ISSN 2515-8260 Volume 09, Issue 08, 2022

Original Research Article

Assessment of upper-extremity inter-limb girth and volume variance to standardize diagnostic cut-offs for detection of upper limb lymphoedema in Indian women population

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Abstract

Background: Due to its diverse appearances and challenges in clinical evaluation, secondary lymphedema is frequently underreported and undertreated. Normative-determined criteria from western population have high sensitivity and specificity for detection of mild lymphedema in western women. It is uncertain if these requirements apply to Indian women, whose body types differ from those of Western women. The purpose of this study was to define the typical upper extremity inter-limb variation in a sample of healthy Indian women and to establish statistically based diagnostic cut-offs for both circumference and volume measures.
Methods: Descriptive research design was adopted. Six hundred and thirty one healthy Indian women, between the age the age of twenty to seventy years, participated in this study. At 5 cm intervals, the upper limb circumference was measured from wrist to above. Each segment of the limb depicted a frustum or truncated cone as a result of the measurement levels dividing the limb into parts. By combining the volumes of the segments individually, the ultimate volume was calculated. Diagnostics cut-offs for lymphoedema were derived by calculating three standard deviations plus the mean difference between the limbs.
Results: Significant differences were revealed by the paired *t*-tests between the dominant and non-dominant circumference and volumetric measurements. Regression analysis found a strong correlation between Age and BMI with the inter-limb circumference and volume difference. The diagnostic cut-offs ranged between 5% for the age 20-25yrs to ≤10% for the age up to 70yrs.
Conclusions: The threshold values provided by this study, taking arm dominance and population specificity into consideration, are likely to be appropriate for accurate diagnosis of changes in limb volume, helping in early detection of lymphoedema and increasing the probability of early intervention. This study delineates the percentage of ≤10% inter upper limb difference to be considered normal and acceptable as non-pathological.

Keywords: Limb volume, lymphoedema, limb dominance, upper limb, Indian women

ISSN 2515-8260 Volume 09, Issue 08, 2022

Introduction

According to Pinar Borman (2018), primary lymphedema is brought on by injury to the lymphatic tissues, whereas secondary lymphedema is brought on by defective lymph vessel or lymph node development. Due to its diverse appearances and challenges in clinical evaluation, secondary lymphedema is frequently underreported and undertreated. Lymphedema that is left untreated increases with time and has a severe impact on quality of life (Lanza *et al*., 2015). Changes in limb volume calculations are often used by clinicians and researchers to diagnose and assess the results of lymphoedema treatment (Chromy *et al*., 2015). Anthropometrically human limbs are symmetrically structured. But due to lifestyle and work style variations muscle mass, limb strength and limb circumference varies from dominant limb to non-dominant limb (Bhat *et al*., 2021). Detection of upper limb lymphedema following treatment for breast cancer typically relies on inter limb circumference-based differences (Katz-Leurer & Bracha, 2012). The most widely accepted measure of arm lymphedema is volume and the most commonly used volume cut-off is a 200 mL volume difference and it was arbitrarily preferred for convenience (MW Kissin, G Querci Della Rovere, D Easton, 1986). Normative-determined criteria from western population have high sensitivity and specificity for detection of mild lymphedema in western women. It is unknown whether these criteria are applicable to Indian women whose body habitus is different from western women. In the Indian Sub-continent, varied climate and dressing cultures exist, difference in limb volume could also be attributed to their bangle or ornaments or tight constricting garment. Presently there is a lack of diagnostic cut-offs for upper limb volumetric and circumference measurements considering ethnic differences and arm dominance specific to Indian women Population; and there is a need to establish validated and reliable reference standard values to accurately diagnose changes in limb volume. Data on cut off volume difference in percentage between dominant and non-dominant limbs enables clinicians to diagnose and vary treatment and improve clinical outcomes that would influence the patient's quality of life.

The purpose of this study was to define the typical upper extremity inter-limb difference in a group of healthy Indian women and to establish statistically based diagnostic cut-offs for circumference and volume measures of upper limb lymphedema.

Methodology

Study design

Descriptive research design was adopted for the present study.

Study sample

The duration to this study was from September 2021 to August 2022. The study participants were 631 healthy Indian women from two north Indian (Rajasthan and Gujarat) and a south Indian state (Tamil Nadu) participating in free general health camps conducted by medical and Physiotherapy colleges. Convenient sampling method was adopted. The inclusion criteria was healthy Indian women aged between 20-70yrs. Exclusion criteria was known cases of filariasis, cellulitis, neurological conditions, hospitalized or vaccinated within a week, new or old fracture of upper limb, rheumatoid conditions or surgery of upper limbs.

ISSN 2515-8260 Volume 09, Issue 08, 2022

Circumference and Volume measurements

Physiotherapist volunteers with more than two years of anthropometric measuring and lymphedema management expertise took measures of both arms. In a predetermined position (Sitting with the shoulder abducted to 90°, elbow extended, and forearm pronated), measurements of the circumference of the upper limbs were collected. With the use of circumferential measurements, arm volume was determined. The limb was split into segments by the measurement levels, and each segment constituted a frustum or truncated cone. Up to the wrist, measurements of the arm's circumference were obtained every 5 cm. The sum of the individual volumes of the segments yielded the final volume.

Data collection

The measurements for comparison between dominant and non-dominant upper limb circumference were taken at three levels-wrist, mid-point forearm and mid-point arm. Limb girth of both the arms was measured (using a flexible measuring tape) at palmar level, wrist level, 5cm above styloid process, 10cm above styloid process, 15 cm above styloid process, at elbow crease level (segment height was noted), 5cm above elbow crease, 10cm above elbow crease 15cm above elbow crease and at axillary level (segment height was noted). Limb volume was calculated using geometrical method of estimation of arm volume (truncated cone method). For the same purpose, the upper limb was divided into segments (cones), starting from the level of the wrist and moving upwards, till the axillary level. The segments for the forearm were divided as Segment A (wrist-5cm), Segment B (5cm to 10cm), Segment C (10 cm-15cm), Segment D (15cm-20cm) and Segment E (20cm to elbow crease). The segments for the arm were divided as Segment F (Elbow crease-5cm), Segment G (5cm to 10cm), Segment H (10 cm-15cm), Segment I (15cm-20cm) and Segment J (20cm to axillary line).
The volume for each segment was calculated using the formula,
$V=h\ (C12 + C1C2 + C22)/12\ \boldsymbol{\pi}$

Where V-volume, H-height of the segment(cone), and C1, C2 are the limb circumference at the either ends of the segment. The volume of the limb was derived by summing up the individual segmental volumes. (Sander *et al*., 2002)

Data analysis

Statistical analysis was performed using SPSS 20 software. The data has been presented as mean ± standard deviation for the dominant and non-dominant arm for circumference and volume calculations. Paired *t*-tests were done to derive the mean for the inter-limb differences. A p-value of 0.01 or less was considered statistically significant. Regression analysis was performed to determine the relationship of age and BMI with the upper limb circumference and volume measurements. Diagnostic cut-offs calculated as mean plus three times standard deviation (Dylke S *et al*., 2011) for circumference and volume measurements of forearm and arm and tabulated based on age and BMI of the participants. The diagnostic cut-offs were expressed as percentage as the cut-offs expressed as volume (ml) may vary as per the BMI.

ISSN 2515-8260 Volume 09, Issue 08, 2022

Ethical considerations

All patients were informed about the nature of the study, and their informed consent was obtained. Their information was solely used for data purposes in the present study. Study approval obtained from IEC, Pacific Medical College and Hospital, Udaipur (PMU/PMCH/IEC/2021/186A/7).

Results

This study had 631 participants with mean age of 47.59 ± 12.87 yrs. (20 - 70 years) and mean BMI 26.73 ± 4.46 (17.10 – 40.60). Single point assessment method for limb dominance identified 96% (n=606) with right hand dominance and only 4% (n= 25) with left hand dominance.

Comparison of circumference and volume measurements of the upper limb based on the limb dominance

The results of the paired '*t'* tests in Table-1 shows the mean, standard deviations and mean of inter-limb differences for the circumference measurements and the volumes of the 10 segments for both the dominant and non-dominant arms for all participants.

Table 1: Comparison of circumference and volume measurements of the upper limb based on the limb dominance

	Dominant		**Non-dominant**		
	Mean	**SD**	**Mean**	**SD**	**Inter-limb Difference Mean (95% confidence interval)**
Circumference (cm)					
Wrist (cm)	15.00	±1.43	14.90	±1.27	0.10(0.02-0.18)*
Mid-point Forearm (cm)	19.43	±2.44	19.285	±2.24	0.15(0.03-0.27)*
Mid-point Arm (cm)	28.11	±3.53	28.19	±3.85	-0.07(-0.24-0.09)
Volume Forearm (mL)					
Segment A (Wrist-5cm above)	98.32	±18.65	96.81	±17.36	1.51(0.71-2.31)*
Segment B (5cm-10cm)	128.83	±29.35	126.60	±27.36	2.23(1.04-3.41)*
Segment C (10 cm-15cm)	178.80	±37.82	175.54	±36.64	3.26(1.80-4.71)*
Segment D (15 cm-20cm)	217.66	±40.62	214.79	±40.14	2.88(1.40-4.35)*
Segment E (20 cm-Elbow Crease)	168.81	±74.96	168.66	±73.90	0.14(-1.28-1.57)
Total Volume Forearm (mL)	792.42	±164.07	782.40	±157.66	10.01(4.80-15.23)**
Volume Arm (mL)					
Segment F (Elbow crease-5cm above)	259.52	±56.02	261.37	±56.44	-1.85(-3.51–0.20)
Segment G (5cm-10cm)	302.70	±73.35	304.42	±74.13	-1.73(-3.90-0.45)
Segment H (10 cm-15cm)	344.49	±82.52	345.74	±83.45	-1.24(-3.32-0.84)
Segment I (15 cm-20cm)	396.98	±92.06	396.50	±91.23	0.48(-1.33-2.29)
Segment J (20 cm-Axillary line)	494.98	±98.29	491.43	±99.63	3.55(1.23-5.87)*
Total Volume Arm (mL)	1798.67	±380.40	1799.47	±381.41	-0.79(-8.40-6.82)
Total Limb Volume (mL)	2591.09	±513.78	2581.87	±512.24	9.22(-2.01-20.45)

Significance at $p<0.01$ denoted by**

Significance at $p<0.05$ denoted by*

ISSN 2515-8260 Volume 09, Issue 08, 2022

Significant differences were revealed by the paired *t*-tests between the dominant and non-dominant circumference and volumetric measurements. The wrist and mid-point forearm circumference measurements for dominant upper limb were higher than the non-dominant upper limb. The mean differences in circumferential measurements for inter-limb girth showed significance at $p<0.05$ for wrist and forearm 0.10cm (*CI* 0.02-0.18) and 0.15cm (CI 0.03-0.27) respectively. There was no significant inter-limb difference for mid-point of arm circumference measurements.

Paired *t*-tests for dominant and non-dominant volumetric measurements showed significance at $p<0.05$ for volume of arm (5cm, 10cm, 15cm and 20cm) and volume at axilla, while significance of $p<0.05$ was noted for volume of forearm.

Diagnostic cut-offs

Three standard deviations plus the mean difference between the limbs were used to calculate diagnostic cut-offs for lymphoedema (Table 2). Regression analysis revealed a significant relationship between age and BMI and inter-limb circumference and volume difference. A significance level of $p<0.01$ was seen for age and BMI as variables in regression. Therefore, the diagnostic cut offs were determined based on age groups and BMI as shown in Table 2. The diagnostic cut-offs were expressed as percentage as the cut-offs expressed as volume (ml) may vary as per the BMI. The diagnostic cut-offs ranged between 5% for the age 20-25yrs to ≤10% for the age up to 70yrs.

Table 2: Diagnostic cut-offs (DC) based on Age and BMI

Age/BMI	N	% Forearm Vol Difference			% Arm Vol difference			% Total ULVol difference			Absolute Forearm Girth Difference			Absolute Arm Girth Difference		
		Mean	SD	DC	Mean	SD	DC	Mean	SD	DC	Mean	SD	DC	Mean	SD	DC
Age																
< 25 years	62	3.56	0.85	6.11	3.43	0.47	4.84	2.85	0.69	4.92	0.46	0.06	0.64	0.95	0.30	1.85
26-35 years	50	3.92	1.11	7.22	2.70	0.72	4.86	2.72	0.58	4.46	0.51	0.15	0.96	0.60	0.11	0.93
36-45 years	127	4.63	1.08	7.87	4.00	1.49	8.47	3.67	1.97	9.58	0.95	0.21	1.58	1.02	0.4	2.22
46-55 years	217	5.34	1.58	10.08	3.98	0.55	5.63	4.25	2.02	10.31	0.91	0.18	1.45	0.95	0.39	2.12
56-65 years	139	4.66	1.37	8.77	3.59	1.16	7.07	3.50	1.05	6.65	0.69	0.10	0.99	0.78	0.25	1.53
>65 years	36	4.84	1.79	10.21	4.27	1.63	9.16	4.66	0.64	6.58	1.03	0.44	2.35	1.20	0.23	1.89
Body Mass Index																
Underweight	14	2.71	0.89	5.38	3.23	0.26	4.01	3.01	0.67	5.02	0.54	0.16	1.02	0.98	0.04	1.1
Normal	230	3.84	1.42	8.1	3.63	0.41	4.86	3.50	2.21	10.13	0.81	0.50	2.31	0.82	0.13	1.21
Overweight	245	4.57	1.89	10.24	3.73	1.48	8.17	3.80	0.81	6.23	0.78	0.10	1.08	1.02	0.09	1.29
Obese	132	4.89	1.97	10.8	4.19	1.45	8.54	4.23	2.04	10.35	0.88	0.15	1.33	1.06	0.17	1.57
Very obese	10	5.91	1.3	9.81	3.10	0.52	4.66	3.19	1.30	7.09	0.75	0.14	1.17	0.65	0.15	1.1

Vol =Volume, UL Vol= Upper Limb Volume

Discussion

The threshold values of normative size and inter-limb difference for diagnosis and evaluation of lymphoedema in Indian women population are generalizable regardless of body habitus. Therefore, the limb volume changes may go undiagnosed or underestimated in early stages of lymphoedema. Secondary upper limb lymphoedema can have detrimental effect on the quality

ISSN 2515-8260 Volume 09, Issue 08, 2022

of life of women. There is a lack of standardized quantification of breast cancer related lymphoedema to help with its early detection, tracking over time and during treatment. A 2 or 3 cm difference in one or more arm circumference measurements or a total difference in circumferential measurements of 5 cm or 5% of an absolute inter-limb arm volume difference ranging from 125 to 200 mL or a 10%-20% inter-limb volume percentage change are commonly used diagnostic criteria for lymphoedema. Volume is the most frequently acknowledged metric of arm lymphedema, and a 200 mL volume difference is the most commonly used volume cut-off. The source of these diagnostic thresholds is unknown. As mentioned by the authors, the 200 mL diagnostic threshold in Kissin *et al*. Publication's was chosen arbitrarily for simplicity (Kissin *et al*., 1986). Measurements of volume derived from circumferences also have a good agreement with both the water displacement method of measuring limb volume, but perometry is often considered the gold standard of assessment (Sander *et al*., 2002). But in Indian health sector a cost effective and a reliable diagnostic measure will be beneficial to patients with lymphoedema. The diagnostic cut-offs derived in the present study ranged between 5% for the age less than 20-25yrs to ≤10% for the age up to 70yrs. This study delineates ≤10% inter upper limb difference to be considered normal and acceptable as non-pathological.

It is observed that normative based threshold is generalized values, regardless of body habitus, dominance of the limb, age and BMI (Thornton & Villamor, 2015). Normative inter-limb differences are likely to be different for Indian women population. Currently, there is a paucity of data on the normative size and inter-limb differences specific to Indian women population. Hence the results from this study can be considered as a cut off value to diagnose lymphoedema based on age and BMI. As in this study BMI was considered an important variable for deriving precise values of diagnostic cut-off. Another study by *Bundred N* found that high BMI predicted lymphoedema diagnosis and progression (Bundred *et al*., 2020). Using bioimpedance spectroscopy, another study discovered that age had a minor but substantial influence on interlimb difference (Ward, 2006; Ward LC, Dylke E, Czerniec S, Isenring E, 2011).

Arm dominance is an important factor in the diagnosis of BCRL as the more dominant arm will usually have larger muscles, and therefore more water, since muscles are 70% water (Arinaga *et al*., 2016). The current study revealed significant differences between dominant and non-dominant arm at few levels of measurements. However, the inter limb total arm volume difference was not significant. Regression analysis confirmed the correlation of inter limb volume differences, age, and BMI.

Further studies using the other diagnostic modalities could be attempted to compare and review the inter-limb variance and diagnostic cut-offs for lymphoedema for the Indian women population. Sample distribution across BMI category is not proportionate and a limitation of the study.

Conclusion

Presently, the inter-limb circumference and volume differences and the threshold values for lymphoedema are generalized, regardless of body habitus and ethnicity. Since, body habitus differs between populations it was imperative to clarify whether these normative values are appropriate for the Indian women population. Considering ethnicity, in India clothing is dependent upon the geography, climate, and cultural traditions of the people of each region of India. The limb volume could differ especially due to bangles or other ornaments or tight constricting garments. Hence, this study emphasized on deriving a set of standardized diagnostic cut-off values for upper limb circumferential and volumetric measurements for

ISSN 2515-8260 Volume 09, Issue 08, 2022

Indian women population. This study concludes the percentage of ≤10% inter upper limb difference to be considered normal and acceptable as non-pathological. The threshold values provided by this study, taking arm dominance and population specificity into consideration, are likely to be appropriate for accurate diagnosis of changes in limb volume, helping in early detection of lymphoedema and thus increasing the probability of early intervention.

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ISSN 2515-8260 Volume 09, Issue 08, 2022

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