

Assessment of Retinal Nerve Fiber Layer Thickness in Nigerian Adults Using Spectral-Domain Optical Coherence Tomography

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Abstract

Objective: To measure the circumpapillary retinal nerve fiber layer (RNFL) thickness in normal eyes of Nigerian adults using spectral-domain optical coherence tomography (SD-OCT). **Materials and methods:** This was a cross-sectional study of normal eyes of Nigerian adults between July and September 2016 at the eye clinic of a tertiary hospital in Nigeria. Sociodemographic data, clinical history, and examination findings were obtained. Dipstick urinalysis and blood pressure measurements were performed. Circumpapillary RNFL thickness was measured with the Topcon 3D OCT-1 Maestro version 8.30 (Topcon Medical Systems, Inc., Oakland, NJ, USA), using the 3D optic nerve head analysis. Data were analyzed using the International Business Machine (IBM) Statistical Package for the Social Sciences (SPSS) Statistics, version 25.0 (IBM Corp., Armonk, NY, USA) and the level of significance was set at $P \leq 0.05$. **Results:** The study included 120 participants (240 eyes) with an age range of 18 to 53 years and a mean age of 34.06 ± 7.64 years. There were 59 (49.17%) males and 61 (50.83%) females. The average RNFL thickness in the right and left eyes was 112.26 ± 9.6 and 110.53 ± 9.14 μm , respectively. The average RNFL thickness for the Igbo ethnic group was 117.5 ± 7.69 and 115.04 ± 7.18 μm in the right and left eyes, respectively. The mean RNFL thickness for the inferior, superior, nasal, and temporal quadrants was 148.92 ± 15.77 , 142.59 ± 16.48 , 85.3 ± 15.39 , and 71.89 ± 9.35 μm in the right eyes and 149.28 ± 16.03 , 141.69 ± 13.33 , 81.82 ± 13.59 , and 68.8 ± 10.17 μm in the left eyes, respectively. **Conclusion:** This study showed the normal circumpapillary RNFL thickness values in Nigerian adults using SD-OCT. There were variations based on ethnicity that suggest it may be important to use ethnic-specific benchmarks when interpreting OCT results for the management of glaucoma.

Keywords: African descent, ethnic group, glaucoma, nerve fiber, optical coherence tomography

INTRODUCTION

Glaucoma is the leading cause of irreversible blindness worldwide and has a more aggressive course in people of African descent.^[1] In Nigeria, glaucoma accounts for 16.7% of blindness in persons 40 years and above.^[2] As a cure for glaucoma is yet to be found, early detection through retinal nerve fiber layer (RNFL) evaluation is one of the keys to reducing the burden of this disease in high-risk populations.^[3]

The RNFL is a layer of the retina located between the inner limiting membrane and the ganglion cell layer.^[4] Its thickness varies significantly based on age, sex, race, eye laterality, and retinal quadrant.^[4-7] Optical coherence tomography (OCT) has been shown to allow for the objective and quantitative estimation of RNFL thickness.^[8] It is a noninvasive and

noncontact imaging system that uses low-coherence interferometry to produce high-resolution cross-sectional images of the retina, vitreous, and optic nerve head (papilla).^[9] There are studies that have reported normal RNFL values measured with the time-domain (TD) OCT technology among subjects from northern Nigeria.^[10,11]

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However, spectral-domain (SD) OCT is a newer technology that has shown an improved capability for the detection of early stage glaucoma compared to the older TD-OCT.^[12]

Appropriate reference values with the SD-OCT that captures the variations of the RNFL in Africans including Nigerians are required for the proper diagnosis and management of glaucoma in this high-risk population. In addition, RNFL measurements between TD- and SD-OCT machines or between different SD-OCT machines are not interchangeable.^[12,13]

This study aimed to measure the circumpapillary RNFL thickness in a sample of normal eyes of Nigerian adults with SD-OCT using the Topcon 3D OCT-1 Maestro version 8.30 (Topcon Medical Systems, Inc., Oakland, NJ, USA).

METHODS

This was a cross-sectional study involving 120 participants aged 18 years and above conducted at the eye clinic of a tertiary hospital in Nigeria. The study participants were drawn from patients booked for the outpatient eye clinic, their relatives, and those referred from the general outpatient department from the period of July to September 2016 at the National Hospital, Abuja.

Participants who met the inclusion criteria were recruited into the study using a systematic random sampling technique. A sample size of 120 was calculated using the standard formula for estimation of mean values in studies.^[14] Ethical approval for the study was obtained from the National Hospital Abuja Health Research Ethics Committee. Written informed consent was obtained from each participant prior to examination and recruitment into the study. The study adhered to the tenets of the Helsinki declaration.

Participants' age, sex, ethnicity, and medical histories were obtained. Detailed ophthalmic examinations including Snellen visual acuity assessment, refraction, slit-lamp biomicroscopy, posterior segment ophthalmoscopy, and Goldmann applanation intraocular pressure measurements were carried out to identify participants with "normal" eyes. Dipstick urinalysis and blood pressure measurements were carried out to check for evidence of diabetes mellitus or systemic hypertension. This was followed by SD-OCT circumpapillary RNFL thickness measurements. Participants underwent all procedures between 8 am and 12 pm on the same day.

An eye was said to be "normal" if a detailed ophthalmic examination found a pink optic nerve head with the absence of atrophy or a tilted disc, a normal retina, a refractive status of ≤ 1 diopter sphere (DS) or cylinder, and intraocular pressures between 10 and 21 mmHg. Participants were eligible if they were Nigerian, aged 18 years or older, had a best-corrected visual acuity of at least 6/6, satisfied the definition of "normal" eyes as stated above, and had an OCT scan image quality score between 50 and 160. Subjective

refraction results were used to calculate the spherical equivalent defined as the sphere plus half of the cylinder.^[15]

Exclusion criteria included a family history of glaucoma; a history of ocular trauma, intraocular surgery or laser treatment; a history or evidence of diabetes mellitus, systemic hypertension, any other significant health problem, or chronic drug use within the last six months; and the presence of a cup-to-disc ratio >0.6 , cup-to-disc ratio asymmetry >0.2 , notching of the optic disc, or disc hemorrhages.

RNFL thickness measurements

This study was conducted using the Topcon 3D OCT-1 Maestro, version 8.30 (Topcon Medical Systems, Inc., Oakland, NJ, USA). The scans were obtained using the 3D optic nerve head analysis of the glaucoma protocol with a scanning diameter (circumpapillary) circle of 3.4 mm from the center of the optic nerve head. Scans were performed on both eyes using standard techniques. Outcome measures obtained from the OCT scans included the average RNFL thickness and mean RNFL thickness of the inferior, superior, nasal, and temporal quadrants. The average RNFL thickness was defined as the calculated mean of the four quadrant RNFL thickness measurements in either eye. A single operator performed all the OCT scans.

Data from both eyes were analyzed using the International Business Machines (IBM) Statistical Package for the Social Sciences (SPSS) Statistics, version 25.0 (IBM Corp., Armonk, NY, USA). Analysis was carried out using descriptive statistics to calculate variable frequencies, percentages, ranges, means, standard deviations, and 95% confidence intervals. The Kolmogorov–Smirnov test was used to assess the normality of distribution of the data. Student *t* test was utilized to compare the average RNFL thickness based on sex. One-way analysis of variance with posthoc test was used to compare average RNFL thickness between ethnic groups. Pearson and Spearman correlation tests were carried out where appropriate to examine the direction and magnitude of the correlation between age, average RNFL thickness, and refractive spherical equivalent. The level of significance was set at $P \leq 0.05$.

RESULTS

Data from 240 eyes of 120 participants were analyzed. Their ages ranged between 18 and 53 years with a mean age of 34.06 ± 7.64 years. There were 59 (49.17%) males and 61 (50.83%) females. The refractive spherical equivalent in the right and left eyes ranged from $-1.375DS$ to $+1.00DS$ and $-1.125DS$ to $+1.00DS$, respectively. The Kolmogorov–Smirnov test indicated that values for age [$D(120) = 0.068, P = 0.2$], right eye average RNFL thickness [$D(120) = 0.048, P = 0.2$], and left eye average RNFL thickness [$D(120) = 0.063, P = 0.2$], followed a normal distribution. The right eye [$D(120) = 0.198, P < 0.001$] and left eye [$D(120) = 0.174, P < 0.001$] refractive spherical equivalent

values did not follow a normal distribution. There was no statistically significant difference in sex between the average RNFL thickness in the right eyes [$t(120) = -0.994, P = 0.322$] [Table 1] or the left eyes [$t(120) = -1.029, P = 0.306$], respectively [Table 2].

The average RNFL was thickest among the Igbo ethnic group compared to the other ethnic groups in this study for both the

right eyes [Figure 1] and the left eyes [Figure 2]. However, in the right eyes of study participants, there was a statistically significant nonlinear relationship among the different ethnic groups [$F(120) = 4.022, P = 0.009, \text{Eta} = 0.316, \text{Eta}^2 = 0.1$]. In addition, one-way analysis of variance and posthoc analysis using the Tamhane T_2 test showed that the heterogeneity in the average RNFL values was between the Igbo and Hausa ethnic groups [$F(120) = 3.196,$

Table 1: Demographic and clinical distribution of average RNFL thickness in right eyes of 120 study participants

Characteristics	n (%) n = 120	Average RNFL thickness	
		Mean ± SD (μm)	95% CI (μm)
<i>Sex</i>			
Male	59 (49.2)	111.37 ± 9.31	108.95–113.80
Female	61 (50.8)	113.11 ± 9.86	110.59–115.64
<i>Age (years)</i>			
≤29	30 (25.0)	113.10 ± 9.04	109.73–116.47
30–39	62 (51.7)	112.02 ± 9.11	109.70–114.33
≥40	28 (23.3)	111.89 ± 11.39	107.48–116.31
<i>Ethnic group</i>			
Idoma	14 (11.7)	112.29 ± 15.05	103.60–120.98
Hausa	17 (14.2)	108.24 ± 9.63	103.29–113.19
Igbo	26 (21.7)	117.50 ± 7.69	114.40–120.60
Yoruba	26 (21.7)	112.04 ± 6.38	109.46–114.61
Others	37 (30.8)	110.57 ± 9.04	107.55–113.58
<i>Refractive SE (D)</i>			
–0.125 to –1.375	39 (32.5)	111.26 ± 8.39	108.54–113.98
Plano	32 (26.7)	112.66 ± 10.16	108.99–116.32
+0.125 to +1.00	49 (40.8)	112.80 ± 10.24	109.86–115.74

Others: Igala, Ebira, Etsako, Ogoja, Urhobo, Nupe, Gbagyi, Tiv, Ishan, Fulani, and Jaba ethnic groups. RNFL, retinal nerve fiber layer; SD, standard deviation; CI, confidence interval; SE, spherical equivalent; D, diopters.

Table 2: Demographic and clinical distribution of average RNFL thickness in the left eyes of 120 study participants

Characteristics	n (%) n = 120	Average RNFL thickness	
		Mean ± SD (μm)	95% CI (μm)
<i>Sex</i>			
Male	59 (49.2)	109.66 ± 9.11	107.29–112.04
Female	61 (50.8)	111.38 ± 9.16	109.03–113.72
<i>Age (years)</i>			
≤29	30 (25.0)	112.83 ± 9.55	109.27–116.4
30–39	62 (51.7)	110.44 ± 8.84	108.19–112.68
≥40	28 (23.3)	109.04 ± 9.8	105.23–112.84
<i>Ethnic group</i>			
Idoma	14 (11.7)	108.29 ± 12.6	101.01–115.56
Hausa	17 (14.2)	108.35 ± 8.95	103.75–112.96
Igbo	26 (21.7)	115.04 ± 7.18	112.14–117.94
Yoruba	26 (21.7)	110.54 ± 6.01	108.11–112.97
Others	37 (30.8)	109.22 ± 10.08	105.86–112.58
<i>Refractive SE (D)</i>			
–0.125 to –1.375	40 (33.3)	110.3 ± 8.36	107.63–112.97
Plano	38 (31.7)	110.68 ± 9.91	107.43–113.94
+0.125 to +1.00	42 (35.0)	110.62 ± 9.34	107.71–113.53

Others: Igala, Ebira, Etsako, Ogoja, Urhobo, Nupe, Gbagyi, Tiv, Ishan, Fulani, and Jaba ethnic groups. RNFL, retinal nerve fiber layer; SD, standard deviation; CI, confidence interval; SE, spherical equivalent; D, diopters.

$P=0.023$]. In contrast, there was no statistically significant heterogeneity in RNFL values based on ethnicity in the left eyes of participants [$F(120) = 2.325, P = 0.061$].

The quadrant RNFL thickness in 130 (54.17%) eyes obeyed the ISNT rule, which states that in normal eyes, the quadrant RNFL thickness decreases in the order of inferior (I), superior (S), nasal (N), and temporal (T). Similarly, the mean RNFL thickness in each of the quadrants obeyed the ISNT rule for both the right and left eyes [Table 3]. There was no significant correlation between age, average RNFL thickness, and refractive spherical equivalent in either the right or left eyes [Table 4].

DISCUSSION

The average RNFL thickness values in this study were higher than those obtained from a previous study using the same type of OCT machine performed in the United States by Chaglasian *et al.*^[16] This finding may be because their measurements were carried out in a population that consisted majorly of Caucasians. The mean inferior RNFL and mean superior RNFL thickness values found in this study were higher than values reported from previous studies in people of African descent,^[17,18] Asians,^[19,20] Middle Easterners,^[7,21] Europeans,^[22] and South Americans.^[23]



Figure 1: A box and whisker chart showing the ethnic distribution of 95% confidence intervals for average retinal nerve fiber layer thickness in the right eyes of study participants.

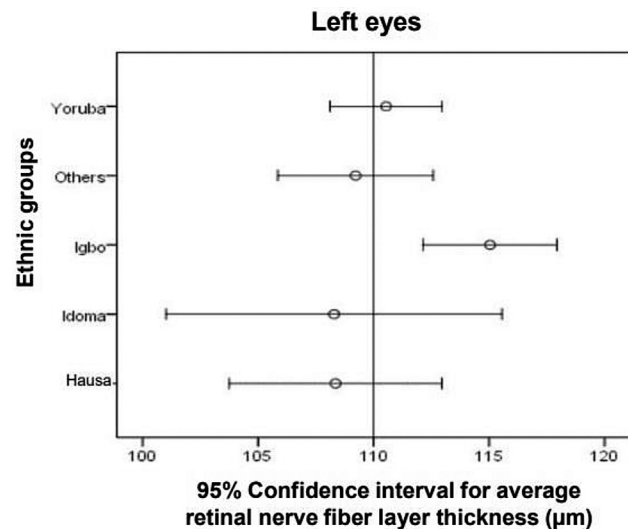


Figure 2: A box and whisker chart showing the ethnic distribution of 95% confidence intervals for average retinal nerve fiber layer thickness in the left eyes of study participants.

Table 3: Distribution of RNFL thickness by eye laterality

	RNFL thickness (μm)			
	Right eye ($n = 120$)		Left eye ($n = 120$)	
RNFL	Mean \pm SD (μm)	95% CI (μm)	Mean \pm SD (μm)	95% CI (μm)
Average	112.26 \pm 9.6	110.52–113.99	110.53 \pm 9.14	108.88–112.19
Inferior	148.92 \pm 15.77	146.07–151.77	149.28 \pm 16.03	146.38–152.17
Superior	142.59 \pm 16.48	139.61–145.57	141.69 \pm 13.33	139.28–144.1
Nasal	85.3 \pm 15.39	82.52–88.08	81.82 \pm 13.59	79.36–84.27
Temporal	71.89 \pm 9.35	70.2–73.58	68.8 \pm 10.17	66.96–70.64

RNFL, retinal nerve fiber layer; SD, standard deviation; CI, confidence interval.

Table 4: Bivariate correlation coefficients between age, average RNFL thickness, and refractive SE

Eye laterality	Age vs. average RNFL		Age vs. refractive SE		Refractive SE vs. average RNFL	
	r^*	P -value	r^\dagger	P -value	r^\dagger	P -value
Right	-0.123	0.184	0.015	0.869	0.071	0.448
Left	-0.11	0.237	-0.001	0.995	0.011	0.909

RNFL, retinal nerve fiber layer; SE, spherical equivalent; vs., versus; r , correlation coefficient. *Pearson correlation coefficient. \dagger Spearman correlation coefficient.

However, this was not the case for the nasal and temporal quadrants. This finding may be due to morphologic differences in the quadrant RNFL among different populations. Although these values were measured using different SD-OCT machines and are not interchangeable, it is important to note that comparing subjects with a normally thick RNFL against a nonrepresentative normative database derived from subjects with a naturally thin RNFL could lead to diagnostic inaccuracies of RNFL thinning in patients with glaucoma.

The RNFL thickness measurements have been documented to vary among different racial or ethnic populations.^[5,6,24,25] Ismail *et al.*^[26] reported that the RNFL of normal Black South Africans was significantly thicker (except in the temporal sector) when compared with an age- and sex-matched normative European database on the Spectralis SD-OCT. A comparative study by Girkin *et al.*^[27] reported that RNFL thickness was higher in subjects of African descent than those of European descent. Furthermore, Murugan *et al.*^[28] found average RNFL thickness was slightly greater among Black South Africans than Indian participants. Sinai,^[25] on the other hand, found that mean RNFL values in Chinese and Hispanic groups were higher than values in participants of African descent. These studies indicate that variations in RNFL thickness could also be due to racial or ethnic differences.

The pattern of average RNFL thickness between the different age groups in this study was in keeping with the well-known decrease in RNFL thickness observed with increasing age.^[7,24,29] There was no sex difference in average RNFL thickness in this study. This could be because the biometric differences due to sex in this study population were not sufficient enough to affect their average RNFL thickness values. This was in contrast to findings conducted among other populations.^[29,30] Similarly, one study found that a thicker RNFL in females was no longer the case after correcting for axial length.^[30]

The right eye average RNFL was found to be thickest among participants in the Igbo ethnic group and thinnest among the Hausa ethnic group participants in this study. The reason for this finding is unclear, but it suggests that there may be ethnic variations in RNFL thickness in this study population. A study with a larger representation of the different ethnic groups in Nigeria may be required to investigate this finding further. Although there is no appropriate RNFL data using SD-OCT from Nigeria with which to make comparisons, there are two studies that reported TD-OCT average RNFL thickness values of $104.17 \pm 10.71 \mu\text{m}$ ^[10] and $107.055 \pm 9.219 \mu\text{m}$ ^[11] from northern Nigeria, an area that is predominantly populated by people of the Hausa ethnic group.

Similarly, Ho *et al.*^[6] reported ethnic differences in RNFL thickness in Singapore. They found that RNFL thickness among Singaporeans was consistently thinner in Indians compared to Chinese and Malay eyes; however, these

ethnic differences were not related to systemic or ocular parameters. These findings further emphasize that normative data from different ethnic groups are required for an accurate interpretation of RNFL thickness measured with SD-OCT.

The quadrant RNFLs in this study were thickest in the inferior quadrant followed by the superior, nasal and temporal quadrants in more than half of the eyes studied; thus, obeying the RNFL ISNT rule, which is the characteristic configuration of a normal healthy RNFL. This proportion was higher than 42% reported by Alasil *et al.*^[24] and 23% reported by Al-Sa'ad *et al.*^[21] This suggests that about half of normal eyes in this study population may have variations in the morphology of the RNFL that do not obey the RNFL ISNT rule. Similarly, the mean RNFL thickness values for all the quadrants obeyed the RNFL ISNT rule. This finding was similar to previous reports in other populations.^[18,20,24] Conversely, Sani *et al.*^[10] and Mahmud-Ajeigbe *et al.*^[11] reported that the mean quadrant RNFL in their study was thickest in the superior quadrant followed by the inferior, nasal and temporal quadrants. Although this pattern is different from what was obtained in this current study, it still conforms to the characteristic double hump configuration in normal eyes where RNFL is thickest vertically, in the superior and inferior quadrants.

There was no significant correlation between age and average RNFL thickness in this study. This was not in keeping with the well-known decrease in RNFL thickness observed with increasing age.^[7,24,29] This may be because of the younger population studied. This finding was similar to the reports by Cubuk *et al.*,^[31] who had a similar age range to that of this study. Similarly, there was no significant correlation between average RNFL thickness and refractive spherical equivalent in this study. This suggests that lower refractive spherical equivalents of $\pm 1.00\text{DS}$ may not affect RNFL thickness to a degree that would require an adjustment of RNFL thickness values unlike the positive correlation that has been reported among patients with higher refractive errors.^[28,30]

The findings from this study suggest that there may be an ethnic variation in RNFL thickness values in Nigerian adults. However, this was an incidental finding, as our sample size was not powered to detect it. A larger study incorporating an equitable number of the different ethnic groups in Nigeria will help to confirm this finding. In addition, a wider age range than what was obtained in this study may have shown a significant correlation between average RNFL thickness and age. Notwithstanding these limitations, the authors believe that this study has provided reference values for RNFL thickness measured with SD-OCT that would buttress the data from previous studies carried out in Nigerian adults.

CONCLUSION

This study describes the circumpapillary RNFL thickness values measured with SD-OCT stratified by age, sex, ethnicity, refractive spherical equivalent, and eye laterality

in normal eyes of Nigerian adults. The mean inferior and superior quadrant RNFL values found in this study were higher than values reported in previous studies. The right eye average RNFL was thickest in the Igbo ethnic group compared to other ethnic groups in this study. Hence, it is important to consider the circumpapillary RNFL values for SD-OCT enumerated in this study when interpreting OCT results for the diagnosis and management of glaucoma.

Authors' contribution

All authors made substantial contributions to the study conception and design. Material preparation and data collection were performed by Habibat Yetunde Daromосу. Data analysis was performed by Bolajoko Abidemi Adewara. The first draft of the manuscript was written by Habibat Yetunde Daromосу. All authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Conflicts of interest

There are no conflicts of interest.

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