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Clinical Application of Electrophysiological Values of Upper and Lower Limb Nerve Conduction Parameters: A Guide for Clinical Decision Making

Deepak Goel[1*], Vikram Sharma[2] and Chandra Prakash[3]

[1]Associate Professor, Neurology, Department of Neurology, Swami Ram Himalayan University (SRHU) Dehradun, india
[2]Consultant Neurology, Sunshine Hospital, Hyderabad, India
[3]Chief technician Neurophysiology lab, Max Institute of Neurosciences Dehradun (MIND), India

***Corresponding author:** Deepak Goel, Associate Professor, Neurology, Department of Neurology, Swami Ram Himalayan University (SRHU) Dehradun, india, Tel: 0135-2471198, E-mail: goeld007in@yahoo.co.in

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Abstract

Objective: our intention was to collect our own normative data of various nerve conduction parameters in upper and lower limb, develop our own reference values and finally compare it with available values for clinical application.

Methods: All nerve conduction reported normal in our lab from 2015-2018 were collected. Means (SD) of normal values for Latency, amplitude, velocity of median, ulnar, peroneal, tibial and sural nerves were collected and upper/lower limits of reference values of all parameters were developed. Finally these parameters were compared with already published values for clinical usage.

Results: Mean (SD) values of all motor and sensory parameters were not different as shown in other studies with normative data. LLN/ULN (Lower/Upper Limit of Normal) values for different parameters were calculated with mean±2SD. Wide variation found in the normative reference values. We had compared these values from three other published reference values showed that mean±2SD values are better than mean±3SD values. 15-34% patients who were normal on mean±2SD values were abnormal on mean±3SD values.

Conclusion: application of LLN/ULN reference values are important to know for better diagnosis of patients based on nerve conduction study. The diagnosis of demyelination versus axonal neuropathy, carpel tunnel syndrome, and conduction block in chronic inflammatory neuropathy requires knowing the above-mentioned parameters.

Keywords: Normative values of nerve conduction, reference limits values of nerve conduction, clinical application of nerve conduction study

Introduction

Clinical utility of nerve conduction studies (NCS) in practice includes; 1) finding the site of nerve lesion: peripheral nerve or root; 2) pathophysiological typing of neuropathy: axonal or demyelinating; 3) distribution of involvement: symmetrical or asymmetrical; 4) severity of nerve lesion: neuraprexia, neurotmesis or axonotmesis; 5) finding out the clinical type of neuropathy: hereditary versus acquired, large- fiber versus small fiber; and 6) to find specific diagnosis like Carpel tunnel syndrome (CTS), Guillain-Barre Syndrome (GBS) or Chronic Inflammatory Demyelinating Polyneuropathy (CIDP). Different types of parameters are recorded in motor and sensory NCS for achieving above mentioned goals [1]. The parameters used in NCS for clinical diagnosis have reference values for upper and lower limit of normal.

In routine clinical practice, parameters used for motor nerve assessment are distal motor latency (DML), compound motor action potential (CMAP) amplitude and duration, motor nerve conduction velocity (MNCV) and motor f wave latency (FWL). For sensory nerve assessment, distal sensory nerve latency (SNL), sensory nerve action potential (SNAP) and sensory nerve conduction velocity (SNCV) are important parameters to record [2].

Other than pathological conditions, various physical factors can also affect the motor and sensory conduction like age, BMI (Body Mass Index) and surrounding temperature. Motor conduction slows down by 0.4 – 1.7 m/s per decade after 20 years age and sensory conduction by 2-4 m/s per decade. Similarly, fastest motor nerve conduction velocity (MNCV) is reduced by approximately 1 m/s per ˚C temperature fall (best results with 34 ˚C) [3].

Normative values of all NCS parameters are essential for differentiating from normal to abnormal. Wide ranges of normative values of various NCS parameters were published in previous studies [4-8]. It is some time difficult for the clinicians to differentiate between normal or abnormal due to wide variation in the values of NCS parameters. For better clinical guidance specific upper and lower limits of normal values in nerve conduction studies were also published. [4-8]. These upper and lower limits of normal were also not based on same formula and were not matching from disease based guidelines. For example one guideline calculated upper and lower limit of normal by mean±3SD formula [4] and other two studies used the formula of mean±2SD [6, 7]. Currently, we also don't know which guideline is better applicable to Indian patients.

The aim of current study was to describe normal range, mean (SD), lower limit of normal (LLN), and upper limit of normal (ULN) for various NCS parameters followed by comparison our LLN and ULN with other reference values given by international bodies or guidelines. Final aim was to assess the clinical utility of these LLN and ULN values of motor and sensory nerve conduction parameters. The assessment and formulation of these reference values will help clinicians for better NCS based decision on Indian patients.

Methods

We have applied four steps approaches to achieve our goals. At first step we collected all nerve conduction studies reported as normal from our lab during last three years and data was analyzed for various motor and sensory parameters of median, ulnar, peroneal, tibial and sural nerves with age and gender. Step 2: we have calculated upper and lower limit of normal (ULN and LLN) values of all NCS parameters with formula of mean±2SD (>95 and <5 percentile). At third step we compared our reference values with ULN and LLN from other available studies. For the comparison of ULN and LLN values of other studies we included three recently published studies. [4, 6-7]. Finally at fourth step we have seen how we can utilize these ULN/LLN parameters of normal nerve conduction studies in clinical practice.

All nerve conduction studies reported normal from our lab were collected from 2015-2018. For doing nerve conduction studies all standard operating procedure to be strictly followed for recording of various parameters for motor nerve conduction studies as described. [3]. Equipment used in study was Dantec key point G4 EMG/ NCS/ EP Workstation.

Findings of median, ulnar, peroneal, tibial and sural nerves were recorded for motor and sensory conduction. We measured DML in milliseconds (ms), CMAP amplitude in milli volts (mV), MNCV in meter/seconds (m/s), and FWL in milliseconds (ms) for motor nerve conduction. Peak sensory nerve latencies (PSNL) in ms, SNAP in microvolts (μV) and SNCV in m/s were recorded for sensory nerve conduction. The range and mean (SD) of all the parameters of motor and sensory conduction in upper and lower limbs were recorded. Percentage of drop of proximal CMAP to distal CMAP in all motor nerve was calculated for motor nerve conduction to decide the criteria for conduction block. Variation of all normative parameters was seen with side of studied limb, age and gender. Age groups were divided in four (< 18, 19-49, 50-79, and > 80 years). Age and gender related changes in mean values were calculated by using IBM SPSS Statistics for Windows version 20 (Armonk NY: IBM Corp.) and p value was calculated using ANOVA test.

The upper limits of normal reference values for DML, FWL and PSNL was calculated by mean+2SD (> 95 percentile); similarly Lower Limit of Normal (LLN) for CMAP, MNCV, SNAP and SNCV was calculated by mean-2SD (< 5 percentile). Finally we had compared the upper and lower reference values of our cohort with reference values given by other researchers [4, 6-7].

Results

Total 493 (209 male and 284 female) upper limb and 477 (231 male and 246 female) lower limb nerve conduction studies were reported normal during study period. Mean (SD) of all parameters according to side, age group and gender are shown in Table 1. Various motor and sensory nerve conduction parameters recorded were having significant variations according to age only. We have not recorded height, weight and body mass index (BMI) in our patients so these parameters were not compared. Mean (SD) values of DML for various nerves are shown in Table 1. Comparisons after ANOVA test showed significant association of age and gender with DML value (p = 0.000).

Table 1: Distribution of Mean (SD) of various nerve conduction parameters according to age, gender and side

Nerve	Variable	DML (ms)	Distal CMAP (mV)	MNCV (m/s)	FWL (ms)	Peak SNL (ms)	SNAP (μV)	SNCV (m/s)	P value
Median	Right side	3.38 (0.38)	10.62 (2.8)	54.19 (5.15)	24.95(3.37)	3.5 (0.41)	32.2(14.2)	54.7(6.7)	0.8
	Left side	3.37 (0.37)	10.54 (2.7)	54.5 (6.2)	24.6 (3.03)	3.5 (0.4)	33.8(14.5)	54.4 (6.4)	
	< 18 years	2.9 (0.54)	10.64(2.97)	55.46(6.9)	21.1 (5.4)	3.01 (0.65)	41.3(10.8)	57.2(8.3)	0.000
	19-49 yrs	3.3(0.34)	11.1(2.8)	55.1(5.3)	24.4(3.3)	3.4(0.37)	36.6(15.3)	55.5(6.3)	
	50-79 yrs	3.5(0.36)	9.9(2.5)	53.4(5.6)	25.5(2.4)	3.6(0.38)	27.5(10.9)	53.3(6.5)	
	> 80 years	3.8(0.1)	6.2(1.9)	44.8(14.1)	25.7(7.1)	3.9(0.43)	18.4(4.01)	48.3(3.02)	
	Male	3.5(0.37)	10.4(2.6)	54(5.9)	25(3.2)	3.5(0.37)	31.4(13.6)	54.7(6.05)	0.000
	Female	3.3(0.37)	10.7(2.8)	54.6(5.5)	24.6(3.2)	3.5(0.43)	34(14.8)	54.5(6.86)	
Total (493)		3.4(0.37)	10.6(2.75)	54.4(5.7)	24.8(3.2)	3.5(0.4)	32.95(14.4)	54.6(6.5)	
Ulnar	Right side	2.7(0.38)	9.9(2.2)	59.6(8.2)	25.9(3.5)	3.1(0.48)	29.8(14.3)	53.9(6.9)	0.7
	Left side	2.8(0.4)	9.2(2.2)	59.9(7.8)	25.8(3.2)	3.08(0.38)	29.7(12.2)	53.9(6.7)	
	< 18 years	2.7(0.65)	8.6(3.0)	59.9(7.2)	22.6(5.8)	2.8(0.75)	35.9(11.6)	54.9(9.3)	0.000
	19-49 yrs	2.7(0.37)	10.1(2.2)	61(7.2)	25.2(3.09)	3.04(0.37)	32(13.0)	54.6(6.4)	
	50-79 yrs	2.8(0.39)	8.9(1.95)	58.1(8.8)	26.9(3.2)	3.2(0.49)	26.3(13.2)	53(7.1)	
	> 80 years	3.2(0.34)	8.05(1.1)	52.4(7.0)	29.8(0.96)	3.4(0.31)	20(7.9)	47.2(4.0)	
	Male	2.9(0.4)	9.39(2.2)	58.4(7.9)	26.2(3.8)	3.09(0.44)	28.5(13.6)	54.2(5.9)	0.5
	Female	2.7(0.36)	9.7(2.2)	60.8(7.9)	25.5(2.98)	3.1(0.44)	30.7(13.1)	53.7(6.7)	
Total (493)		2.75(0.39)	9.6(2.2)	59.8(7.98)	25.8(3.4)	3.1(0.44)	29.75(13.4)	53.9(6.8)	
peroneal	Right side	3.8(0.75)	6.04(1.9)	46.6(4.2)	45.8(4.4)				
	Left side	3.9(0.73)	5.9(1.96)	46.7(4.6)	45.6(4.9)				
	< 18 years	3.8(1.3)	5.3(2.04)	45.8(3.95)	35.1(6.95				0.000
	19-49 yrs	3.9(0.75)	6.3(2.09)	47.4(4.7)	45.4(4.2)				
	50-79 yrs	3.8(0.69)	5.8(1.8)	46.3(4.09)	46.5(4.13)				
	> 80 years	4.2(0.86)	55.7(1.9)	40.3(2.4)	49.7(1.3)				
	Male	3.94(0.75)	6.2(2.03)	45.98(4.6)	46.3(5.08)				0.8
	Female	3.7(0.72)	5.8(1.8)	47.3(4.1)	45.2(4.2)				
Total (477)		3.8(0.74)	5.99(1.9)	46.6(4.4)	45.7(4.7)				
Tibial	Right side	3.9(0.78)	9.9(3.3)	45.8(5.3)	47.3(4.3)				0.8
	Left side	3.9(0.73)	10.8(3.7)	45.8(5.1)	48(4.6)				
	< 18 years	3.6(0.56)	13.3(4.3)	45.98(3.4)	36.9(6.4)				0.000
	19-49 yrs	3.9(0.73)	11.2(3.7)	46.4(5.06)	47.2(3.7)				
	50-79 yrs	3.94(0.76)	9.5(3.2)	45.3(5.4)	48.6(4.0)				
	> 80 years	4.44(1.3)	8.43(1.1)	43.2(2.8)	49.6(3.6)				
	Male	3.9(0.77)	10.6(3.6)	45.5(4.85)	47.6(4.7)				0.4
	Female	3.9(0.74)	9.98(3.4)	46.03(5.5)	47.7(4.1)				
Total(477)		3.9 (0.75)	10.3 (3.5)	45.8(5.2)	47.7(4.4)				

Sural	Right side					2.5(0.5)	19.4(8.3)	74.1(10.9)	
	Left side					2.6(0.44)	19.2(8.8)	72.7(11.6)	
	< 18 years					2.7(0.68)	23.9(7.46)	61.2(9.1)	0.000
	19-49 yrs					2.6(0.55)	20.5(8.8)	72.6(12.3)	
	50-79 yrs					2.5(0.38)	18.2(8.2)	74.8(10.2)	
	> 80 years					2.75(0.19)	12.7(4.6)	70.4(2.5)	
	Male					2.6(0.5)	19.03(9.9)	72.6(11.08)	0.5
	Female					2.5(0.43)	19.5(7.02)	74.2(11.4)	
Total (477)						2.53 (0.47)	19.3(8.5)	73.4(11.3)	

Yrs – years, DML – Distal Motor Latency, CMAP – Compound Muscle Action Potential, MNCV – Motor Nerve Conduction Velocity, FWL – F Wave Latency, SNL – Sensory Nerve Latency, SNAP – Sensory Nerve Action Potential, SNCV – Sensory Nerve Conduction Velocity, ms – milliseconds, mV – millivolts, m/s – meter per seconds, μV – micro-volts.

Means (SD) of all normative values for various motor and sensory conduction parameters were compared from other available studies and comparison is shown in Tables 2-4 [9-20]. Narrow range variation was noted in DML, MNCV, FWL, SNL and SNCV values while wide range of variation is observed in CMAP and SNAP values of different studies.

Upper limit of normal (ULN) and lower limit of normal (LLN) reference values were calculated by adding or subtracting 2-standard deviation from mean value. These values were compared with reference values provided by other guidelines. [4, 6-7] The comparison is given in Table 5. The comparative results showed that except SNAP value, all other parameters were comparable. We had recorded sensory nerve latency (SNL), sensory nerve conduction velocity (SNCV) and sensory nerve action potential (SNAP) for median, ulnar and sural nerve. In our cohort sensory conduction of median, ulnar and sural nerve are shown in Tables 4, 5. Age is significantly associated with values of SNL, SNAP and SNCV (p=0.000) with higher age associated with longer latency, lower amplitude and slower velocity.

Table 2: Comparative analysis of Mean (SD) of upper limb motor conduction

Study [ref]	Mean (SD) of median nerve DML (ms)	Mean (SD) of ulnar nerve DML (ms)	Mean (SD) of Median Nerve CMAP (mV)	Mean (SD) of Ulnar nerve CMAP (mV)	Mean (SD) of Median MNCV (m/s)	Mean (SD) of Ulnar MNCV (m/s)	Mean (SD) of median FWL (ms)	Mean (SD) of ulnar FWL (ms)
Wadoo OK, *et al.* [9]	3.12±0.39	2.59±.39	13.78±2.45	10.16±1.76	56.79±3.68	56.92±3.67	-	-
Pawar, *et al.* [10]	3.25±0.5	2.31±.38	14.00±4.08	13.05±2.76	56.33±4.57	58.13±4.7	25.5	26.09
Robinson, *et al.* [11]	3.6±0.4	2.9±0.4	9.5±2.9	8.4±2.1	54.4±3.8	56.3±6.2	-	-
Kimura J, *et al.* [12]	3.49±34	2.59±.39	7.0±3.0	5.7±2.0	57.7±4.9	58.7±5.1	26.6	27.6
Shahabuddin [13]	3.18±61	2.45±.34	11.79±.59	11.26±1.07	53.59±0.6	55.72±3.24	-	-
Shehab DK [14]	3.1±0.3	2.4±0.3	11.1±2.8	9.2±2.2	56.5±3.5	60.4±52	-	-
Misra and Kalita [15]	3.49±0.34	2.59±0.4	7.0±3.0	8.51±2.03	57.7±4.9	61.45±5.73		
Hennessey, *et al.* [16]	3.2±0.4	2.6±0.3	12.1±3.8	12.6±2.3	59.5±4.4	63±4.8	-	-
Falco, *et al.* [17]	3.5±0.5	2.7±0.3	9.2±3.1	9.9±1.8	54.4±5.4	61.1±4.1	-	-
DeLisa, *et al.* [18]	3.7	3.2	13.2	6.14	56.7	61.8	29.1	30.5
Oh SJ [19]	2.78	2.03	>5	>5	58.78	61.15	25.32	25.68
Current study	3.38±0.38	2.74±.38	10.58±2.8	9.57±2.22	54.35±6.05	59.78±8.18	24.8±3.4	25.8±3.5

DML – Distal Motor Latency, CMAP – Compound Muscle Action Potential, MNCV – Motor Nerve Conduction Velocity, FWL – F Wave Latency, ms – milliseconds, mV – millivolts, m/s – meter per seconds.

Table 3: Comparative analysis of Mean (SD) of lower limb motor conduction

Study (ref)	Mean (SD) of Peroneal nerve DML	Mean (SD) of tibial nerve DML	Mean (SD) of Peroneal Nerve CMAP	Mean (SD) of Tibial nerve CMAP	Mean (SD) of Peroneal motor CV	Mean (SD) of Tibial motor CV	Mean (SD) of Peroneal f wave latency	Mean (SD) of Tibial f wave latency
Kimura J, *et al.* [12]	3.7±0.86	3.9±1.0	5.1±2.3	3.8±1.9	48.3±3.9	48.5±3.6	-	-
Shahabuddin, *et al.* [13]	4.14±0.36	4.77±.036	5.37±.097	4.77±.036	49.01±9.03	45.52±3.04	-	-
Misra and Kalita [15]	4.55±0.59	3.9±0.5	4.23±1.61	-	46.54±4.4	48.3±4.5	-	-
Shehab DK [14]	3.95±0.54	4.2±0.8	-	-	48.2±2.8	46.95±3.35	-	-
Current study	4.83±0.74	3.91±o.75	5.99±1.93	10.3±3.5	46.65±4.41	45.77±5.2	45.74±4.67	47.65±4.43

DML – Distal Motor Latency, CMAP – Compound Muscle Action Potential, MNCV – Motor Nerve Conduction Velocity, FWL – F Wave Latency, ms – milliseconds, mV – millivolts, m/s – meter per seconds.

Table 4: Comparative analysis of mean (SD) of sensory nerve conductions in upper and lower limb

Sensory conduction Study (ref)	Median Peak SNL	Median SNAP	Median SNCV	Ulnar peak SNL	Ulnar SNAP	Ulnar SNCV	Sural Peak SNL	Sural SNAP	Sural SNCV
Misra and Kalita [15]	3.06±0.41	8.91±4.48	45.45±9.4	2.83±0.40	5.54±2.37	54.17±6.1	--	18.0±10.5	50.9±5.4
Johnson and Melvin [20]	--	--	--	3.2±0.25	--	57±5.0			
Kimura et al [12]	2.84±0.34	38.5±15.6	56.2±5.8	2.54±0.29	35±14.7	54.8±5.3			
Shehab DK et al [14]							2.8±0.27		50.1±5.45
Shahabuddin s et al [13]	03.05 ± 0.55	35.21±5.5	56.93±3.5	2.90 ± 0.36	26.73± 0.48	56.52± 0.48	2.47± 0.57	15.63±3.47	50.02±3.45
Current study	3.5±0.4	32.95±14.4	54.6±6.5	3.1±0.44	29.75±13.4	53.9±6.8	2.53±0.47	19.3±8.5	73.4±11.3

SNL – Sensory Nerve Latency, SNAP – Sensory Nerve Action Potential, SNCV – Sensory Nerve Conduction Velocity, ms – milliseconds, mV – millivolts, m/s – meter per seconds, μV – micro-volts.

Table 5: Comparative upper and lower limit of normative values for different nerve conduction parameters in current and three other studies

Parameter of nerve conduction studies (NCS)	Upper and lower limit according to mean±2SD (95 percentile or 5 percentile) in our lab	Mean±3SD Reference values for upper & lower limit of various parameters in a study by Chen S et al 2016 [4]	Upper and lower limit according to mean±2SD (95 percentile or 5 percentile) in study by Shivji Z et al 2019 from Pakistan [6]	Upper and lower limit according to mean±2SD (95 percentile or 5 percentile) in study by Fong SY et al 2016 from Malaysia [7]
Median DML	> 4 ms	>4.5 ms	> 3.8 ms	> 4.1 ms
Ulnar DML	>3.5 ms	>3.7 ms	> 3.1 ms	> 3.0 ms
Peroneal DML	>5.25 ms	>6.5 ms	> 4.5 ms	> 4.2 ms
Tibial DML	>5.31 ms	>6.1 ms	> 5.0	> 4.1 ms
Median CMAP	<6.3 mV	<4.1 mV	< 6.2 mV	< 7.4 mV
Ulnar CMAP	<6.2 mV	<7.9 mV	< 7.4 mV	< 7.0 mV
Peroneal CMAP	<3.4 mV	<1.3 mV	< 3.2 mV	< 3.0 mV
Tibial CMAP	<5.2 mV	<4.4 mV	< 5.7 mV	< 7.5 mV
% of fall in Proximal CMAP (Median)	> 26%			
% of fall in Proximal CMAP (Ulnar)	> 26%			
% of fall in Proximal CMAP (Peroneal)	> 31%	> 32%		
% of fall in Proximal CMAP (Tibial)	> 59%	> 71%		
Median MNCV	<45.8 m/s	<49 m/s	< 51 m/s	< 52 m/s
Ulnar MNCV	<47.97 m/s	<52 m/s	< 54 m/s	< 53 m/s
Peroneal MNCV	<40.4 m/s	<38 m/s	< 45 m/s	< 44 m/s
Tibial MNCV	<38.6 m/s	<39 m/s	< 42 m/s	< 40 m/s
Median FWL	>29.03 ms		> 29 ms	
Ulnar FWL	>30.3 ms		> 29 ms	
Peroneal FWL	>52.6 ms		> 54 ms	
Tibial FWL	>54.3 ms		> 50 ms	
Median PSNL	>4.2 ms	>3.3 ms	> 3.5 ms	
Ulnar PSNL	>3.8 ms	>3.1 ms	> 3.4 ms	
Sural PSNL	>3.3 ms	>3.6 ms	> 3.8 ms	
Median SNAP	<13.7 μV	< 11 μV	< 18 μV	< 7 μV
Ulnar SNAP	<12.2 μV	< 10 μV	< 15 μV	< 6 μV
Sural SNAP	<8.8 μV	< 4 μV	< 12 μV	< 7 μV
Median SNCV	<44.2 m/s		< 52 m/s	< 47 m/s
Ulnar SNCV	<43.3 m/s		< 53.3 m/s	< 48 m/s
Sural SNCV	<54.5 m/s		< 44 m/s	< 41 m/s

DML- distal Motor Latency, CMAP – compound motor action potential, MNCV – motor nerve conduction velocity, FWL – f wave latency, PSNL –peak sensory nerve latency, SNAP – sensory nerve action potential, SNCV – sensory nerve conduction velocity

Table 6: Showing percentage of our patients lying out of reference values provided by other groups.

Parameters	Percentage of patients found out of range according to the criteria of Chen S *et al.* [4]	Percentage of patients found out of range according to the criteria of Shivji Z *et al.* [6]	Percentage of patients found out of range according to the criteria of Fong JY *et al.* [7]
Median MNCV	72 (14.6%) had reading < 49 m/s	133 (27%) had reading < 51 m/s	169 (34.3%) had reading < 52 m/s
Median PSNL	308 (62.5%) had reading > 3.3 ms	226 (45.8%) had reading > 3.5 ms	
Ulnar CMAP	102 (20.7%) had reading < 7.9 mV	67 (13.6%) had reading < 7.4 mV	54 (11%) had reading < 7.0 mV
Ulnar MNCV	82 (16.6%) had reading < 52 m/s	121 (24.5%) had reading < 54 m/s	102 (20.7%) had reading < 53 m/s
Ulnar PSNL	206 (41.8%) had reading > 3.1 ms	94 (19%) had reading > 3.4 ms	

MNCV – Motor Nerve Conduction Velocity, PSNL – Peak Sensory Nerve Latency, CMAP – Compound Muscle Action Potential, ms – milliseconds, m/s – meter/second

The reference values provided by Chen S, *et al.* (mean±3SD) and by Shivji, et al or Fong, *et al.* (Mean±2SD) were applied to our data for finding out percentage of accurate diagnosis of normal study [4, 6, 7] Table 6 is showing the percentage of patients found out of reference values of normal NCS by different guidelines. After application of reference values, most of the parameters had accuracy rate of > 95% except median and ulnar MNCV, median & ulnar PSNL and ulnar CMAP. False normal percentage was ranging from 14.6% - 34.3% for median MNCV, 16.6% - 24.5% for ulnar MNCV, 45.8% - 62.5% for median PSNL, 19% - 41.8% for ulnar PSNL and 11% - 20.7% for ulnar CMAP. Peak sensory latency form median nerve was 4.2 ms (our study), 3.3 ms (USA) and 3.5 ms (Pakistan). PSNL for ulnar nerve was 3.8 ms (our), 3.1 ms (USA) and 3.4 ms (Pakistan). For sural nerve PSNL was 3.3 ms, 3.6 ms and 3.8 ms from our lab, USA and Pakistan respectively (Table 5). Rest all the parameters were having > 95% accuracy by both the parameters (±2SD or ±3SD deviation from means). When compared with other country our data were almost similar to Pakistan population, while few parameters were widely different from USA and Malaysian population. LLN reference values for SNCV in our lab were 44 m/s, 43 m/s and 55 m/s for median, ulnar and sural nerves respectively. Range of SNCV was 52 m/s, 53.3 m/s and 44 m/s from Pakistan form median, ulnar and sural respectively. Form Malaysia SNCV for median, ulnar and sural was 47 m/s, 48 m/s, and 41 m/s respectively.

Discussion

For the diagnosis of demyelinating neuropathy important parameters are; 1) prolong distal latency; 2) decrease nerve conduction velocity; 3) conduction blocks; and 4) prolonged f wave latency. For axonal neuropathy diagnosis is based on reduced CMAP amplitude with normal conduction velocity and reduced SNAP. Clinicians have to quickly decide about abnormal NCS after using reference values. There is wide range of motor and sensory nerve conduction parameters so a chance of false normalcy is possible [1].

We have tried to develop our own reference values and compared with other studies to make better clinical decision on NCS. Among previously available reference values of lower and upper limit were based on mean±3SD in one study. [4] While in two other studies LLN and ULN values were based on mean±2SD for deciding reference values. [6,7] After application of older reference values 15% to 62% of our patients were abnormal. In further discussion we have described normative values of individual NCS parameters in our lab and in other studies for the electro - diagnostic guidelines. Most common clinical setting where clinicians get NCS, are carpel tunnel syndrome (CTS), demyelinating and axonal neuropathies thus we tried to put the normative reference values for accurate diagnosis of the above mentioned conditions.

Distal motor latencies (DML):

DML value is age dependent and found higher with increasing age. The upper limit of normal values for median DML was 4 ms (our study), 3.8 ms (Pakistan) and 4.1 ms (Malaysia) with mean+2SD (95th percentile). Upper limit of median nerve DML by Chen *et al.* (USA) was 4.5 ms with mean+3SD (97 percentile). The electro diagnostic criteria of carpel tunnel syndrome recommended that median nerve DML should be > 4.2 ms for the diagnosis of CTS. [21-22] In other study the criteria for prolong median DML was > 4.6 msec. [23] So we have choices form 3.8-4.6 ms to label median DML abnormal. If age variation is balanced the highest normal value of median DML 4.5 ms can be used with high confidence for clinical application.

For ulnar nerve the upper limit reference value for DML was 3.5 ms (our lab), 3.1 ms (Pakistan), 3.0 ms (Malaysia) (95th percentile) and 3.7 ms (USA) (97th percentile). For the diagnosis of carpel tunnel syndrome difference of median and ulnar DML should be more than 1.8 msec. [23] Our cohort of 493 nerves showed that difference of median and ulnar DML was <1.8 ms in all except one. Therefore, median DML > 4.5 ms, ulnar DML of >

3.7 ms and difference of median & ulnar DML of > 1.8 msec can be taken as abnormal.

For Peroneal DML, upper limit reference value given by Chen S et al was > 6.5 ms (97th percentile) and it was 5.25 ms (Ours), 4.5 ms (Pakistan), 4.2 ms (Malaysia) by 95th percentile. For tibial nerve, upper limit of reference value of DML was 6.1 ms (Chen S et al) and in our cohort it was 5.31 ms, 5.0 ms (Pakistan), and 4.1 from Malaysia. Guidelines for CIDP suggested that values of DML > 50% above the ULN for motor nerves should be selection criteria. Thus absolute value above 5.5 ms (with 2-snadard deviation) and above 6.0 ms (3-standard deviation) would be appropriate for ULN for peroneal and tibial nerve DML.

Compound Motor Action Potential (CMAP) amplitude

Distal and proximal CMAP amplitude are useful for the diagnosis of axonal and demyelinating neuropathy. For median nerve the lowest reference value of distal CMAP amplitude was 4.1 mV (USA) with 3-standard deviation while it was 6.3 mV (ours), 6.2 mV (Pakistan) and 7.4 mV (Malaysia) with 2-standard deviation. For the diagnosis of carpel tunnel syndrome median distal CMAP amplitude of < 5 mV was considered abnormal. [22] The LLN of distal CMAP amplitude of ulnar nerve was 6.2 mV (ours), 7.4 mV (Pakistan) and 7.0 mV (Malaysia) with 5th percentile and it was 7.9 mV (USA) with 3rd percentile. Due to wide variations in LLN values it is difficult to finalize the universally accepted CMAP amplitude and a single value of 6.5 mV can be the option for both median and ulnar nerves.

The lower reference values of CMAP amplitude for peroneal and tibial nerve were 1.3 mV and 4.4 mV respectively in USA (3RD percentile). The LLN values (5th percentile) of CMAP amplitudes for the peroneal and tibial nerves were 3.4 mV & 5.2 mV (ours), 3.2 mV & 5.7 mV (Pakistan) and 3.0 mV & 7.5 mV (Malaysia). There was again wide variation in LLN values of peroneal and tibial CMAP amplitudes. Average LLN values of 3.5 mV for peroneal and 5.5 mV for tibial can be logical for clinical application. It is important to remember that clinical diagnosis should not be based on CMAP of lower limbs alone if CMAP amplitudes are markedly reduced in lower limb and demyelinating neuropathy is suspected then additional upper limb study is important before final decision making. [1]

In clinical practice the distal to proximal drop in CMAP amplitudes value is important for the diagnosis of conduction block for demyelinating neuropathies. There are wide variations in the criteria for conduction block in available literature. [19] The diagnosis of conduction block was based on > 20% fall in CMAP amplitude with normal CMAP duration and > 30% if CMAP duration is prolonged. [3, 24] Another suggested option of 41% fall in proximal CMAP amplitude was there as a single value for conduction block. [19] The upper reference limits of drop in proximal CMAP for peroneal and tibial were 32% and 71% respectively by Chen S *et al.* [4] In our study upper limit (mean+ 2SD) of fall in proximal CMAP for median, ulnar, peroneal and tibial nerve was 26%, 26%, 31% and 59% respectively. For the diagnosis of CIDP, the task force criteria of conduction block was, > 50% fall in proximal CMAP in two nerves when distal CMAP is > 20% above the LLN. [5] Since normal CMAP amplitude fall in tibial nerve was > 50% it is least useful for the diagnosis of conduction block and selection of two other motor nerves should be used. CMAP amplitude fall of > 30% in other nerves can be used for diagnosis of conduction block as suggested by Fisher *et al.* [24]

Motor nerve Conduction velocity (MNCV): The lower (3rd percentile) reference values of MNCV for median, ulnar, peroneal and tibial nerve were; 49 m/sec, 52 m/sec, 38 m/sec and 39 m/sec respectively. [4] In our study, LLN values of MNCV (<5th percentile) for median, ulnar, peroneal and tibial nerves were; 46.8 m/s, 48 m/s, 40.4 m/s and 38.6 m/s respectively. No significant variation noted in LLN values of MNCV was observed in different studies included for analysis (Table 5). Median MNCV < 49 m/s is one of the selected electro-diagnostic criteria for CTS [21]. For the diagnosis of CIDP selected criteria is reduction in MNCV of ≥ 30% below LLN in two nerves. [5] MCV < 50 m/s in upper limb and < 40 m/s in lower limb can be appropriate LLN for clinical application.

F wave latency (FWL)

We could find only one study for the upper reference values for FWL of all motor nerves for comparison. [6] Our study had ULN (> 95th percentile) values of FWL of 29 ms, 30 ms, 53 ms and 54 ms for median, ulnar, peroneal and tibial nerves. In other study from Pakistan, the ULN values of FWL were 29 ms, 29 ms, 54 ms and 50 ms respectively for median, ulnar, peroneal and tibial nerves. [6] Fisher MA suggested that FWL of > 31 ms in upper limb and > 61 ms in lower limb should be considered as prolonged. [25] The European criteria for definite CIDP was F wave latency: ≥ 30% above the ULN in two nerves if CMAP amplitudes are > 80% of LLN and FWL ≥ 50% if CMAP amplitude is < 80% of LLN [5]. We support that FWL > 31 msec for upper limb and > 61 msec for lower limb can be useful ULN value in clinical practice.

Sensory nerve action potential (SNAP)

SNAP is the most important sensory conduction parameter used in clinical practice. Fall in the SNAP is found both in axonal and demyelinating neuropathy. Sensory axonal loss leads to reduction or loss of SNAP, while in demyelinating disorders there is reduction of SNAP with prolong duration. [3] Our LLN reference values of SNAP were 14μV, 12 μV and 9 μV for median, ulnar and sural nerve respectively. From other sources range of lower reference values of SNAP were 7-18 μV for median, 6-15 μV for ulnar and 4-12 μV for sural. Lower range was from USA and Malaysia while higher from India and Pakistan (table 5). Due to high age and BMI dependency and variations in reference values of sensory nerve latencies we have to be decided at local lab level. Clinical utility of SNL and SNCV is less commonly discussed in literature. [8, 26-27] Similar to MNCV, common values for SNCV in upper limb of 50 m/s and in lower limb 40 m/s can be used as lower limit of normal. Utility of SNAP in the diagnosis of CIDP was proposed by Bragg JA and Rajabally. [8, 27] The criterion used for diagnosis of CIDP was: SNCV ≤ 80% of LLN (normal SNAP) or SNCV ≤ 70% of LLN (lower SNAP). [8] Local lab reference values of LLN for SNAP and SNCV used in this study were 20 μV and 50 m/s for median nerve, 29 μV, 14 μV and 9 μV (age < 40, 41- 59 and > 60 years), and 50 m/s for ulnar nerve, 14 μV, 6 μV and 3μV (age < 40, 41-59, 60 years) and 40 m/s for sural nerve. [8] In conclusion, patient with normal SNAP velocity of < 40 m/s and of < 35 m/s with lower SNAP can be taken as abnormal.

Sensory nerve latency (SNL)

Peak SNL is age dependent and in our lab for less than 50 years PSNL for median, ulnar and sural nerve was 4.0 ms, 3.8 ms, and 3.4 ms respectively. For> 50 years PSNL was 4.3 ms, 4.0 ms and 3.2 ms for median, ulnar and sural nerves. Longer duration of sensory latency was not explained in our study but BMI can be contributing factor. In other guidelines, prolonged sural peak SNL (> 2.9 ms) has been linked with diabetic neuropathy. [26] Prolonged median peak SNL (> 3.5 ms) was included in the criteria for carpel tunnel syndrome (CTS) [22]. Peak ulnar SNL of > 3.2 ms with long median SNL (> 3.5 ms) was suggested to be a point towards polyneuropathy. [22] Normally right- left median SNL difference should be less than 0.5 ms and higher difference suggest CTS. [22] Median- ulnar latency difference (MULD) of more than 0.5 ms is also an important criterion for CTS. [23] In our cohort only 267 (54.2%) patients had latency below 3.5 ms latency for median nerve. Finally, ULN values of PSNL of ≥4 ms for median, ulnar and ≥3.5 ms for sural nerve can be used.

Limitation of study

Normative data collected in our study was not on healthy individuals but on patients with some neurological ailment having normal nerve conduction study, although it is more real time data to make decision for normal study. Secondly our data are lab specific and had limitation for general application but other reference lab values and denominators used for clinical diagnosis can be helpful for general practice.

Conclusion

Our study provided comprehensive reviews and guidelines to make correct decisions on patient's findings of nerve conduction studies. Large number of patients data analysed in this study is strength of our paper. Limitations of our study were no data on height, weight and BMI variations of NCS parameters. Not included other nerves like radial, musculocutaneous and axillary. Since the study was done on patients presenting to neurology department not on healthy volunteers, this presents real scenario of variations in different parameters. Our study made clear that wide variation in different parameters of motor and sensory nerves creates a real challenge for the clinicians to decide normal and abnormal study. It is seems important that labs has to have clear cut ULN and LLN reference values of different NCS parameters based on local data or published studies. We could not conclude whether 2-standard deviation is better or 3-standard deviation for deciding ULN and LLN values. Might be in due course of time more studies and meta-analysis would answer this question.

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