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Correlates of Peripheral Neuropathy in Children with Type 1 Diabetes Mellitus

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ABSTRACT
Peripheral neuropathy is one of the commonly encountered complications in children suffering from type 1 diabetes mellitus leading to significant morbidity in children in their growing years, contributing to reduce QALY. Timely intervention and prevention of such complication will not only reduce morbidity but also helps maintain better quality of life. The study design was approved by the institutional ethical committee. Informed written consent was obtained from parents/ care givers of children before enrollment. History, physical and neurological examination findings were recorded on pre structured and predesigned profroma. Children with Type 1 Diabetes Mellitus with the duration of disease being at least 5 years were included in the study and were assessed for eligibility. Mean age at onset of disease in group with normal NCV was 5.1 years with minimum and maximum age at onset being 1 and 12 years, respectively. Mean age at onset of disease in group with neuropathy was 6 years with minimum and maximum age at onset being 1 and 13 years, respectively.

INTRODUCTION

Estimated 97,700 children in India are afflicted by Type 1 Diabetes mellitus with increasing prevalence. World over, approximately 11, 06,500 children are living with type 1 diabetes mellitus according to World Health Organization report of the International Diabetes Federation for the South East Asian Region[1]. Prevalence rates are expected to raise with easy access to insulin therapy and better survival rates owing to advancements in healthcare delivery and are responsible for a growing proportion of global health expenditure[2]. Basic pathology in type 1 diabetes mellitus is inadequate Insulin release with consequent rise in blood sugars., if poorly controlled, incites cascade of immunological response leading to micro and macro-vascular complications like, neuropathy, retinopathy and nephropathy[3]. Complications are expected earlier in patients with poor glycemic control and with increasing duration of illness. Peripheral neuropathy is one of the commonly encountered complications in children suffering from type 1 diabetes mellitus leading to significant morbidity in children in their growing years, contributing to reduce QALY. Timely intervention and prevention of such complication will not only reduce morbidity but also helps maintain better quality of life[4]. Preventive strategy shall be based on screening by nerve conduction study and specific intervention by rehabilitation, better glycemic control and hence formulate a screening protocol. Nerve conduction study, is a non-invasive technique that helps diagnose neuropathy in sub-clinical stage, there-by guiding therapeutic interventions in the window period to prevent clinical neuropathy. Clinical examination and nerve conduction study was carried out in children with type 1 diabetes mellitus to establish prevalence rates of neuropathy as a primary outcome measure.

MATERIALS AND METHODS

Children with Type 1 diabetes mellitus (with duration >5 years) attending diabetic clinic were enrolled into the study. The study design was approved by the institutional ethical committee. Informed written consent was obtained from parents/care givers of children before enrollment. History, physical and neurological examination findings were recorded on pre structured and predesigned profroma. Children with Type 1 Diabetes Mellitus with the duration of disease being at least 5 years were included in the study and were assessed for eligibility.

Nerve Conduction Study: NCS was performed after explaining the procedure to the parents and the child. It was done by using standard "Allengers Scorpio Electromyography machine". Stimulating electrode was placed on the nerve surface and the response was recorded by placing two electrodes G1 and G2. Median and ulnar nerves from the upper limb and tibial, sural and peroneal nerve from the lower limb were selected. NCS was conducted by the same technician and reporting was done by the same Paediatric neurologist for all 95 patients. At the time of visit, samples for blood glucose, HbA1c, liver function test, urea and creatinine were sent. Along with this, all children were subjected for ophthalmological examination by experienced ophthalmologists to look for diabetic changes. HbA1c reports of previous one year were collected and mean was calculated and were designated, good control, fair control and poor control based on HbA1c range of $\leq$7.5, 7.6-9.9 and $\geq$10 respectively.

Inclusion Criteria: Children diagnosed with Type 1 Diabetes Mellitus with duration of illness >5 years enrolled in Diabetic clinic of Indira Gandhi Institute of Child Health.

Exclusion Criteria: Children with Type 1 Diabetes Mellitus with history and examination suggestive of other neuropathies.

- Malnutrition.
- Neuromuscular diseases.
- Connective tissue disorders.
- Prolonged hospitalization for any reason.

RESULTS AND DISCUSSIONS

Table 1: Comparison of Mean Age Among Study Population

NCV	N	Mean	SD	Median	Min.	Max.	't' value*	'p' value
Normal	49	11.1	3.416	10.0	6	18	5.073	0.027
Neuropathic	46	12.6	3.367	13.0	7	18		
Total	95	11.8	3.465	12.0	6	18		

Mean age of study population was 11.8 years. Mean age in neuropathic and normal group was 12.6 years and 11.1 years respectively, indicating advancing age as a risk factor (p-value-0.027).

Table 2: Age Wise Comparison Between Normal and Neuropathic Population

	Age					
	6-10 Years	10-15 Years	15-18 Years	Total	2 value*	p value
Normal	25	17	7	49	11.275	0.004
	51.0%	34.7%	14.3%	100.0%		
Neuropathic	13	20	13	46		
	28.3%	43.5%	28.3%	100.0%		
Total	38	37	20	95		
	40.0%	38.9%	21.1%	100.0%		

Of the 46 participants with neuropathy, 13 (28.3%), 20 (43.5%) and 13 (28.3%) belonged to age group of 6-10 years, 10-15 years and >15 years, respectively, reflecting higher prevalence rates as the age progressed with significant p-value of 0.004. Out of 49 participants with normal nerve conduction, 25 (51%) were between 6-10 years, 17 (34.7%) were between 10-15 years and 7 (14.3%) were above 15 years, showing reduced proportion with normal NCV as the age progressed (p-value-0.004).

Table 3: Comparison of Mean Age of Onset Between Normal and Neuropathic Population

NCV	N	Mean	SD	Median	Min.	Max.	't' value*	'p' value
Normal	49	5.1	3.266	4.0	1	12	1.877	0.174
Neuropathic	46	6.0	3.432	6.3	1	13		
Total	95	5.6	3.363	5.0	1	13		

Mean age at onset of disease in group with normal NCV was 5.1 years with minimum and maximum age at onset being 1 and 12 years, respectively. Mean age at onset of disease in group with neuropathy was 6 years with minimum and maximum age at onset being 1 and 13 years, respectively.

Table 4: Age Wise Comparison of Duration of Illness between Normal and Neuropathic Population

	Duration of Illness					
	5-9 years	10-14 years	>14 years	Total	2 value*	P value
Normal	47	2	0	49	3.138	0.208
	95.9%	4.1%	.0%	100.0%		
Neuropathic	40	4	2	46		
	87.0%	8.7%	4.3%	100.0%		
Total	87	6	2	95		
	91.6%	6.3%	2.1%	100.0%		

Out of 49 participants with normal NCS, 47 (95.9%) belong to duration of illness between 5-9 years and remaining 2 (4.1%) belong to duration of illness between 10-14 years. Out of 46 participants with neuropathy, 40 (87%) belong to duration of illness between 5-9years, 4 (8.7%) belong to duration of illness between 10-14 years and 2 (4.3%) belong to duration of illness >14 years.

Table 5: Distribution of Duration of Illness Among the Study Population

Duration of illness	Normal	Neuropathy	Total
5-9 years	47 (54%)	40 (46%)	87 (100%)
10-14 years	2 (33.3%)	4 (66.6%)	6 (100%)
>14 years	0	2 (100%)	2 (100%)

87 participants with duration of illness between 5-9 years, 46% (40) had neuropathy. 6 participants with duration of illness between 10-14 years, 66.6% (4) had neuropathy. 2 participants with duration of illness of >14 years, 100% (2) had neuropathy.

Table 6: Sex Distribution Among Normal and Neuropathic Population

	Gender				
	Male	Female	Total	2 value*	P-value
Normal	22	27	49	0.324	0.569
	44.9%	55.1%	100.0%		
Neuropathic	18	28	46		
	39.1%	60.9%	100.0%		
Total	40	55	95		
	42.1%	57.9%	100.0%		

In participants with normal NCS, 22 (44.9%) were males and 27 (55.1%) were females. In neuropathic participants, 18 (39.1%) were males and 28 (60.9%) were females.

Table 7: Distribution of Age (Years) Between Types of Neuropathy

		Age				
		6 to 10 Years	10 to 15 Years	15 to 18 Years	Total	P- value
Normal	Count	25	17	7	49	0.219
	% of Total	26.3%	17.9%	7.4%	51.6%	
Motor Axonal Neuropathy	Count	2	3	2	7	
	% of Total	2.1%	3.2%	2.1%	7.4%	
Mild Demyelinating Motor Neuropathy	Count	11	17	11	39	
	% of Total	11.6%	17.9%	11.6%	41.1%	
Total	Count	38	37	20	95	
	% of Total	40.0%	38.9%	21.1%	100.0%	

Total of 7 patients had motor axonal neuropathy, 2 each from the age groups of 6-10 years and 15-18years. 3 from the age group of 10-15 years39 patients had demyelinating motor neuropathy, of which 11 were from age group of 6-10years, 17 and 11 patients were from 10-15 years and 15-18 years respectively.

Table 8: Comparison of Mean Age (Years) Between Types of Neuropathy

NCV	N	Mean	SD	Min	Max
Normal	49	5.1	3.266	1	12
Motor axonal	7	7.42	4.033	1	12
Mild demyelinating motor	39	5.8	3.373	1	13
Total	95	5.6	3.363	1	13

Mean age of patients with motor axonal neuropathy and demyelinating motor neuropathy was 7.42 years and 5.8 years respectively.

Table 9: Comparison of Baseline Characteristics with Other Studies

	Vahideh Too pchizadeh *et al.*[4]	Xin-Hua Bao *et al.*[5]	Funda Cenesiz *et al.*[6]	Sang-Soo Lee *et al.*[8]	Present study
Type of Study	Cross sectional study	Cross sectional study	Cross sectional study	Prospective study	Cross sectional study
Sample Size	40	38	40	37	95
M:F	15:25	18:20	17:23	14:23	40:55
Age Group Studied	<18 years	4-21 years	4-18 years	3-19 years	6-18 yeas
Mean Age	12.73±0.43 years	12.7 years	11.9±3.6 years	12±3.7 years	11.8±3.465 years

Current study included 95 children with disease duration of >5 years, which is the largest among the studies compared, to evaluate neuropathy in type 1 diabetes mellitus. Out of 95 children, 40 were males and 55 were females with male to female ratio of 1:1.3, similar female predominance was noted in other studies, though majority of the studies didn't show statistically significant correlation. Mean age of the present study population was 11.8±3.46 years, which was comparable to other studies[7].

CONCLUSION

Total of 7 patients had motor axonal neuropathy, 2 each from the age groups of 6-10 years and 15-18 years. 3 from the age group of 10-15 years 39 patients had demyelinating motor neuropathy, of which 11 were from age group of 6-10 years, 17 and 11 patients were from 10-15 years and 15-18 years respectively

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