Subcommittee of the Indian Academy of Paediatrics.[20] Nerve Conduction Velocity study was performed on median, ulnar and common peroneal nerves with Neuroperfect EMG/NCV/EP System. Nerves were stimulated by applying depolarising square wave electrical pulses to the skin over the peripheral nerves. The surface recording electrodes used for measuring Motor Nerve Conduction Velocity (MNCV) were placed in belly-tendon montage; keeping the active electrode close to the motor point and the reference to the tendon.

Statistical Package for Social Science (SPSS 17.0) for Windows Software was used for the statistical analysis. One-Way ANOVA and Tukey-Kramer post-hoc test were applied to analyse the statistical significance of changes in the MNCV. P value of less than 0.05 was taken as statistically significant.

RESULTS

As the nerve conduction velocity varies with age,[21] children were divided into four age groups for statistical analysis: - Group 1: 06 - 12 months, Group 2: 13 - 24 months, Group 3: 25 - 36 months and Group 4: 37 - 48 months. 60 healthy children (n= 15 for each age group) without any nutritional problems served as control subjects. Within each age group the patients were further divided into 2 groups on the basis of severity of malnutrition, first as suffering from mild-to-moderate malnutrition (grade 1 and 2 malnutrition) and second as suffering from severe malnutrition (grades 3 and 4 malnutrition). In Group 1 with PEM grade 1 and 2, number of cases (n)= 11 and with PEM grade 3 and 4, n= 10 ; Group 2 with PEM grade 1 and 2, n= 12 and with PEM grade 3 and 4, n= 13 ; Group 3 with PEM grade 1 and 2, n= 10 and with PEM grade 3 and 4 n= 9 ; Group 4 with PEM grade 1 and 2, n= 9 and with PEM grade 3 and 4 n= 8 were taken up for the study.

Groups	Age (Months)	Sex (Controls)		Sex (PEM 1 and 2)		Sex (PEM 3 and 4)	
		Male	Female	Male	Female	Male	Female
Group 1	6-12	9	6	7	4	6	4
Group 2	13-24	9	6	7	5	5	8
Group 3	25-36	9	6	6	4	6	3
Group 4	37-48	9	6	5	4	5	3

Table 1. Age and Sex distribution of Controls and Cases

PEM= Protein Energy Malnutrition.

Age Groups	Control	PEM Grade (1 and 2)	PEM Grade (3 and 4)	P-value	Statistical Significance
Group 1	41.58 ± 3.16	39.26 ± 2.84	35.18 ± 2.22	< 0.001	Significant
Group 2	47.06 ± 2.37	46.10 ± 2.65	37.25 ± 2.38	< 0.001	Significant
Group 3	50.03 ± 2.37	48.75 ± 2.87	38.14 ± 1.80	< 0.001	Significant
Group 4	52.71 ± 2.54	50.93 ± 1.79	37.78 ± 1.20	< 0.001	Significant

Table 2A. One-Way ANOVA comparing Mean MNCV (m/s) of Median Nerve between Control Group and Two Groups of Cases (PEM Grade 1 and 2 and PEM Grade 3 and 4) in Four Age Groups

MNCV= Motor Nerve Conduction Velocity, PEM= Protein Energy Malnutrition.

Age Groups	Control	PEM Grade (1 and 2)	PEM Grade (3 and 4)	P-Value	Statistical Significance
Group 1	44.84 ± 3.11	42.57 ± 3.08	38.10 ± 2.75	< 0.001	Significant
Group 2	51.17 ± 2.87	49.56 ± 3.10	39.6 5± 2.35	< 0.001	Significant
Group 3	53.13 ± 2.61	50.85 ± 3.48	39.05 ± 1.85	< 0.001	Significant
Group 4	54.80 ± 1.64	53.61 ± 1.90	39.19 ± 1.22	< 0.001	Significant

Table 2B. One-Way ANOVA comparing Mean MNCV (m/s) of Ulnar Nerve between Control Group and Two Groups of Cases (PEM Grade 1 and 2 and PEM Grade 3 and 4) in Four Age Groups

MNCV= Motor Nerve Conduction Velocity, PEM= Protein Energy Malnutrition.

Age Groups	Control	PEM Grade (1 and 2)	PEM Grade (3 and 4)	P-value	Statistical Significance
Group 1	43.53 ± 3.19	41.30 ± 3.08	36.30 ± 3.15	< 0.001	Significant
Group 2	48.24 ± 3.62	46.27 ± 3.42	37.34 ± 2.36	< 0.001	Significant
Group 3	50.07 ± 1.92	48.78 ± 2.79	38.05 ± 1.70	< 0.001	Significant
Group 4	51.99 ± 1.71	50.71 ± 1.53	37.92 ± 1.32	< 0.001	Significant

Table 2C. One-Way ANOVA comparing Mean MNCV (m/s) of Common Peroneal Nerve between Control Group and Two Groups of Cases (PEM Grade 1 and 2 and PEM Grade 3 and 4) in Four Age Groups

MNCV= Motor Nerve Conduction Velocity, PEM= Protein Energy Malnutrition.

Age Groups	Groups Compared	Dependent Variable		
		MNCV Ulnar Nerve	MNCV Median Nerve	MNCV CPN Nerve
		P value	P value	P value
Group 1	Control- PEM Grade (1 and 2)	.156 *	.113*	.190*
	Control - PEM Grade (3 and 4)	< 0.001†	< 0.001†	< 0.001†
	PEM Grade (1 and 2)- PEM Grade (3 and 4	.005†	.006†	.003†
Group 2	Control- PEM Grade (1 and 2)	.305*	.575*	.261*
	Control- PEM Grade (3 and 4)	< 0.001†	< 0.001†	< 0.001†
	PEM Grade (1 and 2)- PEM Grade (3 and 4	< 0.001†	< 0.001†	< 0.001†
Group 3	Control- PEM Grade (1 and 2)	.119*	.401*	.324*
	Control- PEM Grade (3 and 4)	< 0.001†	< 0.001†	< 0.001†
	PEM Grade (1 and 2)- PEM Grade (3 and 4)	< 0.001†	< 0.001†	< 0.001†
Group 4	Control- PEM Grade (1 and 2)	.216*	.124*	.152*
	Control- PEM Grade (3 and 4)	< 0.001†	< 0.001†	< 0.001†
	PEM Grade (1 and 2)- PEM Grade (3 and 4)	< 0.001†	< 0.001†	< 0.001†

Table 3. Post Hoc Analysis showing Multiple Comparisons of Mean MNCV (m/s) of Ulnar Nerve, Median Nerve and Common Peroneal Nerve between Three Children Groups (Control, PEM Grade 1 and 2 and PEM Grade 3 and 4) in Four Age Groups. (Tukey-Kramer Test)

* Not Significant, † Significant, MNCV= Motor Nerve Conduction Velocity, PEM= Protein Energy Malnutrition.

Table 2A, 2B, 2C and 3 gives statistical analysis of the results using One-Way ANOVA followed by Tukey-Kramer Post-Hoc test. In One-Way ANOVA test, comparison of mean MNCV of Ulnar nerve, Median nerve and Common Peroneal nerve between control group and two groups of cases (PEM grade 1 and 2 and PEM grade 3 and 4) was statistically significant ($p < 0.05$) in all the four age groups. In Post-Hoc Tukey-Kramer test, comparison of mean MNCV of all 3 nerves in PEM grade 3 and 4 group with that of control group was statistically significant ($p < 0.05$) in all the four age groups. However, comparison of mean MNCV of all 3 nerves in PEM grade 1 and 2 group with that of control group was not statistically significant ($p > 0.05$) in all the four age groups.

DISCUSSION

Maturation of peripheral nervous system in the form of myelination begins during the fourth month of foetal life and it is complete at around 5 years of age.[22] As majority of myelin is assembled during the first years of postnatal life, a great magnitude of tasks is performed by glial cells during this short period of time. Very rapid myelin synthesis early in development has been demonstrated biochemically by the very rapid incorporation of radioactive precursors into myelin and substantial increase of enzymes involved in synthesising myelin components.[23] The axons also mature during the prenatal and postnatal periods, beginning at 20 weeks' gestation and reaching a maximum between ages 2 and 5 years.[24] Nerve Conduction velocity is a dependent variable of myelination, diameter of the fibre and internodal differences. Conduction velocity increases in proportion to the diameter of the nerve fibres, the ratio being about 6: 1.[25] There is a direct relationship between the diameter of the axon and the thickness of the myelin sheath. The diameters of peripheral nerves range from 1 to 3 µm in the newborn and between 1 and 7 µm in children of 4 years of age. The Nodes of Ranvier are remodelled during maturation with the maximum internodal distances occurring at 5 years.[26] Malnutrition can affect this ongoing maturation of peripheral nerves in children. Chopra et al[19] studied sural nerve biopsies and reported significant segmental demyelination in about 50 percent of cases in group consisting of children with severe PEM. Moreover, in this group, the normal developmental pattern for myelinated fibre size distribution was impaired with a persistence of small myelinated fibres and there was a failure of internodal segments on large fibres to elongate with increase in age. Sural nerve biopsies from children with mild-to-moderate PEM were characterised by normal developmental changes in myelinated fibres with an increasing proportion of medium and large size fibres, and an appropriate relationship of internodal length to fibre diameter. They reported evidence of mild segmental demyelination in only one child of mild-to-moderate PEM.

The present study has shown significant reduction in motor nerve conduction velocity in children with severe PEM. No significant difference in MNCV was found in children with mild-to-moderate PEM. The result was similar in all age groups of this study ranging from 6 months to 4 years. Similar findings were reported by Ghosh S et al.[27] They reported significant reduction in motor nerve conduction velocity in children with severe PEM and ongoing long-term malnutrition. Osuntokun BO[28] reported that motor nerve conduction velocity was decreased to the greatest extent in the more severe cases of PEM and the slowest mean rate was that in 7 patients who subsequently died. Significant effects on peripheral nerve function have been pointed out by various other motor nerve conduction studies in malnourished children.[29-31]

Protein energy malnutrition during the first years of postnatal life can have limiting effect on the process of myelination as demonstrated earlier.[19] This might be the cause for significantly decreased conduction velocity in severely malnourished children.

CONCLUSION

Malnutrition affects maturation of peripheral nerves as indicated in the present study by significant decrease in motor nerve conduction velocity in severely malnourished children. There was no significant decrease in motor nerve conduction velocity in children with mild-to-moderate malnutrition. It indicates an association between severity of malnutrition with changes in nerve conduction. The detrimental effects of malnutrition may be the cause for long-term neurological deficits in children with PEM, but further studies should assess children who have recovered from malnutrition.

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