

Cross-Sectional Area Reference Values of Nerves in the Upper and Lower Extremities using Ultrasonography in the Indian Population

DM Sindhu¹, Akshata Huddar¹, Jitender Saini², Seena Vengalil¹, Saraswati Nashi¹, Mainak Bardhan^{1,3}, Gopikrishnan Unnikrishnan¹, Rahul Reddy Rajula¹, Thennarasu Kandavel⁴, Lokesh Bathala⁵, Leo H. Visser⁶, Atchayaram Nalini¹

Departments of ¹Neurology, ²Neuro Imaging and Interventional Radiology and ⁴Biostatistics, National Institute of Mental Health and Neurosciences, Bengaluru, Karnataka, India, ⁵Department of Neurology, Aster CMI Hospital, Bangalore, Karnataka, India, ⁶Departments of Neurology and Clinical Neurophysiology, ETZ, St. Elisabeth Hospital, Tilburg, Netherlands, ³ICMR-National Institute of Cholera and Enteric Diseases (NICED), Kolkata, West Bengal, India

Abstract

Background and Purpose: Cross-sectional area (CSA) is the most important parameter to study peripheral nerves by high-resolution ultrasonography. The aim was to acquire normative data of CSA of the main upper and lower limb nerves in the Indian population. **Methods:** CSA of nerves was determined in 100 healthy volunteers at 11 predetermined sites: median and ulnar at the wrist, mid-forearm, elbow; radial (spiral groove); tibial (popliteal fossa, medial malleolus); common peroneal (CPN, fibular head) and sural (lateral malleolus). **Results:** The mean age of participants was 40.7 ± 13.0 years (range: 18-79). Fifty were < 40 years of age. The mean height, weight and BMI were 161.5 ± 8.3 centimeters (range: 145–179), 58.6 ± 10.1 kilograms (range: 32-90) and 22.4 ± 3.2 kilogram/square meter (range: 14.03-30.44), respectively. The median and ulnar nerve measurements were non-uniform throughout its course, and the CSA was largest at the elbow and ulnar groove, respectively. With advancing age, there was a significant difference for median and ulnar nerves at the wrist (median $P = 0.002$, ulnar $P = 0.009$) and tibial nerve (popliteal fossa, $P = 0.045$, medial malleolus, $P = 0.005$), CPN ($P = 0.047$). Men had greater CSA of upper limb nerves and tibial nerves at popliteal fossa ($P < 0.05$) as compared to women. A positive correlation was noted with weight. **Conclusion:** It is apt for every defined population to have its own set of normative data of CSA as it varies with ethnicity, age, and the built of individuals. We provide a valuable set of CSA data for nerves in the Indian population, which can be used for comparison while investigating peripheral nerve disorders.

Keywords: Cross-sectional area, India, normative data, peripheral nerve, ultrasound

INTRODUCTION

High-resolution ultrasonography (HRU) is a rapidly evolving technique for assessing the peripheral nerves and brachial plexus in several disease conditions like nerve entrapment, hereditary, inflammatory, demyelinating, infectious (leprosy), and diabetic neuropathies.^[1,2] Prior to the advent of HRU, evaluation of peripheral nerve disease primarily consisted of history, clinical examination, and electrodiagnostic studies. However, electrodiagnostic studies evaluate only the functional aspects of the nerve. HRU addresses this limitation by permitting direct assessment of nerve anatomy and its surrounding structures.^[3] It is non-invasive and easy to perform. Ultrasound machines are radiation-free, compatible with metal implants, and portable, allowing fieldwork. They provide dynamic real-time high-resolution imaging of the peripheral nerves.^[2] When compared with magnetic resonance imaging (MRI), HRU has a higher sensitivity and equivalent specificity in clinically accessible regions and in detecting multifocal nerve lesions.^[4]

The most widely used parameter to assess the peripheral nerve is the cross-sectional area (CSA). Normative data of nerves in a population is crucial in differentiating from pathological conditions. Studies have shown significant differences in the normative data of the CSA, depending on gender, physical and

geographic differences.^[5-7] A study from India reported that CSA of the median and ulnar nerve was largest at the wrist and was proportional to aging.^[8,9] In contrast, constant median nerve CSA was reported throughout its course in another study.^[10] Hence, there is a need to explore the implications of the differences that have been inferred from the studies.

There are a limited number of studies on the CSA of various nerves in the Indian population.^[5,8,9] The aim of this study was to acquire normative data of CSA of upper and lower limbs nerves at predetermined sites in healthy Indian adult subjects and to correlate with age, gender, height, and body

Address for correspondence: Dr. Atchayaram Nalini,
Department of Neurology, National Institute of Mental Health and
Neurosciences, Hosur Road, Bengaluru - 560 029, Karnataka, India.
E-mail: atchayaramnalini@yahoo.co.in

Submitted: 12-Aug-2021 **Revised:** 05-Oct-2021 **Accepted:** 03-Nov-2021

Published: 01-Apr-2022

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: WKHLRPMedknow_reprints@wolterskluwer.com

DOI: 10.4103/aian.aian_727_21

mass index (BMI). These normative data are important for the assessment of abnormal nerves in patients with entrapment neuropathies, mononeuritis multiplex, and polyneuropathies.

METHODS

This prospective, cross-sectional study was carried at a quaternary care center for neurological disorders in India between January 2019 and August 2020. Around 100 to 150 cases with neurological disorders are evaluated daily at the outpatient services, and 3-4% of the cases are likely to have acquired or inherited peripheral nerve disorders. This study was approved by the institutional ethics committee [NO.NIMH/DO/IEC (BS & NS DIV)/2018-19]. Informed written consent was obtained from all the participants.

Healthy adult volunteers (18-80 years) who are residents of India, including relatives and caregivers of the in-patients, admitted to our hospital, institute employees, and medical students were recruited. Pregnant women, alcoholics (>14 units/week for men and >7 units/week for women),^[11] subjects with co-morbidities (diabetes, hypothyroidism, obesity (BMI > 30)), preceding neurological illness or history of paresthesias, fasciculations, thinning, weakness, trauma, sensory loss, hereditary neurological illness in the family, abnormal neurological examination or electrophysiological studies were excluded from the study.

Demographic and anthropometric data were collected regarding age, gender, handedness, height, weight, BMI, along with symptoms of systemic and neurological illness. A systemic and neurologic examination was performed. Participants underwent random blood sugar testing (RBS) to look for undetected diabetes (glucometry) and motor conduction of the right ulnar nerve and common peroneal nerve (CPN) using the belly tendon method. The compound muscle action potential (CMAP) latency, amplitude, and velocity were noted.

Ultrasonography of the right upper and lower limb nerves was performed using Philips Diagnostic scanner EPIQ 7 using 8-15 MHz linear transducer or Esaote My lab gamma using 3-13 MHz linear transducer. A total of 11 sites were assessed in each subject, and at each site, an average of three readings was taken. CSA for the various nerves was measured at the following sites: median (wrist crease, mid-forearm- at the midpoint between the wrist crease and elbow crease, elbow -medial to the brachial artery), ulnar (wrist crease, mid-forearm - at the midpoint between the medial epicondyle and ulnar styloid, elbow-at the ulnar groove), radial (spiral groove), tibial (popliteal fossa, posterior to medial malleolus), CPN (fibular head), and sural (lateral malleolus) [Figures 1 and 2].

Upper limb nerves were scanned with the patient in supine position, and the arm abducted to 60° at the shoulder and forearm in supine position. The tibial CPN nerve at the popliteal fossa was scanned with patient lying in prone position. The sural and CPN at the fibular head were scanned with the patient lying in lateral position. Power and color doppler modes were used. In order to avoid anisotropy, the transducer was placed perpendicular to the nerve, and pressure applied was minimized to prevent deformation of the structures underneath. The inner border of the thin hyperechoic epineural rim was traced at every site using the trace function. The intra-observer variability was assessed by repeat ultrasonography on 10 participants after a minimum time gap of 1 month. Inter-observer variability was assessed on 10 participants by another ultrasonographer (JS) who was blinded to the values obtained by the first examiner.

Statistics were performed using IBM SPSS version 22 for windows. Descriptive statistics were used to present basic demographic data of the study population. The mean and standard deviation for age, height, weight, BMI, and CSA of nerves were calculated. The reference range was calculated as mean \pm 2 standard deviations. Normality was tested using the Shapiro-Wilk test, and as some of the values did not

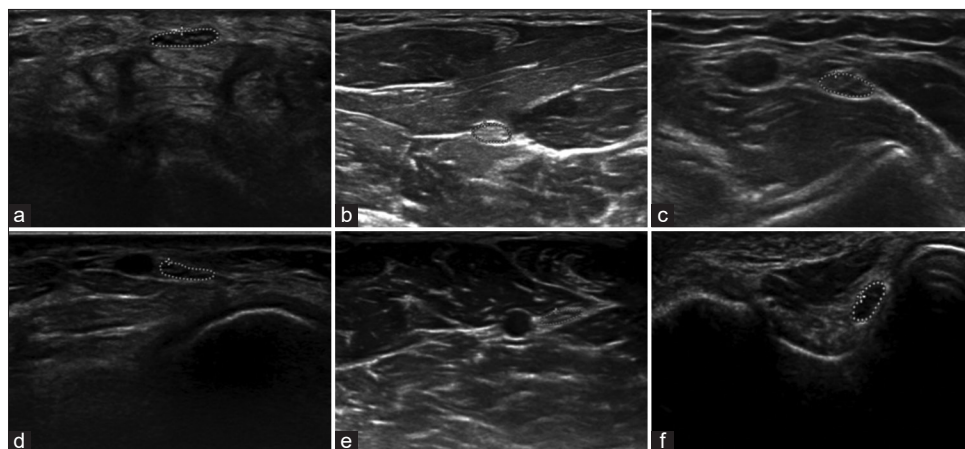


Figure 1: USG cross section images of median and Ulnar nerves: Median nerve at wrist (a), at mid forearm between the flexor digitorum superficialis and flexor digitorum profundus (b) and at the elbow medial to the brachial artery (c), Ulnar nerve at the wrist beside the ulnar artery (d), at the mid forearm beside the ulnar artery (e) and at the elbow between the olecranon and medial epicondyle (f).

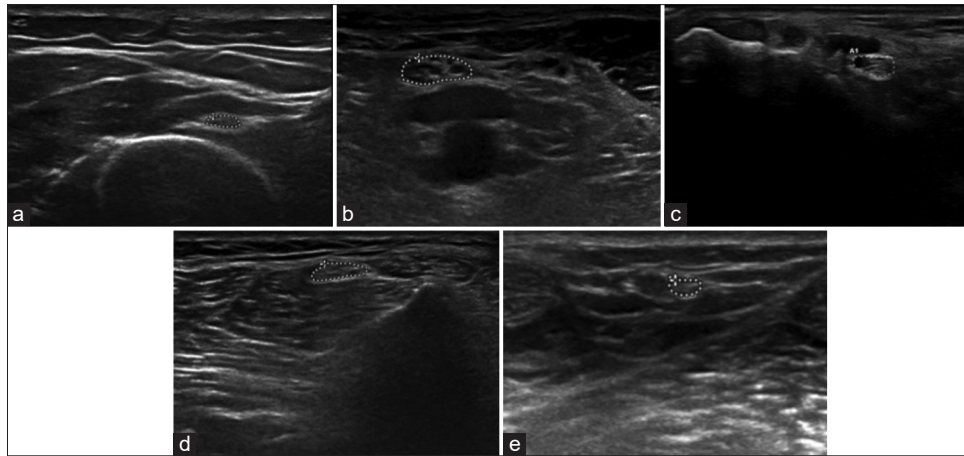


Figure 2: USG cross section images of radial and lower limb nerves: Radial nerve at the spiral groove (a), Tibial nerve at the popliteal fossa, just above the popliteal vein (b) and posterior to the medial malleolus in relation to the posterior artery and vein (c), Common peroneal nerve lateral to the fibular head (d) and Sural nerve at the lateral aspect of the distal leg, lateral to the lesser saphenous vein (e)

follow a normal distribution, non-parametric tests were used. Spearman's rank correlation coefficient and multivariate linear regression analysis were used to evaluate the relation between CSA and age, gender, weight, and height. Mann-Whitney U test was used to compare the variation in CSA of nerve segments with respect to the gender of the participants. Chi-square and Friedman tests with Dunn's correction were used to compare the CSA at various levels of median and ulnar nerves. Inter-rater variability was evaluated using intraclass correlation coefficient, and intra-rater variability was evaluated using Wilcoxon signed-rank test.

RESULTS

A total of 105 participants were recruited for the study. Five participants were excluded: abnormal conductions ($n = 2$), newly detected diabetes mellitus ($n = 2$), and bifid median nerve ($n = 1$). Hundred healthy participants (M:F = 1:1) underwent ultrasonography of nerves of the right upper and lower limb.

The mean age of the healthy participants was 40.7 ± 13.0 years (range, 18-79). Among the 100 participants, 50 (50%) were less than 40 years of age. The mean height, weight and BMI was 161.5 ± 8.3 centimeters (range: 145-179), 58.6 ± 10.1 kilograms (range: 32-90) and 22.4 ± 3.2 kilogram/square meter (range: 14.03-30.44), respectively.

The mean, standard deviation, and range of CSA measurements of all 11 nerve segments for men ($n = 50$) and women ($n = 50$) are presented in Table 1, Figures 1 and 2. The CSA of the median nerve was not uniform. It was greatest at the elbow and least at the forearm. The CSA of the ulnar nerve was greatest at the ulnar groove, with uniform CSA between the wrist and mid-forearm level.

Mann-Whitney U test was used to compare the variation in CSA of nerve segments with respect to the gender of the participants. Men had significantly higher CSA values compared to women

at all sites except the median nerve at the wrist and posterior tibial nerve at the medial malleolus [Table 1].

A statistically significant and positive weak to fair correlation was found between age and the CSA of median and ulnar nerve at the wrist, the tibial nerve at popliteal fossa, and medial malleolus and CPN at the fibular head. A statistically significant and weak positive correlation was seen between the height and CSA at all measured sites except the median nerve at the wrist. A moderate positive correlation was seen between the CSA of the tibial nerve at popliteal fossa and weight. All the other nerves except the radial nerve showed a weak positive correlation with weight [Table 2].

Multivariate regression analysis showed a significant association between the age and CSA of nerves at entrapment sites in the upper limb like median and ulnar at the wrist, ulnar at the elbow, tibial at popliteal fossa and medial malleolus, and CPN at the fibular head. Regression analysis also showed that men, in general, had larger CSA for upper limb nerves and also for the tibial nerve at the popliteal fossa. The weight of the subjects showed consistent relation with nerve CSA at most sites. However, the relation between height and CSA was inconsistent in the regression analysis [Table 3].

Intra-rater variability was evaluated using Wilcoxon signed-rank test, and there was no significant difference between the values obtained by a single observer at two-time frames [Table 4]. Inter-rater variability was evaluated using the intraclass correlation coefficient (ICC). The coefficient values were between 0.86 and 1, which indicated a good reliability [Table 5].

DISCUSSION

This study aimed at providing reference values of the common upper and lower limb nerve CSAs for the Indian population. We recruited 100 healthy participants to generate reference values for CSA of nerves at 11 predetermined

Table 1: CSA values (mm²) and variability with gender of 11 nerve segments with reference ranges in 100 healthy subjects

Recording Positions Nerve/site	Males (mm ² , n=50)			Females (mm ² n=50)			Male vs Female		Total (mm ² n=100)			Reference range (mm ²)
	Mean	SD	Range	Mean	SD	Range	Mann-Whitney U	P	Mean	SD	Range	
Median wrist	7.72	1.51	5.1-11.0	7.12	1.53	4.7-9.0	992.000	0.072	7.42	1.39	4.7-11.0	4.64-10.2
Median forearm	5.37	0.92	4.0-7.0	4.84	1.02	3.0-7.0	898.000	0.013	5.10	0.91	3.0-7.0	3.28-6.92
Median elbow	8.28	1.61	5.4-12.0	7.25	1.75	5.0-12.0	788.000	0.001	7.77	1.60	5.0-12.0	4.57-10.97
Ulnar wrist	4.75	0.76	3.0-6.2	4.10	0.88	3.0-6.0	708.000	<0.001	4.43	0.79	3.0-6.2	2.85-6.01
Ulnar forearm	4.89	0.76	3.0-7.0	4.15	0.95	3.0-6.0	612.000	<0.001	4.52	0.83	3.0-7.0	2.86-6.18
Ulnar elbow	6.16	1.29	3.6-10.0	5.11	1.41	3.0-7.0	658.500	<0.001	5.64	1.26	3.0-10.0	3.12-8.16
Radial arm	4.50	0.68	3.0-6.5	4.05	0.78	3.0-5.5	785.000	0.001	4.28	0.69	3.0-6.5	2.9-5.66
Tibial popliteal fossa	22.71	3.89	15.7-32.2	18.68	4.84	10.0-27.0	597.500	<0.001	20.70	4.41	10.0-32.2	11.88-29.52
PTN medial malleolus	10.54	2.36	6.7-15.0	9.67	2.39	5.9-16.0	1000.500	0.083	10.10	2.23	5.9-16.0	5.56-14.56
CPN fibula	9.86	2.24	5.0-15.0	8.92	2.32	6.0-15.0	907.000	0.017	9.39	2.12	5.0-15.0	5.15-13.63
Sural	1.98	0.38	1.0-3.0	1.72	0.48	1.0-3.0	946.500	0.018	1.85	0.45	1.0-3.0	0.95-2.75

Table 2: Correlation between CSA at various sites and age, height, weight and BMI using Spearman's correlation

Parameters	Age		Height		Weight		BMI	
	CC	P	CC	P	CC	P	CC	P
Median Wrist	0.380**	<0.001	0.176	0.080	0.303**	0.002	0.305**	0.002
Median forearm	0.174	0.083	0.249*	0.013	0.269**	0.007	0.190	0.058
Median elbow	0.174	0.084	0.320**	0.001	0.507**	<0.001	0.354**	<0.001
Ulnar wrist	0.273**	0.006	0.298**	0.003	0.309**	0.002	0.187	0.063
Ulnar forearm	0.099	0.326	0.355**	<0.001	0.375**	<0.001	0.221*	0.027
Ulnar elbow	0.174	0.084	0.426**	<0.001	0.340**	0.001	0.141	0.162
Radial arm	-0.146	0.147	0.210*	0.036	0.193	0.054	0.107	0.289
Tibial popliteal fossa	0.246*	0.013	0.388**	<0.001	0.602**	<0.001	0.455**	<0.001
PTN medial malleolus	0.314**	0.001	0.296**	0.003	0.470**	<0.001	0.384**	<0.001
CPN fibula	0.217*	0.030	0.278**	0.005	0.449**	<0.001	0.321**	0.001
Sural	-0.054	0.596	0.358**	<0.001	0.268**	0.007	0.084	0.406

**Correlation is significant at the 0.01 level (2-tailed). *Correlation is significant at the 0.05 level (2-tailed). CC - correlation coefficient

Table 3: Multivariate linear regression model for CSA at various sites and age, gender weight and height

Parameters	Age		Gender		Weight		Height	
	Beta	P	Beta	P	Beta	P	Beta	P
Median wrist	0.03	0.002	-0.49	0.14	0.036	0.023	0.008	0.715
Median forearm	0.011	0.085	-0.445	0.047	0.022	0.042	-0.004	0.772
Median elbow	0.014	0.215	-0.86	0.02	0.070	<0.001	0.026	0.312
Ulnar wrist	0.015	0.009	-0.60	0.001	0.01	0.255	0.004	0.974
Ulnar forearm	0.002	0.631	-0.708	<0.001	0.028	0.003	0.014	0.289
Ulnar elbow	0.019	0.037	-0.633	0.030	0.016	0.259	0.032	0.126
Radial arm	-0.007	0.152	-0.524	0.002	0.017	0.043	0.018	0.129
Tibial popliteal fossa	0.051	0.045	-3.502	<0.001	0.26	<0.001	-0.108	0.068
PTN medial malleolus	0.045	0.005	-0.067	0.895	0.077	0.002	0.033	0.372
CPN fibula	0.031	0.047	-0.69	0.175	0.07	0.005	0.017	0.634
Sural	0.001	0.718	0.053	0.625	0.007	0.171	0.015	0.059

sites: median and ulnar at the wrist, mid-forearm and elbow, radial (spiral groove), tibial (popliteal fossa, medial malleolus), CPN (fibular head), and sural (lateral malleolus). The group represented an equal number of men and women with ages ranging from 18 to 79 years. The demographics of our cohort more or less represent the average demographic values of the population.^[12] Our study evaluated CSA only on

the right side as previous studies have shown no significant side-to-side variation in CSA of nerves.^[13-16] Inter-observer variability of nerve ultrasound in peripheral neuropathy is generally limited, especially for nerves in the arm. Different devices and a multicenter setting have shown no effect on the inter-observer variability. Therefore, nerve ultrasound is a reproducible investigational method for diagnostics in routine

Table 4: Intra-rater variability for CSA at various sites using Wilcoxon signed rank test

Parameters	R1	R2	Z	P
Median wrist	0.07 (0.068, 0.093)	0.07 (0.06, 0.093)	-1	0.317
Median forearm	0.06 (0.05, 0.06)	0.06 (0.05, 0.06)	-1	0.317
Median elbow	0.085 (0.068, 0.1)	0.08 (0.068, 0.1)	-1.414	0.157
Ulnar wrist	0.04 (0.04, 0.05)	0.04 (0.04, 0.05)	-1	0.317
Ulnar forearm	0.04 (0.038, 0.053)	0.04 (0.038, 0.053)	0	1.000
Ulnar elbow	0.06 (0.05, 0.073)	0.06 (0.05, 0.073)	0	1.000
Radial arm	0.04 (0.038, 0.05)	0.04 (0.038, 0.05)	0	1.000
Tibial popliteal fossa	0.205 (0.188, 0.29)	0.205 (0.18, 0.28)	-1.3	0.194
PTN medial malleolus	0.105 (0.09, 0.115)	0.105 (0.098, 0.115)	-1	0.317
CPN fibula	0.1 (0.09, 0.113)	0.105 (0.09, 0.12)	-1	0.317
Sural	0.02 (0.02, 0.02)	0.02 (0.02, 0.02)	0	1.000

R1 - First reading, R2 - Second reading obtained by same observer after a time period

Table 5: Inter-rater variability for CSA at various sites using intraclass correlation coefficient

Parameters	ICC
Median wrist	0.90
Median forearm	0.86
Median elbow	0.92
Ulnar wrist	0.88
Ulnar forearm	1.00
Ulnar elbow	0.94
Radial arm	0.95
Tibial popliteal fossa	0.98
PTN medial malleolus	0.95
CPN fibula	0.90
Sural	1.00

clinical practice and multicenter research.^[17] We performed the intra-observer and inter-observer variability in our study to check the reliability of the values obtained. We obtained high intraclass correlation coefficient values between 0.86 – 1.0, as reported previously.^[18,19] The lowest interrater variability was for the ulnar nerve at mid-forearm, followed by the radial and sural nerves. This emphasizes that the CSA of nerves can be measured reliably with HRU. However, reference values of CSA of lower limb nerves vary considerably among different studies.^[1,6,7,13,14,16,19] The borders of the nerves of the lower limbs are not clearly visible due to the echogenic properties of the surrounding tissues. The CPN at the fibular head has an oblique course, and hence minimal tilting of the probe can lead to discrepancies in the values of the CSA. These reasons account for the wide variability in the CSA values in different studies of the lower limb nerves.

The CSA values in the present study correlated well with previous studies from India and China,^[8,9,20] while other studies have reported marginally greater values.^[1,6,7,13-16,21] This variation is probably due to the difference in body habitus and ethnicity. The weight of the participants in these studies (74-77 kg) was higher compared to the mean weight of our cohort (58.6 kg). The CSA values of the nerves in previous studies and the present study are summarized in Table 6.

The CSA of median and ulnar nerves were not uniform throughout their course in the current study. The CSA of the median nerve was largest at the elbow, followed by CSA at the wrist and mid-forearm. This may be due to the measurement of the nerve prior to branching and the increased CSA at the wrist due to branching of the nerve fibres within the nerve distally.^[9] In another Indian study, the CSA of the median nerve was largest at the wrist, but in their study, the CSA at the elbow was not evaluated.^[9] The largest CSA of the ulnar nerve was at the ulnar groove, which is consistent with findings from other studies.^[8,18,20] The ulnar nerve at the ulnar groove is a common site of entrapment which explains the larger CSA compared to the other sites. However, in few previous reports, the median and ulnar nerve did not vary widely in CSA throughout their course.^[10,22]

In the current study, median and ulnar nerves at the wrist and all lower limb nerves were larger with advancing age except the sural nerve, which is similar to findings in earlier studies.^[8,9,14-16,20] However, few studies found no correlation with age.^[11,19,21] A study from Germany reported that median nerve in the axilla and radial nerve in spiral groove had decreased CSA with advancing age, and tibial nerve at the ankle showed higher CSA with advancing age.^[7] The possible explanations given for lower CSA were loss of nerve fibres and degeneration as the age advances and increase in the non-neural elements like connective tissue within the nerve, presence of macrophages, onion bulbs etc., for increased CSA.^[7] The age group in the above study was a decade higher than most of the studies, including the present study. However, another study with a similar age group did not find any correlation with age.^[11] In our study, the CSA of radial nerve did not correlate with age as shown in the previous studies.^[14,15,21,23] Nevertheless, another study reported a statistically significant weak positive correlation between age and radial nerve at spiral groove.^[6]

The men in our study had a greater CSA when compared to women in the median and ulnar measurements, except the median nerve at the wrist, which is consistent with the previous reports.^[8-10,15,18,20] However, a German study reported no correlation of gender with CSA at most sites in the upper limb

Table 6: Comparison table showing CSA of upper and lower limb nerves with other published studies

Para meters	Present study	Bathala et al ^[8,9]	Boehm et al ^[1]	Cartwright et al ^[6]	Bedewi et al ^[14,15]	Kerasnoudis et al ^[7]	Seok et al ^[20]	Qrimli et al ^[13]	Taglificio et al ^[12]	Won et al ^[17]	Sugi moto et al ^[18]	Niu J et al ^[16]
Year	2021	2014/2012	2014	2008	2018	2013	2014	2016	2013	2013	2013	2020
Country	India	India	Hungary	USA	Egypt	Germany	South Korea	Canada	Italy	South Korea	Japan	China
Number	100	100	56	60	69	75	94	100	60	97	60	111
Age (years)	40.7±13.01	39±14	51.8±16.4	45.9	38.33±12.13	53.46±14.8	43.9±14.4	44.1±18.4	44.3±14.4	44.3±14.4	35.4±9.7	41.69±15.80
Height (cm)	161.51±8.28	160±10	171±9	168	161.48±9.8	175±9	165.2±9.0	165.2±9.0	165.2±9.0	165.2±9.0	164±10	167.07±8.31
Weight (kg)	58.6±10.06	59.3±11.3	75.4±13	74.5	77.14±18.4	77.9±10.68	62.8±12.2	62.8±12.2	63.1±12.2	63.1±12.2	60.0±12.1	65.34±11.06
BMI (kg/m ²)	22.41±3.15	22.95±3.50	26.30	26.5	29.31±6.64	45.30	22.9±3.1	25.3±5.3	22.9±3.1	22.9±3.1	22.3±3.6	23.32±2.86
M/F	50:50	50:50	26:30	22:38	9.77±2.88	45:30	44:50	30:70	47:50	47:50	29:31	
Wrist level Median (mm ²)	7.42±1.39	7.2±1	8.5±1.8	9.8 ± 2.4	9.77±2.88	8.43±2.07	44:50	10.0±2.4	8.2±2.3	8.33±1.52	8.5±1.7	6.0±0.9
Forearm Median (mm ²)	5.1±0.91	4.8±0.9	5.7±1.3	7.5±1.6 (mid forearm)	6.46±2.05 (10cm from wrist)	6.6±1.6		7.3±1.7	5.5±2.2	6.53±1.05	5.6±1.1	5.4±0.8
Elbow Median (mm ²)	7.77±1.6		8.9±1.8	7.6±1.7 (proximal forearm)	11.12±3.94			10.3±3.4		8.12±1.58	9.1±2.2	7.8±1.1
Arm Median (mm ²)		6.1±1	8.9±1.8	8.6±2.3				9.4±3.1		9.44±1.40	8.2±1.7	7.3±1.1
Axilla Median (mm ²)	4.43±0.79	5.9±0.9	7.9±1.9	8.9±2.1	4.07±1.56	8.4±2.87		5.0±1.7	3.1±1.0	4.28±0.78	4.1±1.0	2.9±0.5
Wrist Ulnar (mm ²)	4.52±0.83	4.1±0.6	5.2±1.3	5.9±1.1	5.52±1.90 (10cm from guyon canal)	5.16±1.03		6.2±1.5		6.30±1.01	4.6±0.8	4.2±0.8
Forearm Ulnar (mm ²)	5.64±1.26	4.7±0.6	7.6±2.1	6.3±1.0 (midforearm)	7.49±2.35 (1 inch above medial epicondyle)	5.33±1.4		6.9±2.3	5.9±3.0	7.49±1.42	6.7±1.9	5.2±1.0
Arm Ulnar (mm ²)	4.28±0.69	4.4±0.6	6.3±1.7	6.7±1.1 (2 cm distal to ME)	7.55±2.60			6.8±2.3		5.85±1.05	4.8±1.0	4.2±0.8
Axilla Ulnar (mm ²)		4.3±0.5	4.2±1.0	(2cm proximal to ME) 6.1±0.9 (midarm)								
Arm Radial (mm ²)			2.3±0.7	6.2±1.1		6.53±1.82				4.58±0.85		4.2±0.8
Forearm Superficial radial (mm ²)				7.9±2.7		3.26±1.52				2.00±0.53		3.4±0.7
Popliteal fossa Tibial (mm ²)	20.70±4.41		9.6±2.2	35.3 ± 10.3	19.07±6.88	8.43±2.68	24.4±4.4					
Posterior tibial (mm ²)	10.10±2.23		11.7 ± 4.6	13.7± 4.3	12.66±4.45	6.36±1.45	12.1±3.1	12.7±3.4	9.6±4			
Popliteal fossa CPN (mm ²)	9.39±2.12		8.9±2.0	11.2±3.3	9.71±4.07	8.6±1.77	10.4±2.7	11.8±3.8				
Fibula head CPN (mm ²)	1.85±0.45		1.8±0.6	5.3±1.8 (distal calf)	8.89±3.23	7.1±2.3	9.2±2.9	11.1±3.5	13.2±14			
Sural (mm ²)					3.52±1.40 (distalleg)	1.82±0.64 (between the heads of gastrocnemius)	2.6±0.6 (distal calf)	2.1±0.8 (above lateral malleolus)	3.6±1.1			

except for the ulnar nerve at the wrist. In this report, women had higher values of intra-nerve CSA variability compared to men.^[7] In our study, the CSA of the radial nerve correlated with gender, similar to a previous study.^[23] However, most of the studies reported no correlation with gender and CSA of radial nerve.^[6,14,15,21] In our study, all lower limb nerves were larger in men except the posterior tibial nerve at the medial malleolus, which is similar to the previous studies.^[7,14] This is in contrast to a few other studies.^[1,6,16,19]

In parallel to previous studies, the CSA at most of the sites in the median, ulnar and lower limb nerves showed a statistically significant weak correlation with weight.^[10,14-16,18,21] Few studies have reported a positive correlation with both height and weight,^[19,20] few only with height,^[24] and the remaining did not find any correlation.^[1,8,9,25] The CSA of radial nerve at spiral groove did not correlate with height and weight as reported in a previous study,^[15] but a few other studies on radial nerve showed a strong correlation between CSA of the radial nerve and the individual's weight and height.^[14,21,23]

This study has a few limitations. Nerves were evaluated only on one side, and hence side to side variability was not assessed. Earlier studies have reported a strong correlation between wrist circumference and CSA of median and ulnar nerves.^[18,26] Unfortunately, in the current study, the wrist circumference was not measured.

In conclusion, focal or diffuse thickening of a particular nerve can be easily appreciated or confirmed only when there is a set of established normative data for the given population. Reference values that have been established in previous reports from different countries show variation in the values and correlation studies due to different ethnicity, age and built of the participants, technique and the equipment used, different sites of measurement, and the skill of the examiner. Hence it is apt for every defined population to have its own set of normative data of ultrasonographic reference values of the nerves and this has been well established in the current study for Indians.

Abbreviations

BMI: Body Mass Index, CMAP: Compound Motor Action Potential, CPN: Common Peroneal Nerve, CSA: Cross Sectional Area, kg: kilogram, HRU: High Resolution Ultrasonography, MHz: Megahertz, mm: millimeter, MRI: Magnetic Resonance Imaging, RBS: Random Blood Sugar.

Acknowledgements

We thank all volunteers for participating in the study.

Ethical publication statement

We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

Declaration of patient consent

The authors certify that they have obtained all appropriate consent forms. In the form the participants (s) has/have given his/her/their consent for his/her/their images and other clinical

information to be reported in the journal. The participants understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

- Boehm J, Scheidl E, Bereczki D, Schelle T, Arányi Z. High-resolution ultrasonography of peripheral nerves: Measurements on 14 nerve segments in 56 healthy subjects and reliability assessments. *Ultraschall Med* 2014;35:459-67.
- Walker FO, Cartwright MS, Alter KE, Visser LH, Hobson-Webb LD, Padua L, *et al.* Indications for neuromuscular ultrasound: Expert opinion and review of the literature. *Clin Neurophysiol* 2018;129:2658-79.
- Suk JI, Walker FO, Cartwright MS. Ultrasonography of peripheral nerves. *Curr Neurol Neurosci Rep* 2013;13:328.
- Zaidman CM, Seelig MJ, Baker JC, Mackinnon SE, Pestronk A. Detection of peripheral nerve pathology: comparison of ultrasound and MRI. *Neurology* 2013;80:1634-40.
- Burg EW, Bathala L, Visser LH. Difference in normal values of median nerve cross-sectional area between Dutch and Indian subjects. *Muscle Nerve* 2014;50:129-32.
- Cartwright MS, Passmore LV, Yoon JS, Brown ME, Caress JB, Walker FO. Cross-sectional area reference values for nerve ultrasonography. *Muscle Nerve* 2008;37:566-71.
- Kerasnoudis A, Pitarokoili K, Behrendt V, Gold R, Yoon MS. Cross sectional area reference values for sonography of peripheral nerves and brachial plexus. *Clin Neurophysiol* 2013;124:1881-8.
- Bathala L, Kumar P, Kumar K, Visser LH. Ultrasonographic cross-sectional area normal values of the ulnar nerve along its course in the arm with electrophysiological correlations in 100 Asian subjects. *Muscle Nerve* 2013;47:673-6.
- Bathala L, Kumar P, Kumar K, Shaik A, Visser LH. Normal values of median nerve cross-sectional area obtained by ultrasound along its course in the arm with electrophysiological correlations, in 100 Asian subjects. *Muscle Nerve* 2014;49:284-6.
- Cartwright MS, Shin HW, Passmore LV, Walker FO. Ultrasonographic reference values for assessing the normal median nerve in adults. *J Neuroimaging* 2009;19:47-51.
- Topiwala A, Allan CL, Valkanova V, Zsoldos E, Filippini N, Sexton C, *et al.* Moderate alcohol consumption as risk factor for adverse brain outcomes and cognitive decline: Longitudinal cohort study. *BMJ* 2017;357:j2353. doi: 10.1136/bmj.j2353.
- Mamidi RS, Kulkarni B, Singh A. Secular trends in height in different states of India in relation to socioeconomic characteristics and dietary intakes. *Food Nutr Bull* 2011;32:23-34.
- Tagliafico A, Cadoni A, Fiscì E, Bignotti B, Padua L, Martinoli C. Reliability of side-to-side ultrasound cross-sectional area measurements of lower extremity nerves in healthy subjects. *Muscle Nerve* 2012;46:717-22.
- Qrimli M, Ebadi H, Breiner A, Siddiqui H, Alabdali M, Abraham A, *et al.* Reference values for ultrasonography of peripheral nerves. *Muscle Nerve* 2016;53:538-44.
- Bedewi MA, Abodonya A, Kotb M, Mahmoud G, Kamal S, Alqabbani A, *et al.* Estimation of ultrasound reference values for the upper limb peripheral nerves in adults: A cross-sectional study. *Medicine (Baltimore)* 2017;96:e9306. doi: 10.1097/MD.00000000000009306.
- Bedewi MA, Abodonya A, Kotb M, Kamal S, Mahmoud G, Aldossari K, *et al.* Estimation of ultrasound reference values for the lower limb peripheral nerves in adults: A cross-sectional study. *Medicine (Baltimore)* 2018;97:e0179. doi: 10.1097/MD.00000000000010179.

17. Telleman JA, Herraets IJT, Goedee HS, Verhamme C, Nikolakopoulos S, van Asseldonk JH, *et al.* Nerve ultrasound: A reproducible diagnostic tool in peripheral neuropathy [published online ahead of print, 2018 Dec 28]. *Neurology*. 2018;10.1212/WNL.0000000000006856. doi:10.1212/WNL.000000000000685600000000006856..
18. Sugimoto T, Ochi K, Hosomi N, Mukai T, Ueno H, Takahashi T, *et al.* Ultrasonographic reference sizes of the median and ulnar nerves and the cervical nerve roots in healthy Japanese adults. *Ultrasound Med Biol* 2013;39:1560-70.
19. Seok HY, Jang JH, Won SJ, Yoon JS, Park KS, Kim BJ. Cross-sectional area reference values of nerves in the lower extremities using ultrasonography. *Muscle Nerve* 2014;50:564-70.
20. Niu J, Li Y, Zhang L, Ding Q, Cui L, Liu M. Cross-sectional area reference values for sonography of nerves in the upper extremities. *Muscle Nerve* 2020;61:338-46.
21. Won SJ, Kim BJ, Park KS, Yoon JS, Choi H. Reference values for nerve ultrasonography in the upper extremity. *Muscle Nerve* 2013;47:864-71.
22. Cartwright MS, Shin HW, Passmore LV, Walker FO. Ultrasonographic findings of the normal ulnar nerve in adults. *Arch Phys Med Rehabil* 2007;88:394-6.
23. Chen J, Wu S, Ren J. Ultrasonographic reference values for assessing normal radial nerve ultrasonography in the normal population. *Neural Regen Res* 2014;9:1844-9.
24. Zaidman CM, Al-Lozi M, Pestronk A. Peripheral nerve size in normals and patients with polyneuropathy: An ultrasound study. *Muscle Nerve* 2009;40:960-6.
25. Heinemeyer O, Reimers CD. Ultrasound of radial, ulnar, median, and sciatic nerves in healthy subjects and patients with hereditary motor and sensory neuropathies. *Ultrasound Med Biol* 1999;25:481-5.
26. Claes F, Meulstee J, Claessen-Oude Luttikhuis TT, Huygen PL, Verhagen WI. Usefulness of additional measurements of the median nerve with ultrasonography. *Neurol Sci* 2010;31:721-5.