ORIGINAL ARTICLE

DEFINING NORMAL REFERENCE RANGE FOR THE CROSS-SECTIONAL AREA OF THE MEDIAN NERVE AT THE WRIST AND FOREARM USING HIGH-RESOLUTION ULTRASONOGRAPHY IN ASYMPTOMATIC PAKISTANI ADULTS

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Background: Carpal tunnel syndrome (CTS) can be diagnosed easily on ultrasonography (USG); which is a cheap, non-invasive and readily available modality. However, there is wide normal variation in the normal values of cross-sectional area (CSA) of median nerve among different populations; therefore, its necessary to establish a normal range of variability in median nerve dimensions in different populations. **Method:** A total of 500 asymptomatic patients i.e., 1000 median nerves were evaluated at the distal wrist crease and mid-forearm by 3 expert radiologists independently. All patients having a positive nerve conduction study or history of carpal tunnel syndrome and wrist trauma were excluded. Ultrasound was performed with a 7.5–15 MHz high-frequency linear probe. SPSS v 20 was used to analyze data. **Results:** The study population had a mean age of 31.40±10.11 years with a female-to-male ratio of 1.36:1. Mean BMI was 22.15±4.34 Kg/m^2. The mean cross-section area of the median nerve at the right wrist was calculated to be 6.8±1.96 mm^2 and the left wrist was 6.6±1.96 mm^2. The mean median nerve cross-section area at the right mid-forearm was 5.3±1.46 mm^2 and the left mid-forearm was 5.2±1.50 mm^2. A decrease in mean median nerve cross-section areas was noted by moving from wrist to forearm. Similarly, males showed higher median nerve CSA than females. **Conclusion:** Mean median nerve cross-section area was found to be different from Western countries. This warrants the utilization of the data of the Pakistani population to establish our own normal reference range for median nerve cross-sectional area to avoid misdiagnoses.

Keywords: Median Nerve; Wrist; Fore-arm; Ultrasonography; Cross-sectional Area

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INTRODUCTION

Median nerve compression in the carpal tunnel at the wrist is often debilitating and results in carpal tunnel syndrome. Electrophysiological testing in association with clinical features had remained the mainstay of carpal tunnel syndrome (CTS) diagnosis for a long time.[1] However, the recent advances in the discovery of ultrasonography's role as a diagnostic tool in the assessment of CTS have shifted the attention from nerve conduction studies to non-invasive and painless use of sound waves for its diagnosis.[2–6]

Literature documents that the assessment of cross-sectional area (CSA) of the median nerve at the level of distal wrist crease/ at the level of pisiform bone has the best diagnostic ability for CTS. The studies document notable differences in the normal value of CSA of the median nerve across the globe; ranging from 7 to 9.4 mm2 in different populations.[7–9] The differences in the threshold value of CSA of the median nerve for the establishment of CTS diagnoses is multifaceted including both individual and population-based factors including body habitus, degree of nerve inflammation and site of CSA measurement. Ethnicity/ racial difference is also an important factor that applies generally to a population group.[10] Therefore, it is important to define the normal reference range for each population subset so that ultrasound's diagnostic accuracy for CTS detection could be optimized.

A study conducted by Ellen Walhout-van burg, *et al*, found out median nerve CSA at the wrist in the Indian cohort to be 7.0 ± 1.1 mm^2 which was lower when compared to the Dutch population (8.3 ± 1.9 mm^2; $p < 0.05$).[11] Our experience also suggests that the normal average median nerve CSA at distal wrist crease and forearm in our population are smaller than in

European people. This descriptive study is conducted to determine the reference range for the normal value of median nerve CSA in the Pakistani adult population.

MATERIAL AND METHODS

Ethical clearance was taken from IRB and EC (Institutional Review Board and ethical committee) reference IRB# 186-676-2019. The descriptive study was conducted over a 2-year time period from July 2017 to July 2019. A total of 500 asymptomatic patients, i.e., 1000 median nerves were evaluated at the distal wrist crease and mid-forearm by 3 expert radiologists independently. Informed written consent was obtained from all subjects prior to median nerve evaluation.

All patients having a positive nerve conduction study or history of carpal tunnel syndrome and wrist trauma were excluded. For Ultrasonography, patients were comfortably seated on the ultrasound couch with their arms extended on a pillow placed on their thighs. All scans were performed on 500 Aplio Toshiba ultrasound machines. The median nerve was identified by a characteristic appearance and internal stippling. High-frequency linear transducer having 7.5-15 MHz frequency was used for acquiring

CSA of the median nerve at the level of the distal crease of the wrist and 12 cm proximal to distal wrist crease in the forearm by continuously outlining the nerve circumference drawn immediately inner to the echogenic epineurium as shown in figure-1 and figure-2. The system-generated area was recorded on performed proformas. The same procedure was repeated on another upper limb. The scans were performed by 3 expert radiologists independently.

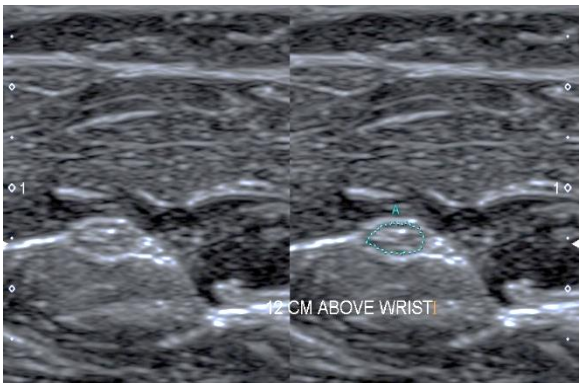

Figure-1: Measurement of median nerve CSA 12 cm above the distal wrist crease on ultrasound.

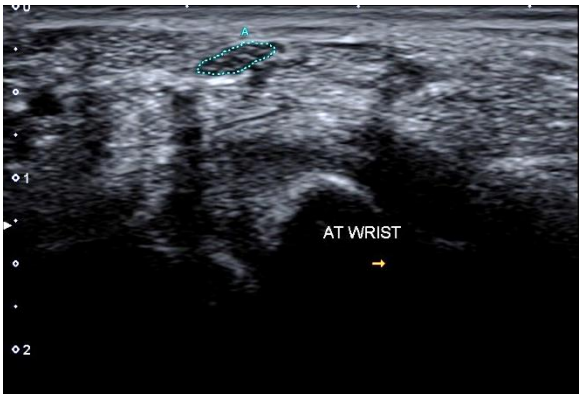

Figure-2: Measurement of median nerve CSA at the level of distal wrist crease on ultrasound.

Data was analyzed via SPSS v 20. For quantitative data; standard deviations and mean were calculated, i.e., median nerve CSA at the level of the distal crease of the wrist and 12 cm above the distal wrist crease in the forearm. To establish the significance of median nerve CSA in males versus females, and among BMI groups unpaired T-Test was applied. To determine the significant change of median nerve CSA from wrist to forearm, paired T-Test was applied. For checking the correlation between age, BMI and cross-sectional area, the Pearson correlation coefficient was calculated. Findings were considered significant at *p*-value<0.01.

RESULTS

The mean age of the population enrolled was 31.40±10.11 years with male to female ratio of 1: 1.36. The mean BMI was 22.15±4.34 Kg/m^2. The mean median nerve CSA at the right wrist was calculated to be 6.8±1.96 mm^2 and the left wrist was 6.6±1.96 mm^2. The mean median nerve cross-section area at the right mid-forearm was 5.3±1.46 mm^2 and the left mid-forearm was 5.2±1.50 mm^2.

A decrease in mean median nerve cross-section areas was noted by moving from wrist to forearm. Table 1: establishes the significant change in the median nerve cross-section area via paired T-test.

A significant difference in median nerve mean CSA was found between males and females through the range remained the same. Table-2 depicts the independent T-Test findings of these variables.

Median nerve CSA for the right wrist was 7.536±1.65 in males at the wrist compared to 6.066±1.38 in the forearm. The values for Median nerve CSA increased in both genders while moving from wrist to forearm. Histogram shows the distribution of median nerve CSA for the right and

left arms at the wrist and mid-forearm with respect to gender (Figure-3).

There was a significant correlation between the increase in median nerve CSA and an increase in BMI (r = 0.324, p<0.01). Both genders had the same distribution of BMI (p<0.341) (Figure-4).

A positive correlation was found between an increase in age and an increase in median nerve CSA (r-0.377, p<0.001).

Table-1: Paired Samples Statistics

		Mean	N	Std. Deviation	T-score	*p*-value
Pair 1	**Left wrist**	6.620	500	1.9655	23.744	0.0001
	Left forearm	5.26	500	1.504		
Pair 2	**Right wrist**	6.828	500	1.9488	26.195	0.0001
	Right forearm	5.342	500	1.4647		

Table-2 Group Statistics

	Gender	N	Mean	Std. Deviation	T-score	Significance
Right wrist	Male	211	7.536	1.6540	7.290	0.0001
	Female	289	6.311	1.9878		
Left wrist	Male	211	7.398	1.6103	8.030	0.0001
	Female	289	6.051	2.0088		
Right forearm	Male	211	6.066	1.3854	10.417	0.0001
	Female	289	4.813	1.2855		
Left forearm	Male	211	5.94	1.398	9.447	0.0001
	Female	289	4.76	1.378		

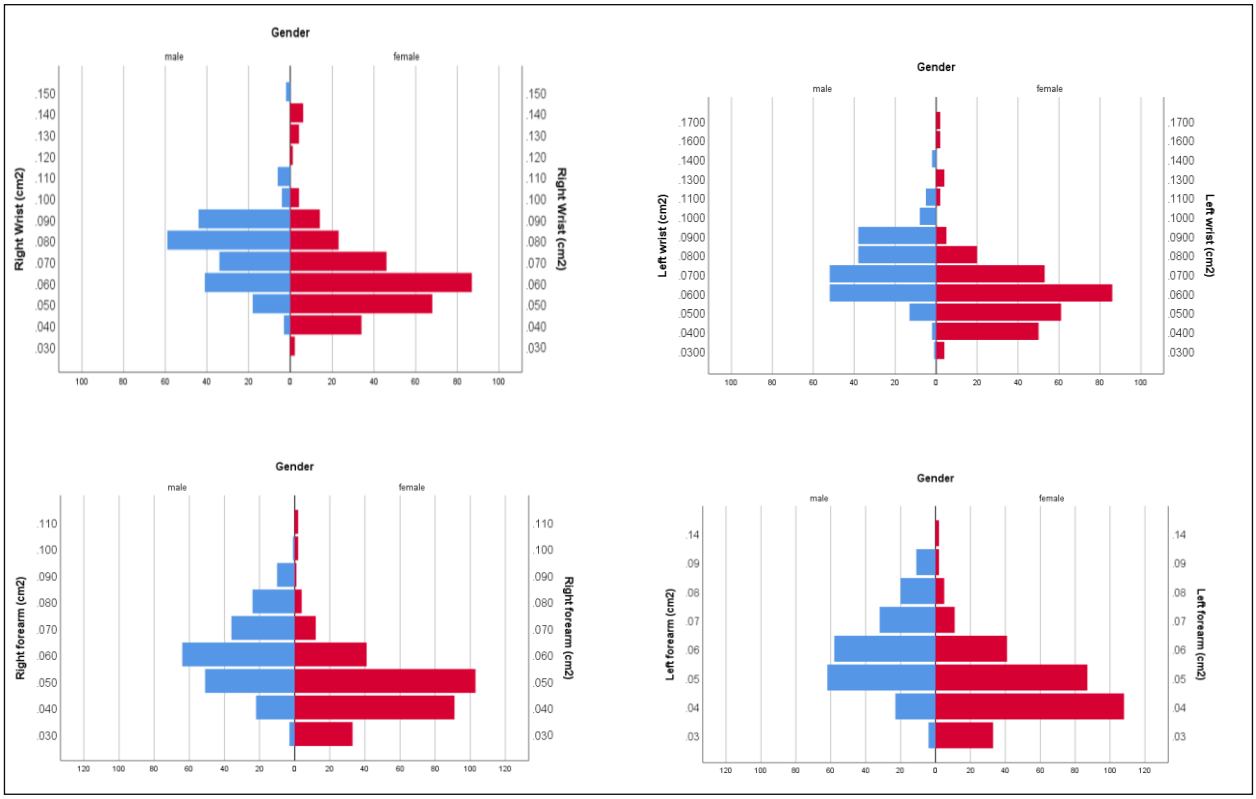

Figure-3: Histogram analysis showing the gender-wise distribution of median nerve cross-section area at right and left wrist and forearm.

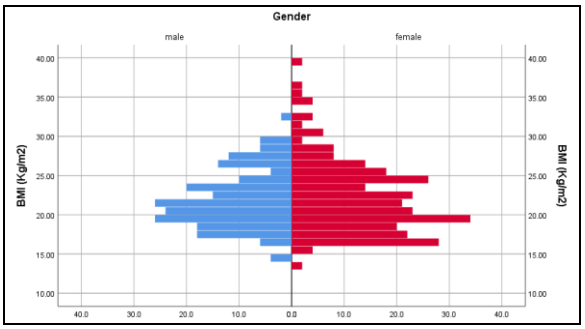

Figure-4: Gender-wise histogram of BMI

DISCUSSION

The optimal method for validating a clinical diagnosis of CTS has not been established and is under debate for a long time.[12] The results of physical examinations, numerous electrodiagnostic testing, and postoperative betterment have all been used and tested as diagnostic means. Recent additions to the novel diagnostic techniques include median nerve sonography.[13] As pointed out previously in multiple studies, the increase in CSA of the median nerve at the wrist/enlargement on ultrasound appears promising but rather challenging in clinical practice to adapt due to differing results in different studies. One of the reasons for this variability in results is due to different populations being studied in different studies. A study conducted by Ellen Walhout-van burg, *et al*, showed median nerve CSA at the wrist in the Indian cohort (7.0±1.1 mm^2) was notably lower when compared to CSA at the wrist measured in the Dutch cohort (8.3±1.9 mm^2; $p<0.05$).[11] This difference in mean nerve circumference implies the need to develop different reference CSA values in different populations including Pakistan.

In our study, the mean median cross-section at the right wrist was greater than the left wrist and the mean cross-section area reduced as the observation moved from the wrist towards the forearm. The *p*-value was less than 0.001 which shows that this observation was highly significant. This finding is in line with a study conducted comparing the CSA values of patients in India and the Netherlands. The Indian cohort had lower CSA values (7.2 mm2 on the right; 7.0 mm^2 on the left) which are quite near to the values we obtained for the Pakistani population, i.e., (6.82 mm^2 on the right; 6.62 mm^2 on the left) as compared to the Dutch population which had greater CSA values (8.1 mm^2 in right; 8.3 mm^2 in left).[11] The reason for this similarity can be attributed to hard ethnicities, and gene pool owing to the similar geographical locations of India and Pakistan as compared to the Netherlands.

The CSA values are also comparable to another study conducted in Iran where the mean median nerve CSA came out to be 5.78 mm2 which is quite near to the CSA values in our study population from Pakistan.[14] However, there is a study that contradicts this observation of differing CSA values in different areas. In a study conducted with one patient group in the US while the other one in Italy, showed quite similar mean values of median nerve CSA at distal wrist crease and forearm.[10] Therefore, these differing observations in different studies prove that there is a need to determine individual reference CSA values for individual populations.

In a recent meta-analysis and systemic review conducted on 28 published studies by Costoso *et al*., it was concluded that carpal tunnel syndrome can be diagnosed reliably on ultrasonography measurements with high specificity and sensitivity in both inlet and outlet measurements. The inlet-level ultrasonography, however, showed better results as compared to outlet measurements with high diagnostic accuracy.[15] Another meta-analysis conducted recently including 74 studies focused on the reference values of the median cross-sectional area and found high variability and heterogeneity in the radial nerve and low variability and heterogeneity in other nerve sites.[16] Although there are multiple benefits of ultrasonography for the diagnosis of CTS, there are still hurdles to its widespread acceptance and clinical utility for CTS patients. These include the unclear relationship of CTS with other factors of the patients like age, sex technique of sonography and comorbidities. Similarly, the CSA values obtained by ultrasonography do not hint at the level of severity of the disease as well as other subjective and objective outcomes related to CTS.[17] Moreover, the US measurements of the median nerve are also found to be less correlated with the gold standard cadaveric measurements as compared to MRI.[18] These results and different studies stress the need for the development of normal reference range values of median nerve CSA so that CTS can be diagnosed via ultrasonography reliably.

The limitations of our study included a unicentric study; median nerve CSA was measured at our hospital only where the majority of people residing in Islamabad were scanned. The study needs to be performed in different cities and regions of Pakistan to validate and further strengthen the reference range for median nerve CSA across the country.

CONCLUSION

The mean median nerve cross-section area was found to be different and smaller than in Western countries. Therefore, there is a need to design reference values for all countries and then develop the universal

criterion for carpal tunnel syndrome diagnosis via ultrasonography.

AUTHORS' CONTRIBUTION

RN: Conceptualization, data collection, proofreading. MR: Data analysis and write-up. FR: Write-up, data interpretation. BYF: Literature search, write-up. MSW: Data collection, proofreading. RA: Data collection and proofreading.

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