

Developing Normative Reference Values for Nerve Conduction Studies of Commonly Tested Nerves among a Sample Pakistani Population

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ABSTRACT

Introduction: Most neurophysiology departments around the world establish their own normative data. However, ethnic differences are not taken into account. Our aim was to establish normal nerve conduction studies (NCS) data for routinely tested nerves in individuals of Pakistani (South Asian) origin and to compare with Western published data. **Materials and Methods:** One hundred healthy adults' nerves were assessed, using standardized techniques. Individuals were grouped into age groups. Gender differences were assessed. **Results:** Of the 100 volunteers, 49 were female and 51 were male. Their mean age was 39.8 years. Findings showed statistically significant prolongation of median distal motor latency (DML) and F-wave latency with age and reduction of median, ulnar, and sural sensory amplitudes as age increased. Gender differences showed consistent difference in the normal values for median, ulnar, and peroneal DMLs and respective F-wave latencies, which were significantly shorter in females. Sensory amplitudes of tested upper extremity nerves were significantly lower in males. Comparing with available data, our findings are similar to the Saudi population but significantly different from the American and multiethnic Malaysian populations. Pakistani individuals generally have significantly higher amplitudes and faster conduction velocities with similarities to South Asian studies. **Conclusions:** We recommend normative NCS parameters for commonly tested nerves for the Pakistani population, using standardized techniques to ensure highest quality testing and outcomes.

KEYWORDS: Nerve conduction studies, normal values, normative data, practices standards, reference values

INTRODUCTION

Nerve conduction studies (NCS) are an important diagnostic tool in the assessment of peripheral nervous system disorders and helps in diagnosis, prognostication, and longitudinal monitoring of a disease process.^[1,2] In order to identify abnormal values, a set of “normative” or “reference” values need to be determined.^[3,4] The latter are derived from a healthy subject population that approximates the demographics of the patients. Age, gender, temperature, techniques, and possibly ethnicity may affect the results.

With the dearth of published data on reference values that can be widely used, most neurophysiology departments around the world tend to identify their

own reference values^[3,5] or use established Western values. The neurophysiology department at the Aga Khan University Hospital (AKUH), Karachi, was established over 20 years ago. The aim of our study is to help establish NCS normative data that could be applicable in the Pakistani population and can be used in neurophysiology departments around the country. We also aim to compare our findings with the existing published data from different populations.

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MATERIALS AND METHODS

A prospective, descriptive study of willing healthy controls was undertaken over a 3-year period (2014–2017). Each individual was administered a standard screening questionnaire and only those individuals meeting the inclusion criteria were included in the study. Written consent was obtained. This study was approved by the Ethical Review Committee of the AKUH.

One hundred asymptomatic adult volunteers, over the age of 18 years, willing to consent, and without known sensory symptoms, neurologic disorders, or other medical issues that could affect peripheral nerves such as diabetes mellitus, thyroid disorders, Vitamin B12 deficiency, cancer with or without chemotherapy, or other such medications were enrolled. Participants underwent neurological examination, height and weight determinations, and NCS using standard methodology for sensory (median, ulnar, radial, median palmar, ulnar palmar, and sural) and motor (median, ulnar, peroneal, and tibial) nerves.

For NCS and electromyography, a Nicolet Viking machine was used. Low- and high-pass filters were set at 2 Hz and 10 kHz and 20 Hz and 3 kHz for motor studies and sensory studies, respectively, with a sweep speed of 2 ms/division.

Nerve conduction responses were recorded using standardized techniques. All responses were obtained using supramaximal stimulation and proper placement of electrodes. Data were collected for the following parameters: onset and peak latencies, amplitude, amplitude drop, conduction velocity (CV), and F-waves. All sensory nerves were examined antidromically. Amplitudes for the sensory nerve action potential (SNAP) were measured from the peak of the negative potential to the peak of the positive potential. SNAP peak and onset latencies were noted. Sensory median and ulnar nerves were stimulated at the wrist and recorded from the 2nd and 5th digits, respectively, at a distance of 14 cm. Distance for stimulation for palmar responses was 8 cm. The radial nerve was stimulated 10 cm proximal to the active electrode on the dorsolateral aspect of the distal forearm.

Median and ulnar motor nerves were tested with the active electrode over the motor point of the abductor pollicis brevis and the abductor digiti minimi muscles, respectively. In the lower limbs, for the tibial and peroneal nerves, the active electrodes were over the adductor hallucis and extensor digitorum brevis, respectively. The reference electrodes were placed on the tendon of the muscle in question. Distal stimulations

were 8 cm proximal to the active electrode for motor median, ulnar, and peroneal nerves and 9 cm for the tibial nerve. The acceptable limb temperature for performing NCS was $\geq 32^{\circ}\text{C}$. In the event of cool limb temperatures, the participant was warmed up using hot water bags or a heating pad to maintain the temperature, as needed.

Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics for Windows, Version 19.0. (Armonk, NY: IBM Corp). Continuous variables were reported as mean and standard deviation. Independent sample *t*-test was used to assess differences between sexes and age groups. Reference value was set to outside the mean ± 2 standard deviations. $P < 0.05$ was taken as cutoff level for statistical significance.

RESULTS

Of the 100 healthy volunteers, 49 (49%) were female and 51 (51%) were male. Their mean age was 39.8 ± 12.3 years (range 18–67). Participants were grouped in the age groups of <30 ($n = 24$), 30–39 ($n = 28$), 40–49 ($n = 20$), and >50 ($n = 28$) years. Male and female differences were assessed. Normal values for motor nerve and sensory nerve conduction are summarized in Tables 1 and 2, respectively.

Tables 3 and 4 show the variation in normal values of motor and sensory findings among various age groups.

Variations with age

There is a significant increase in the median distal motor latency and F-wave latency with age (>40 years) [Table 3]. Median SNAP from digit II and ulnar SNAP from digit V showed significantly higher amplitudes in the younger age groups (<40 years). Sural sensory amplitudes also decreased with increasing age ($P < 0.003$) [Table 4]. Tibial motor amplitudes decreased with age ($P 0.005$). Although peroneal motor CVs statistically increased with age, the increase through age groups is not consistent and therefore not clinically significant.

Variations with gender

Gender differences (adjusted for height) showed consistent difference in the normal values for median, ulnar, and peroneal distal motor latencies and respective F-wave latencies, which were significantly shorter in females for median, ulnar, and peroneal nerves [Table 5]. No significant gender differences were noted for motor conduction velocities.

Sensory amplitudes of median (digit II), ulnar (digit V), and radial were significantly lower in males [Table 6]. Amplitude and peak latency of ulnar palmar responses was also significantly different in males, with a lower

Table 1: Motor nerve conduction study findings of upper and lower limbs

	Distance	DML±SD (ms)	DML 95 th	Amp±SD (µV)	Amp 5 th	CV±SD (m/s)	CV 5 th	F-wave±SD (ms)	F-wave 95 th
Median	8.0	3.1±0.40	3.8	10.5±2.8	6.2	58.7±4.3	51	24.9±2.1	29
Ulnar	8.0	2.5±0.30	3.1	10.4±2.0	7.4	61.3±3.9	54	25.3±2.2	29
Tibial	9.0	3.9±0.6	5.0	12.5±4.5	5.7	48.6±4.1	42	45.4±4.1	54
Peroneal	8.0	3.4±0.5	4.5	6.1±2.0	3.2	50.7±3.9	45	44.7±3.7	50

DML: Distal motor latency, Amp: Amplitude, CV: Conduction velocity, SD: Standard deviation, 95th: 95th percentile, 5th: 5th percentile

Table 2: Sensory nerve conduction study findings of upper and lower limbs

	Onset DL (95 th)	Mean±SD	Peak DL (95 th)	Mean±SD	Amp (5 th)	Mean±SD	CV (5 th)	Mean±SD
Median								
Palmar	1.6	1.3±0.14	2.1	1.9±0.15	40.1	98±39.3	51.6	63±7.3
Digit II	2.7	2.3±0.18	3.5	3.0±0.27	18.0	41±15.1	52.0	60.4±4.5
Ulnar								
Palmar	1.5	1.2±0.13	2.0	1.7±0.15	18.1	44.1±19.5	53.3	66.1±6.6
Digit V	2.7	2.3±0.24	3.4	3.0±0.30	15.0	35.0±13.0		60.0±5.6
Radial - forearm	2.0	1.6±0.18	2.5	2.1±0.19	25.0	45.5±14.2	60.0	71.7±6.0
Sural - calf	3.0	2.4±0.3	3.8	3.2±0.32	12.0	22.5±8.8	44.0	57±6.3

DL: Distal latency, Amp: Amplitude, CV: Conduction velocity, SD: Standard deviation, 95th: 95th percentile, 5th: 5th percentile

Table 3: Motor nerve conduction study findings of upper and lower limbs grouped by age

Age	DML (ms) 95 th	DML±SD	Amp (µV) 5 th	Amp±SD	CV (m/s) 5 th	CV±SD	F-wave (ms)±SD	F-wave 95 th
Median (years)								
<30	3.7	3.0±0.32	7.0	11.0±2.5	52.2	59.6±3.4	25±2.2	29
30-39	3.6	3.0±0.37	6.8	11.2±2.6	50.4	60.0±4.1	24±2.2	29
40-49	4.0	3.2±0.36	6.2	10.2±2.5	51.0	58.1±4.7	25±1.4	28
≥50	4.0	3.2±0.43	4.6	10.0±3.3	51.0	57.8±5.0	26±2.0	29
<i>P</i>		0.02		0.33		0.36	0.01	
Ulnar (years)								
<30	3.3	2.7±0.33	6.9	10.2±2.2	54	61.3±4.1	25.1±2.2	29
30-39	3.1	2.4±0.28	7.2	11.0±2.3	54.4	61.1±3.7	25.1±2.4	30
40-49	3.1	2.6±0.28	7.5	10.5±1.5	54.2	63.2±3.5	25.2±2.2	28
≥50	3.1	2.5±0.28	5.8	10.1±2.0	54	60.1±3.7	25.8±2.2	29
<i>P</i>		0.059		0.38		0.06	0.62	
Tibial (years)								
<30	5.0	3.8±0.57	5.8	13.4±4.7	42.2	49.2±3.8	45.3±4.3	57.1
30-39	5.0	4.0±0.55	5.7	14.5±5.1	42.0	49.4±4.5	43.9±4.1	54.1
40-49	5.5	3.8±0.6	4.5	11.4±2.8	42.0	49.0±4.6	45.6±3.1	51.0
≥50	5.5	4.0±0.7	5.4	10.6±3.8	41.8	47.1±3.3	47±4.1	54.5
<i>P</i>		0.59		0.005		0.13	0.06	
Peroneal (years)								
<30	5.2	3.6±0.7	2.9	6.6±2.3	44.2	50.4±3.8	44.1±3.2	49.7
30-39	4.3	3.4±0.5	3.7	56.1±1.7	46.4	52.4±3.3	43.8±4.0	51.4
40-49	4.2	3.4±0.4	3.2	5.8±1.7	46.0	50.3±3.2	44.1±4.1	54.7
≥50	4.4	3.4±0.52	2.4	5.7±2.2	44.0	49.6±4.5	46±3.3	51.2
<i>P</i>		0.64		0.45		0.04	0.12	

DML: Distal motor latency, Amp: Amplitude, CV: Conduction velocity, SD: Standard deviation, 95th: 95th percentile, 5th: 5th percentile

amplitude and longer latency ($P = 0.03$, amplitude: male = 40.2 ± 19.6 and female = 48.4 ± 18.8 , peak latency: male = 1.8 ± 0.15 and female = 1.7 ± 0.14).

DISCUSSION

NCS are an important tool for the evaluation of peripheral nervous system disorders. The main aim of our study

was to provide reference NCS values for commonly tested nerves in normal Pakistani adult volunteers and to compare with published normative values, using standardized techniques. Falck and Stalberg^[6] determined that "Reference values in one laboratory can be used in others when techniques are standardized." Normative data for NCS to our knowledge have not been formally

Table 4: Sensory nerve conduction study findings of upper and lower limbs grouped by age

Age	DL (ms) 95 th	Peak DL±SD	Amp (µV) 5 th	Amp±SD	CV (m/s) 5 th	CV±SD
Median digit II (years)						
<30	3.5	3.0±0.37	18.6	43.6±13.2	52	59.2±4.8
30-39	3.4	3.0±0.24	34.4	51.0±16.2	53.4	61.7±4.0
40-49	3.4	3.1±0.19	16.3	35.4±10	53	60.2±3.8
≥50	3.5	3.1±0.21	15.4	32.5±12.0	53	60.2±12
<i>P</i>		0.06		<0.0001		0.27
Ulnar digit V (years)						
<30	3.4	3.0±0.38	13.2	37.8±14.5	51	61.6±5.7
30-39	3.4	3.0±0.21	22.9	39.5±11.6	53	61.2±5.3
40-49	3.4	3.1±0.31	20.0	34.8±10.1	50	57.4±4.1
≥50	3.5	3.1±0.24	14.0	27.7±11.8	50.4	58.7±6.1
<i>P</i>		0.052		0.003		0.03
Radial (years)						
<30	2.5	2.1±0.18	24	47.0±16.7	60	71.4±6.1
30-39	2.4	2.0±0.18	28.1	49.5±14.5	63	72.0±4.5
40-49	2.8	2.1±0.24	30	43.5±11.6	57.1	71.5±7.0
≥50	2.6	2.1±0.19	30	41.6±12.5	55.3	72.0±6.5
<i>P</i>		0.38		0.18		0.97
Sural (years)						
<30	3.0	2.4±0.20	10.5	24.5±10.8	49	57.7±4.2
30-39	3.6	3.1±0.27	15.4	26.2±8.2	45.8	57.7±4.2
40-49	4.0	3.1±0.31	10.1	21.0±7.6	56	57.5±7.1
≥50	4.1	3.2±0.4	9.3	18.2±6.0	51	56.2±8.1
<i>P</i>		0.94		0.003		0.62

DL: Distal latency, Amp: Amplitude, CV: Conduction velocity, SD: Standard deviation, 95th: 95th percentile, 5th: 5th percentile

Table 5: Motor nerve conduction study findings of upper and lower limbs grouped by gender

Gender	DL (ms) 95 th	DML±SD	Amp (µV) 5 th	Amp±SD	CV (m/s) 5 th	CV±SD	F-wave (ms) 95 th	F-wave±SD
Median								
Male	4.0	3.3±0.36	6.2	10.3±2.90	51.0	58.7±4.76	28.6	25.5±1.89
Female	3.6	2.9±0.35	7.4	10.6±2.81	51.3	58.7±4.0	29.1	24.3±2.21
<i>P</i>		<0.001		0.058		0.98		0.003
Ulnar								
Male	3.2	2.7±0.29	7.2	10.3±2.08	54.0	60.7±3.90	29.0	26.1±1.94
Female	3.1	2.5±0.29	7.3	10.7±2.11	54.0	62.0±3.85	28.5	24.5±2.36
<i>P</i>		0.001		0.33		0.24		<0.001
Tibial								
Male	5.0	4.0±0.63	7.6	12.2±3.73	43.0	48.0±3.45	53.3	46.4±3.50
Female	5.4	4.0±0.60	6.4	12.8±5.29	43.0	49.4±4.68	55.0	44.5±4.53
<i>P</i>		0.72		0.51		0.09		0.02
Peroneal								
Male	4.7	3.6±0.52	3.2	6.2±2.02	44.6	51.8±4.32	51.2	46.3±3.24
Female	4.5	3.3±0.54	3.0	5.9±2.07	45.5	53.2±3.76	50.0	43.1±3.66
<i>P</i>		0.002		0.50		0.08		<0.001

DML: Distal motor latency, Amp: Amplitude, CV: Conduction velocity, SD: Standard deviation, 95th: 95th percentile, 5th: 5th percentile

performed previously in our population. The reference values currently used in Pakistan are either established by individual institutions based on a very small sample size or based on Western data. We determined that there are some differences between the two groups.

Our reference values were compared to normative nerve conduction values from other population-based studies

that investigated asymptomatic healthy controls, using standardized techniques. The results of our study show similar findings to that described (taking variation in measurements techniques into consideration) in the Saudi and Indian population and somewhat to the Kuwaiti population^[7-9] but significantly different for sensory studies in the American and multi-ethnic Malaysian

Table 6: Sensory nerve conduction study findings of upper and lower limbs grouped by gender

Gender	Peak DL (ms)		Amp (μ V)		CV (m/s)	
	95 th	\pm SD	5 th	\pm SD	5 th	\pm SD
Median digit II						
Male	3.5	3.1 \pm 0.28	16.0	37.7 \pm 11.52	52.0	59.7 \pm 4.53
Female	3.4	3.0 \pm 0.25	22.0	45.5 \pm 17.17	52.5	61.2 \pm 4.52
<i>P</i>		0.10		0.004		0.12
Ulnar digit V						
Male	3.4	3.1 \pm 0.27	14	30.8 \pm 10.51	50.0	59.0 \pm 5.34
Female	3.4	3.0 \pm 0.30	15	39.2 \pm 14.0	52.0	60.7 \pm 5.87
<i>P</i>		0.02		0.001		0.07
Radial						
Male	2.5	2.2 \pm 0.18	24	40.9 \pm 12.30	58.5	71.1 \pm 5.92
Female	2.4	2.1 \pm 0.21	31	50.34 \pm 14.59	61.5	72.53 \pm 6.07
<i>P</i>		0.26		0.001		0.22
Sural						
Male	3.9	3.2 \pm 0.34	11.6	21.74 \pm 8.92	43.0	56.3 \pm 6.06
Female	3.8	3.2 \pm 0.30	11.0	23.38 \pm 8.73	43.5	57.4 \pm 7.11
<i>P</i>		0.78		0.35		0.40

95th: 95th percentile, 5th: 5th percentile. DL: Distal latency, Amp: Amplitude, CV: Conduction velocity, SD: Standard deviation

population^[10-12] when comparing with published data [Table 7]. CVs in our participants were comparable to the CVs reported in a study from India;^[13] however, we were not able to compare amplitudes as their measuring technique was baseline to peak. Pakistani individuals generally have significantly increased sensory amplitudes and faster conduction velocities. Sensory distal latencies were slightly increased which we believe could be related to the variations in distal distances used or whether onset or peak latency was used. For this reason, we opted to make note of both latencies.

Amplitude drop was also noted as the age increased [Table 4]. This could be explained secondary to the natural loss of axons with aging. Similar to previous studies,^[14] SNAP amplitudes decreased with age, significantly for median, ulnar, and sural SNAPs. Females had consistently higher SNAP amplitudes compared to males, most significantly in upper-limb nerves. This is similar to findings described in other populations.^[15,16] Median and ulnar SNAP (digit II and V) showed statistically significant amplitude decrease in males [Table 6]. Bolton and Carter^[17] suggested this to be possibly because of varying finger circumference. Variation in SNAP amplitude from other studies could also be because of different methods of measurement.^[7] We used peak-to-peak amplitude measurement, the peak latency for distal latency, and onset latency for CV of sensory nerves studies. Males had higher normal values for median, ulnar, and peroneal F-wave latency, which has also been described in a study from India.^[9]

Some of these differences may be due to body habitus, genetic factors, lifestyle, and dietary

differences.^[8] Furthermore, factors such as the filter setting of the high frequencies and low frequencies make significant difference in the NCS values; therefore, filter settings should be specified.^[18] Albers^[10] used filter settings of 2 Hz and 10 kHz and 20 Hz and 2 kHz for motor and sensory studies, respectively, for their laboratory.

Another important factor that can make a difference is the need for standardized techniques. They include accurate and standardized distal distances, supramaximal stimulation but preventing excessive stimulation or overstimulation. Temperature is an important factor. Electrode application and impedance is another technical factor to consider. Standardization of techniques ensures quality of nerve conduction studies. It helps in comparing studies over periods of time with easier comparison of outcome measures and effectiveness of treatment.^[18]

There is considerable mention in literature about the effect of age, gender, height, and other individual related variables, but little information on how ethnicity affects the NCS. Fong *et al.*^[11] have demonstrated the ethnic/racial differences in their article. Yet, others have failed to demonstrate that ethnicity^[19,20] makes a difference. Therefore, as suggested by Lahoria *et al.* "highly developed reference values with correction for applicable variables may be used for cohorts of mixed ethnicity."^[20]

Normative reference values of commonly tested peripheral nerves were established for a sample healthy adult population in Karachi, Pakistan. Values for sensory NCS for most nerves tested varied from published data.^[10-12] This study showed that amplitudes were higher and CVs were faster. Our data have similarities to the

Table 7: Comparison of current study data of motor and sensory nerves with published data from other regions of the world

Motor	Present study AKUH (mean±SD)	Albers (US) (range)^[10]	Rasheedi^[8] (KFSH SA) (mean±SD)	Kimura^[12] (mean±SD)	Fong (Malaysian)^[11] Reference limits	
Median nerve						
DML -	3.1±0.4	2.3-4.3 -	3.00±0.40	3.49±0.34	4.1	
MNCV	58.7±4.3	48-73	59±4.33	57.7±4.9	52	
CMAP A	10.5±2.8	3.0-20	10.4±2.27	7.0±3.0	7.4	
Ulnar nerve						
DML	2.5±0.3	1.9-3.8 -	2.5±0.36	2.59±0.39	3.0	
MNCV	61.3±3.9	46-71	59.8±4.86	58.7±5.1	53	
CMAP A	10.4±2.0	5.7-22	10.9±1.96	5.7±2.0	7.0	
Tibial nerve						
DML -	3.9±0.6	3.0-6.3 -	3.5±0.61	3.96±1.0	4.1	
MNCV	48.6±4.1	40-60	48.7±4.6	48.5±3.6	40	
CMAP A	12.5±4.5	3.0-30	12.1±3.30	5.8±1.9	7.5	
Peroneal nerve						
DML -	3.4±0.5	3.3-6.4 -	3.7±0.5	3.77±0.86	4.2	
MNCV	50.7±3.9	39-58	50.9±3.86	48.3±3.9	44	
CMAP A	6.1±2.0	2.0-11	5.4±2.13	5.1±2.3	3.0	
Sensory	Present study AKUH peak DL for sensories (mean±SD)	Present study AKUH onset DL for sensories (mean±SD)	Albers^[10] (US) (range)	Rasheedi^[8] (KFSH SA) onset DL (mean±SD)	Kimura^[12] onset DL (mean±SD)	Fong (Malaysia)^[11] mean±2SD*
Median nerve						
DL digit II	3.0±0.27	2.3±0.18	2.3-3.9	1.76±0.31	2.84±0.34	
SNCV	60.4±4.5	60.4±4.5	51-71	62.5±9.28	56.2±5.8	47
SNAP A	41±15.1	41±15.1	15-90	59.47±25.76	38.5±15.6	7
Ulnar nerve						
DL digit V	3.0±0.30	2.3±0.24	2.3-3.7	1.69±0.25	2.54±0.29	
SNCV	60.0±5.6	60±5.6	49-77	66.85±8.77	54.8±5.3	48
SNAP A	35±13	35±13	17-70	25.01±8.25	35.0±13.4	6
Radial nerve						
DL	2.1±0.19	1.6±0.18		2.30±0.29		
SNCV	71.7±6.0	71.7±6.0		67.16±6.62		50
SNAP A	45.5±14.2	45.5±14.2		42.56±13.20		20
Sural nerve						
DL Lat	3.2±0.32	2.4±0.3	2.5-4.4			
SNCV	57±6.3	57±6.3	40-58			41
SNAP A	22.5±8.8	22.5±8.8	5.0-50			7

DML: Distal motor latency, MNCV: Motor nerve conduction velocity, CMAP: Compound motor action potential, SD: Standard deviation, DL: Distal latency, SNCV: Sensory conduction velocity, SNAP: Sensory nerve action potential, *SNAP A by log transformation, AKUH: Aga Khan University Hospital, KFSH: King Faisal Specialist Hospital

South Asian studies we reviewed. The motor studies, though, were comparable to reported normative nerve conduction values, with variations according to sex and age. Amplitude variations could be explained by the different methods of amplitude measurement, distal latency variations by differences in distal distances used, techniques and equipment settings, genetic factors, lifestyle, dietary differences, and possibly ethnicity. It is, therefore, highly recommended and encouraged to obtain our own reference values for NCS. It would be interesting to do a normal NCS for the South Asian population.

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Conflicts of interest

There are no conflicts of interest.

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