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Normal Cerebral Blood Flow Volume in Healthy Nigerian Adults

Akeem Babatunde Bello[1], Temitope O. Bello[1], Ademola Adegoke Aremu[2*] and Victor A. Adetiloye[3]

[1]*Department of Radiology, Ladoke Akintola University Teaching Hospital, Osogbo, Osun State, Nigeria.*
[2]*Department of Radiology, Ladoke Akintola University Teaching Hospital, Ogbomoso, Oyo State, Nigeria.*
[3]*Department of Radiology, Obafemi Awolowo University Teaching Hospital, Ile-Ife, Osun State, Nigeria.*

Authors' contributions

This work was collaboration between all the authors, who were involved in all the aspects. They all contributed to conception and design of the study. Author ABB acquired the data, analysed and drafted the manuscript. Author TOB was involved in data analysis, interpretation, proof reading and editing of the manuscript. Author AAA did the literature search, was involved in data analysis and interpretation, proofreading, critically revision and final correction of the manuscript. Author VAA critically revised the manuscript and final approval of the submitted manuscript. All authors read and approved the final manuscript.

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ABSTRACT

Background: Blood supply to the brain is very vital for its functions. Most of the pathologic processes that affect the acutely injured brain eventually results in impairment of cerebral blood flow (CBF). Early identification of the ischaemic or hyperemic conditions is critical to define the most appropriate therapeutic strategies. However, there is paucity of data on the normal cerebral blood volume in Sub Saharan Africa; we therefore employed the use of a safe, practical, economical, repeatable and readily available Doppler ultrasonography to evaluate CBF.

**Corresponding author: E-mail: aaaremu@lauech.edu.ng, lamode70@yahoo.com;*

Aims and Objectives: The main aim of the study was to determine age and sex specific normal cerebral blood flow volume by Doppler ultrasonography of the extracranial carotid and vertebral arteries in healthy Nigerian adults.
Methodology: Three hundred and ninety six (396) subjects that met the inclusion criteria were examined with the aid of Doppler ultrasound machine. All the subjects were scanned by the same radiologist, thereby avoiding inter observer variability and each measurement was taken thrice and an average found. The flowmetry values from the carotid and vertebral arteries were statistically analyzed using SPSS version 16.
Results: The total cerebral blood flow volume was 624.90±115.57 ml/min with the mean blood flow volumes of 226.57±32.03 ml/min and 226.85±31.58 ml/min (right and left internal carotid arteries); 85.59±27.81 ml/min, and 85.59±27.20 ml/min (right and left vertebral arteries). The mean total cerebral blood flow volume was more in the males (625.64±116.38 ml/min) than the females (624.75±115.06 ml/min), decreasing with increasing age in both sexes with associated increase in vessels diameters with age. Although, statistically significant differences ($P<0.001$) were seen in the Peak.
Systolic velocities (PSV), End diastolic velocities (EDV) and Resistive Indexes (RI) of the internal carotid arteries in Males and Females, the difference in the total cerebral blood volume was not significant. The intra rater reliability showed an almost perfect agreement with an average Kappa coefficient of 0.88.
Conclusion: Our study has provided a safe, economical and repeatable age, sex and side specific extracranial normogram of flowmetries of individual and total cerebral blood vascular supplies to the brain which is essential in successful management of cerebrovascular diseases.

Keywords: Normal cerebral blood; volume; doppler ultrasound; carotid arteries; vertebral arteries; healthy adults.

1. INTRODUCTION

Blood flow to the brain is very vital for its functions, although the brain weighs 2% of the total body weight, it receives about 15% of the body's supply [1], therefore early detection of changes in cerebral blood flow is an essential step in management of acutely injured brain.

Several imaging modalities like Positron emission tomography (PET), Single photon emission tomography (SPECT), Stable xenon computer tomography and Magnetic resonance Imaging have been used to provide reliable and accurate measurements of cerebral blood flow. All of these techniques however are cumbersome, expensive, not readily available in developing countries and most importantly not mobile as the critically ill, often sedated and ventilated patients will have to be transferred to the imaging or radionuclear facility. They are not easy to repeat as often as clinically indicated, therefore are of limited use in setting up of intensive care.

Doppler ultrasound on the other hand is a user friendly, portable system that produces rapid and frequent measurement of cerebral blood flow at bed side. The initial measurements of cerebral blood flow volume by Duplex ultrasound were limited to the estimation of common carotid arteries and the internal carotid arteries, until in 1994 when Schoning et al. [2] discovered that the common carotid artery flow volume were not representative and approximately one- quarter of the cerebral blood flow volume is transported through the vertebrobasilar system [2].

Duplex flowmetry of the extracranial cerebral vessels (internal carotid and vertebral arteries) permits estimation of intravascular flow and total cerebral blood flow volume(millimeter per minute) by summing the flow volumes measured in each of the four extracranial vessels has been proven to be precise, reliable [1-4] and an index of total brain perfusion [3,4].

Few data concerning normal cerebral blood flow volume have been reported worldwide and a decline of flow volume with age has been a subject of controversy [1-4], therefore there is a need to record the normal cerebral blood flow volume in healthy adults, the effects of age and sex on the flow velocimetry by Doppler ultrasonography which has not been widely explored.

2. METHODOLOGY

A cross-sectional one-year prospective study in which duplex velocimetry measurements were taken in healthy adult volunteers recruited through advertisement notices on the hospital boards.

Three hundred and ninety-six consecutive adults who gave informed consent, without history of brain and or neck surgery, no clinical features of cerebrovascular disease, trauma or neurodegenerative disease and with normal Body Mass Index (BMI) were included. Also excluded were anaemic, hypertensive and diabetic subjects; subjects with history of cigarettes smoking, alcohol consumption, steroid and oral contraceptives; congenital or acquired heart diseases. Those with plaque or stenosis were also screened out with colour and spectral Doppler Ultrasound.

Cerebral blood flow measurements were performed according to the protocol proposed by Schoning et al. [2], using a Sonoace X-8 (Medison, South Korea) duplex ultrasound machine with a standard 5-12MHz transducer. All the patients were scanned by the same radiologist to avoid interobserver variability and the premenopausal women were scanned at the mid follicular phase of the menstral cycle.

After the procedure was explained to the volunteers, he or she lied supine on the couch and rested for 15 minutes before the commencement of the examination. The head was slightly turned away from the side being examined, the neck slightly hyperextended in majority of cases by placing a pillow under the subject’s shoulder and coupling gel applied to the region of the neck to be examined before placing a high frequency transducer.

The examination started with a transverse scan of the carotid artery as low in the neck as possible to as high as possible behind the angle of the mandible.

Blood flow measurements were done (on right and left) at segment located 2 cm proximal to the bifurcation in the common carotid artery (CCA); 1-2 cm distal to the bifurcation in the internal carotid (ICA) and the external carotid artery (ECA). For the vertebral artery (VA) measurements were done bilaterally at the center of the arterial segment between 4th and 5th cervical vertebral transverse processes in the sagittal plane. The head was slightly turned about 10 degrees to the contralateral side for the carotid arteries measurement and between 25 degrees to 40 degrees to the contra-lateral side for the vertebral arteries measurement. In order to obtain error free measurements, arterial diameters were calculated on magnified mode images at the end of the diastole as a vertical line through the lumen, between the echogenic intima layer (Fig. 1, Fig. 2).

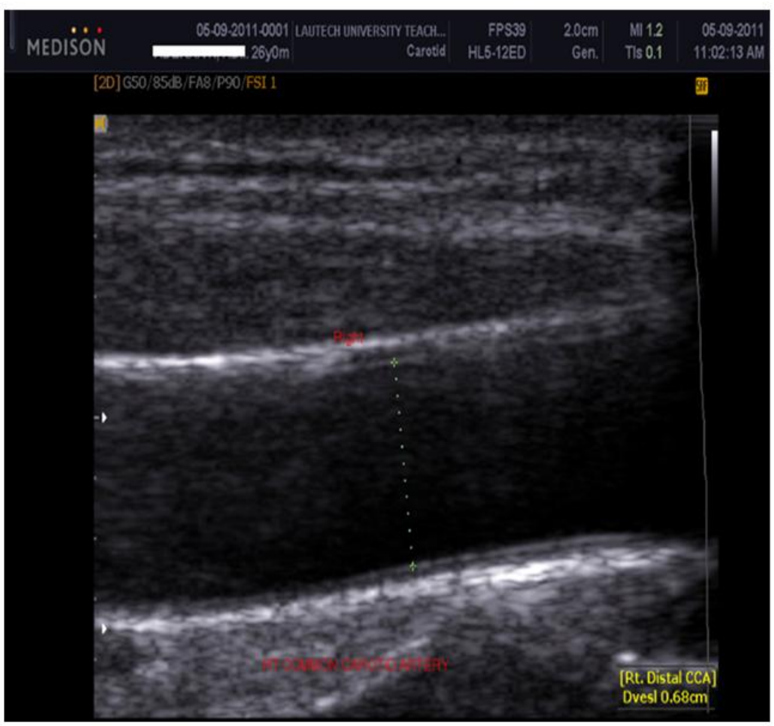


Fig. 1. Measurement of vessel diameter 0n magnified B- mode image

The Color Doppler was used to locate the vessel and the flow direction after which the Pulse Doppler was used to obtain the flow velocities at a constant Doppler insonation angle of 60 degree (Fig. 3).

Fig. 2. B- mode image at the birfucation of common carotid artery

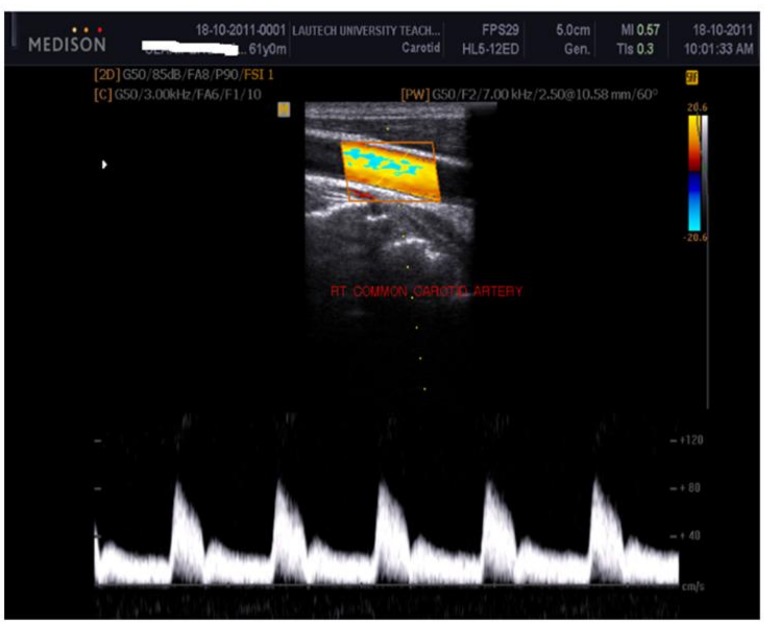


Fig. 3. Normal flow parttern in the rt. common carotid artery

The Doppler sample volume was kept at less than the vessel diameter and at the middle of the flow channel. Three consecutive blood flow velocity waveforms were considered as the correct spectral samples. The peak systolic velocity (PSV), End diastolic velocity (EDV), resistance index (RI) and blood flow volume (ml/min) were automatically calculated. Total cerebral blood flow volumes were obtained by summing the bilateral internal carotid and vertebral arteries blood flow volumes. All the measurements were done three times and the mean recorded. Other necessary information were derived with the aid of a questionnaire and the data analysis was done using statistical packaging for social sciences (SPSS) version 16, multivariate regression analysis and flow chart were also done.

3. RESULTS

A total of three hundred and ninety six (396) subjects -198 males (50%) and 198 females (50%) were included with age range of 21-80years (mean of 50.2 years±17.1 years). The subjects were divided into three age groups; 21-40 years, 41-60 years and 61-80 years with equal proportion of subjects (both males and females) in each group (Fig. 4).

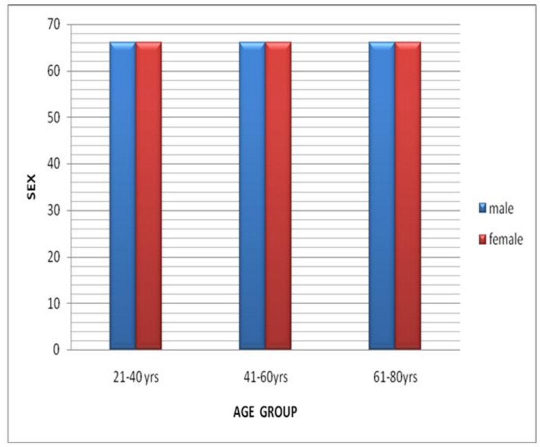


Fig. 4. Age and sex distribution of the subjects

The average total cerebral blood flow volume was 624.90±115.57 ml/min with the mean blood flow volume in the internal carotid arteries (ICA) of 226.57±32.03 ml/min and 226.85±31.58 ml/min for the right and left respectively; 85.59±27.81 ml/min and 85.59±27.20 ml/min for the right and left Vertebral arteries (RVA, LVA).

The mean total cerebral blood flow volume in the male was 625.84±116.38 ml/min and in the female it was 624.75±115.06 ml/min. The pattern of cerebral blood flow was similar in the right and left sides within the same age groups and also between both sexes. However reduction in flow volumes of right and left ICA and VA were noted with increasing age; this is however more significant in the total cerebral blood flow (CBF). In males the cerebral blood flow (CBF) in the right internal carotid artery (Rt.ICA) was 239.15±26.01 ml/min in the 21-40 yrs age group reduced to 224.64±30.71 ml/min in the 41-60 yrs group and 215.56±35.17 mls/min in 61-80 yrs. In the female, similar reduction was seen with advance in age 238.66±25.69 ml/min (21-40 yrs), 223.95±29.90 ml/min (41-60 yrs) and 217.44±35.83 ml/min (61-80 yrs).

The vessel were generally larger in males with an increase in the average vessel diameters (AVD) with age on both sides and in both sexes but no significant difference between the right and left sides.

Thus the average vessel diameter in males and females (Rt.ICA) respectively was 4.48±0.17 cm and 4.34±0.14 (21-40 yrs); 4.59±0.21 cm and 4.46±0.16 cm (41-60 yrs) and 4.71±0.26 cm 4.52±0.20 cm (61-80 yrs).

In the male subjects, the flow velocimetry values of the right and left were similar but there are statistically significant difference in the EDV and RI (of VA); PSV, RI and EDV (of the ICA) (Table 1). However in the female statistically significant differences were obtain between the right and left sides in the PSV, EDV, RI (ICA) and cerebral blood flow of ICA and VA (Tables 2 and 3).

While comparing velocimetry values between the two sexes (Tables 2 and 3), higher values were recorded in females (Rt and Lt) with statistically significant differences in PSV, EDV and RI (ICA). The PSV of the ICA was higher in females on both sides: Rt.ICA 72.70±9.60 cm/s and 66.61±7.85 cm/s ($p < 0.001$); Lt. ICA, 72.35±9.56 cm/s and 66.47±7.88 cm/s ($p< 0.001$). No statistically significant differences were obtained in the CBF (ICA, VA) and also PSV, EDV and RI (VA) in the between sexes (Tables 2 and 3).

High correlation and significant values were obtained while the PSV, EDV and RI were correlated with Global Cerebral blood flow volume (Table 4 and Fig. 5). The intra rater reliability showed an almost perfect agreement with an average Kappa coefficient of 0.88. The multivariate regression analysis with anova, f and p value for total Cerebral blood flow was only significant (p value of 0.006) for age group and not for BMI and sex. (Table 5).The flow chart of the study is depicted by Figs. 6a,b and c.

Table 1. Flow velocimetry value of the right and left internal carotid and vertebral arteries in both the male and female sex

Flow velocimetry	Right side male	Right side female	Left side male	Left side female
PSV – ICA (cm/s)	66.61±7.85	72.70±9.60	66.47±7.88	72.35±9.56
EDV – ICA (cm/s)	26.62±2.53	27.90±2.83	26.76±2.54	28.18±3.11
RI – ICA	0.60±0.04	0.61±0.03	0.60±0.03	0.61±0.03
CBF – ICA (ml/min)	226.45±32.27	226.68±31.87	226.28±31.36	227.43±31.86
PSV – VA (cm/s)	44.34±8.36	43.85±7.97	44.20±8.23	44.03±8.12
EDV – VA (cm/s)	14.93±2.13	15.14±2.27	15.18±2.26	15.23±2.32
RI – VA	0.66±0.03	0.65±0.03	0.65±0.03	0.65±0.03
CBF – VA (ml/min)	86.38±28.18	84.77±27.47	85.93±27.54	85.86±29.93

PSV – ICA = Peak systolic velocity – internal carotid artery, PSV –VA = peak systolic velocity – vertebral artery
EDV – ICA = end diastolic velocity – internal carotid artery, EDV – VA = end diastolic velocity – vertebral artery
RI – ICA = resistivity index – internal carotid artery, RI- VA = resistivity index – vertebral artery
CBF – ICA = cerebral blood flow – internal carotid artery, CBF – VA = cerebral blood flow – vertebral artery

Table 2. Significant differences of the velocimetry between male and female on the left side

Flow velocimetry	Male	Female	t-value	p-value
PSV – ICA (cm/s)	66.47±7.88	72.35±9.56	6.675	0.001
EDV – ICA (cm/s)	26.76±2.54	28.18±3.11	4.992	0.001
RI – ICA	0.60±0.03	0.61±0.03	4.080	0.001
CBF – ICA (ml/min)	226.28±31.36	227.43±31.86	0.361	0.718
PSV – VA (cm/s)	44.20±8.23	44.03±8.12	0.256	0.789
EDV – VA (cm/s)	15.18±2.26	15.23±2.32	0.221	0.825
RI – VA	0.65±0.003	0.65±0.03	0.797	0.426
CBF – VA (ml/min)	85.93±27.54	85.86±29.93	0.026	0.979

PSV – ICA = Peak systolic velocity – internal carotid artery, PSV –VA = peak systolic velocity – vertebral artery
EDV – ICA = end diastolic velocity – internal carotid artery, EDV – VA = end diastolic velocity – vertebral artery
RI – ICA = resistivity index – internal carotid artery, RI- VA = resistivity index – vertebral artery
CBF – ICA = cerebral blood flow – internal carotid artery, CBF – VA = cerebral blood flow – vertebral artery

Table 3. Significant differences of the velocimetry between male and female on the right side

Flow velocimetry	Male	Female	t-Value	p-Value
PSV – ICA (cm/s)	66.61±7.85	72.70±9.60	6.932	0.001
EDV – ICA (cm/s)	26.62±2.53	27.90±2.83	4.764	0.001
RI – ICA	0.60±0.04	0.61±0.03	4.309	0.001
CBF – ICA (ml/min)	226.45±32.27	226.68±31.87	0.072	0.942
PSV – VA (cm/s)	44.34±8.36	43.85±7.97	0.604	0.546
EDV – VA (cm/s)	14.93±2.13	15.14±2.27	1.957	0.335
RI – VA	0.66±0.03	0.65±0.03	2.275	0.023
CBF – VA (ml/min)	86.38±28.18	84.77±27.47	0.571	0.568

PSV – ICA = Peak systolic velocity – internal carotid artery, PSV –VA = peak systolic velocity – vertebral artery
EDV – ICA = end diastolic velocity – internal carotid artery, EDV – VA = end diastolic velocity – vertebral artery
RI – ICA = resistivity index – internal carotid artery, RI- VA = resistivity index – vertebral artery
CBF – ICA = cerebral blood flow – internal carotid artery, CBF – VA = cerebral blood flow – vertebral artery

Table 4. Correlation values: PSV, EDV, RI VS CBF

Flow velocimetry	R	p-value
PSV – Rt. ICA	0.883	0.001
PSV – Lt. ICA	0.879	0.001
EDV – Rt.ICA	0.587	0.001
PSV – Lt. ICA	0.632	0.001
RI – Rt. ICA	0.635	0.001
RI – Lt. ICA	0.613	0.001
PSV – Rt. VA	0.964	0.001
PSV – Lt. VA	0.965	0.001
EDV – Rt. VA	0.815	0.001
EDV - Lt. VA	0.825	0.001
RI – Rt. VA	0.660	0.001
RI – Lt. VA	0.627	0.001

4. DISCUSSION

Numerous imaging modalities are available to accurately evaluate the cerebral blood flow. Isotopic studies (positron emission tomography, single photon emission tomography) and imaging studies such as stable xenon computer tomography and magnetic resonance imaging-based technology have all proved to achieve reliable and accurate measurements of cerebral blood flow. They are however cumbersome and expensive; the critically ill, sedated and or ventilated patients will have to be transferred to the imaging or radio nuclear facility. As such these techniques cannot be repeated as clinically indicated and are of limited use for intensive care patients. Most of the published articles [5-7] on cerebral blood flow were based on ultrasound assessment of only common carotid arteries because of its ease of performance. However, this method was found to be less precise than measuring the internal and external carotid arteries separately [2]. The common carotid artery vessel diameter substantially changes during a cardiac cycle, and it has been shown that the mean flow volume can be higher in the common carotid artery than the sum of the flow volumes in the internal carotid and external carotid arteries [2]. Furthermore, summing up of flow volumes of both internal carotid and vertebral arteries as in this study had been reported to be accurate and reliable [2,8].

Accurate evaluation of velocimetry values was achieved in this study by using a linear array high frequency probe which allowed adequate penetration of the sound waves thereby preventing under or overestimation of the flow velocities and flow volumes. The insonating angle was set at 60 degrees because the Doppler signals are strong at 0 to 60 degrees angle to flow but weak at 60 to 90 degrees).

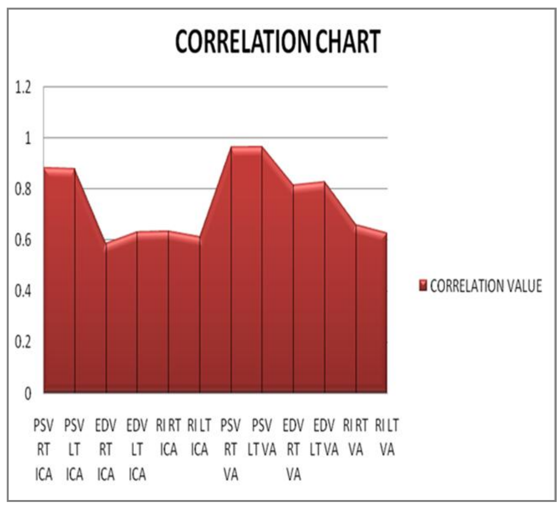


Fig. 5. Correlation chart

Table 5. Multivariate regression analysis for CBF volume with sex, BMI, age

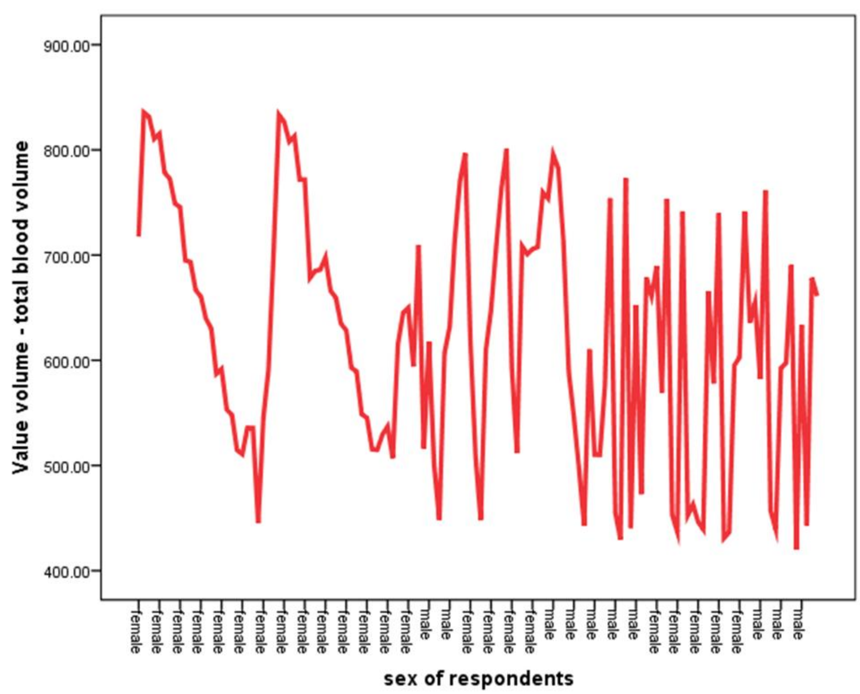
	Sample Size	CBF	F value	P value
Sex				
Male	66	625±16.97	0.0001	0.989
Female	66	624.75±115.63		
BMI				
Underweight	2	628.69±259.87		
Normal	124	622.94±116.59	0.370	0.691
Overweight	6	664.79±42.06		
Age group				
21-40	44	662.88±108.03		
41-60	44	626.82±109.66	5.308	0.006
61-80	44	584.99±118.69		

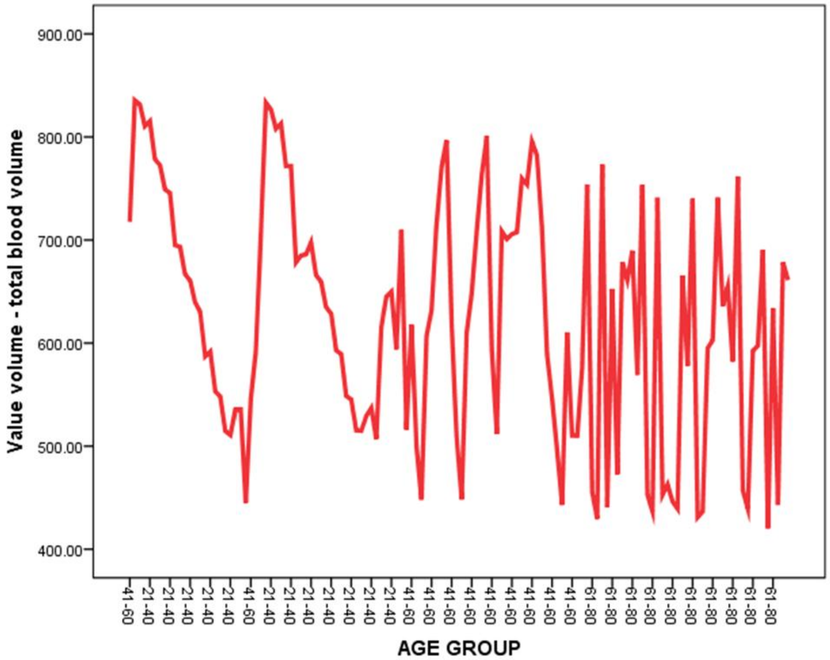
The total cerebral blood flow volume of 624.90±115.57 ml/min. that was obtained in this study was similar to results obtained from other previous studies [2,6,9,10]. The total cerebral blood flow volume was reported as 640±105 ml/min by Yazici et al. [9], 630±97 ml/min by Dorfler et al. [6], 701±104 ml/min by Schoning et al. [2] and 644±123 ml/min by Scheel et al. [10].

There is no consensus about age related changes in cerebral blood flow of healthy adults; it was observed by some authors [2,5,8] while others reported a constant volume throughout lifetime [11-13]. We however recorded a decline in cerebral blood flow volume with advancement in age. There was significant decrease in total cerebral blood flow volume, blood flow velocities and the flow volume in the internal carotid and vertebral arteries relative to increased age. Several studies on cerebral blood flow on healthy individuals also reported similar age variation [2,9,10,14,15]. The decrease in the cerebral blood flow volume with aging was reportedly due to a decrease in the perfusion demand of the brain secondary to atrophy from progressive neuronal loss [10,14,15]. However this hypothesis would require more patho-anatomical data.

The right internal carotid artery (Rt. ICA) blood flow volume of 226.57±32.03 ml/min and the right vertebral artery (Rt. VA) blood flow volume of 85.59 ml/min agreed with the Edrisson L, et al. [16] that approximately one-quarter of the cerebral blood flow volume is transported through the vertebro- basilar system. The gender differences in total cerebral blood, internal carotid artery (ICA) and vertebral artery (VA) blood flow volumes recorded in this study were not statistically significant; also no statistically significant difference was seen between the right and left sides. These results were in concordance with previous reports [9,10,17,18] though few authors [6,10] recorded lesser carotid and vertebral arteries blood flow volumes in women compared with men.

Although no significant difference was found between the genders regarding the blood flow volume, it was discovered that the ICA's peak systolic velocity (PSV) and end diastolic velocity (EDV) in internal carotid arteries were higher in the females than in males but the luminal diameter is however larger in males than females. This is similar to what was obtained by Yazici et al. [9] this has been attributed to the volume which is equal to the vessel diameters multiplied by the blood flow velocity. Blood flow velocity should be higher when the vessel diameter is narrowed to keep the equilibrium of flow volume.





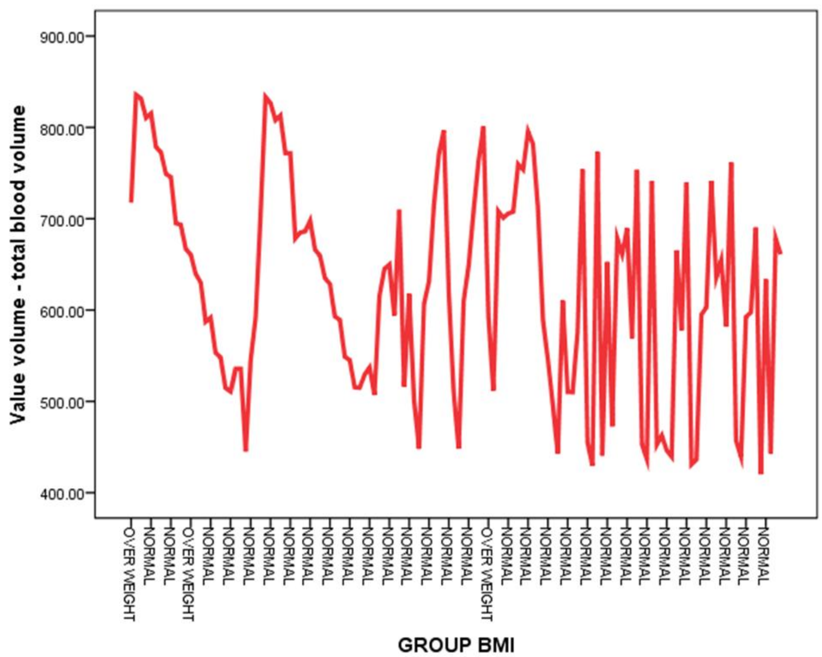


Fig. 6. A, B and C shows the flow chart of the study for sex, age group and BMI respectively

This may be responsible for the similar total cerebral blood flow in males and females despites the larger diameters in males. This study implies that vascular narrowing should be given more urgent attention in females compared to males.

The luminal diameter of the internal carotid arteries (ICA) is significantly increased in males than in females. The observed increase in vessel diameter associated with ageing in this study and other similar studies have been attributed to atherosclerotic change that causes a decrease in the vessel wall elasticity.

Conflicting results have been reported about vertebral artery diameters. Some authors including Agunloye A. M. et al. [19] suggested that the right vertebral artery (Rt. VA) or the Left vertebral artery (Lt. VA) has a narrow caliber, while others stated that no significant difference exists. In this study no significant difference in diameter was present between the right and the left vertebral arteries.

Measurement of flow volume may be helpful in defining vertebral hypoplasia. To date, this has been done by diameter {below 3 mm [6] or 2 mm [10]} or quantitatively as a thin string of color by use of maximum sensitivity in color – coded duplex sonography.

The age related vertebral blood flow decrease, noted in this study was previously reported [6,10]. A threshold of 200 ml/min had been proposed for net vertebral artery flow volume by the conventional duplex sonographic method; patients are said to exhibit symptoms of vertebrobasilar ischaemia below this threshold [6].

The average (normal) net vertebral flow in this study is less than 200 ml/min though more than 100 ml/min (average of 85.59±27.81 and 85.79±27.20 ml/ min, RVA and LVA respectively) and none of our subjects had symptoms of vertebrobasilar ischaemia. It is however worthy of note that some authors had also reported a normal net vertebral blood flow of 100 mls/min [18].

A lot of previous studies had measured cerebral blood flow to the brain using various imaging modalities [2,5,6,8,10,20] but ultrasound was found to be excellent [2,5,6,10,18]. It is cheap, readily available, non-invasive and does not possess any hazardous radiation effect. Hence this study was carried out with ultrasound which is an established technique for evaluation of extracranial portion of the carotid and vertebral arteries [2,5,6,10,18]. A study had shown that the number of arteriograms with normal findings decrease significantly (from 49% to 19%) when patients undergo effective non invasive sonographic screening for carotid disease [6].

Other imaging methods which may be used to measure cerebral blood flow volume include Magnetic Resonance Imaging [8,11], Computerized Tomography [20] and Positron Emission Tomography [15]. All of them have been proved to achieve reliable and accurate measurement of cerebral blood flow. However they are expensive and not readily available in most developing countries. Moreso, computerized tomography and positron emission tomography will subject the patients to ionizing radiation. Angiography also has been used in the study of blood flow to the brain, but subjecting healthy individuals to an invasive examination may not be ethical. The main disadvantage of ultrasound is that the accuracy of the method depends highly on the experience and the skill of the examiner [9,10].

5. CONCLUSION

Ultrasonographic measurement of the cerebral blood flow volume according to this study is a reliable and invaluable investigation in the work-up of the patients with cerebrovascular disorders. We have been able to provide age specific baseline for healthy adults and also revealed a decrease in cerebral blood flow volume with age.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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