

Retinal Nerve Fiber Layer Thickness and Optic Disc Parameters measured by Cirrus HD OCT among adults attending St. Paul's Hospital Medical College

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Abstract

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Background: Optic nerve structures and Retinal nerve fiber layer thicknesses variations have been suggested as an essential factor for the glaucoma occurrence and progression in different types of population.

Objectives: This study aimed to determine the normative value for Retinal nerve fiber layer (RNFL) thickness and optic disc 30 parameters and their corresponding correlation with each other and socio-demography.

Materials and Methods: Cross-sectional design study was conducted between September 2019 and January 2020 on 330 eyes of 165 patients among conveniently available subjects. Data were analyzed by SPSS version 20 using simple and multivariable linear regression. The statistical significance was considered at p -value < 0.05 .

Results: The mean of age was 40.79 (± 11.0) years and ranged from 18 to 69 years. The mean vertical disc diameter was 1.50mm, and the average cup disc ratio was 0.48. Mean Disc area and neuroretinal rim area were 2.01mm² and 1.45mm² respectively. The inferior nerve fiber layer was thickest (131.19 μ m), followed by superior (122.14 μ m), nasal (76.51 μ m) and temporal quadrants (65.42 μ m). The mean of the average nerve fiber layer was 98.54 μ m. Age ($p=0.002$), axial length ($p=0.01$) and horizontal disc diameter ($p<0.001$) were negatively associated with average nerve fiber layer thickness. Vertical disc diameter ($p<0.001$) and rim area ($p=0.025$) were positively associated with average nerve fiber layer thickness.

Conclusion: The mean average RNFL thickness was 131.19 μ m. It is inversely correlated with age increment and elongation of axial length of the eye. The RNFL was thickest inferiorly, followed by superior, nasal, and temporal quadrants.

Key words: Glaucoma, Optic disc parameter, Retinal nerve fiber layer

Background

Glaucoma is one of the leading causes of irreversible blindness globally. People of African descent have been found to be more susceptible to, and have a higher rate of blindness from, primary open-angle glaucoma (POAG) (1, 2). POAG is associated with characteristic optic nerve changes. In order to diagnose it, one must first be able to recognize the normal nerve appearance. . People of African race have been shown to have a greater susceptibility and also higher rates of blindness due to primary open-angle glaucoma (POAG) (1, 2). POAG is associated with characteristic optic nerve changes. For early detection and management of glaucoma utilizing optic nerve appearance and other factors are essential to avoid preventable blindness in preventing needless blindness due to the disease. However, these parameters can vary with age, sex, race, axial length and optic disc dimensions (3).

Quantitative in vivo topographic measurements of optic disc structure and retinal nerve fiber layer (RNFL) thickness using various imaging techniques plays an vital role in order to improving the ability to detect glaucoma and progressive glaucomatous damage. Optical coherence Tomography (OCT) was first introduced in 1991 and designed with an age-matched normative database used to interpret RNFL thickness for each individual of a certain age (4). The measurements and interpretation of the data is done by comparing each one individual parameter with other normative values which stored on the instrument soft wares from different ethnicity and age.

Majority of subjects in the normative database were selected from European descent. However, adequate numbers of black subjects have not been represented in most studies using these instruments to evaluate the role of quantitative optic disc analysis and the RNFL. Thus further normative data is required to use as the standard for other ethnic backgrounds, specifically, Ethiopian people or black Africans. By doing so, physicians will be able to better differentiate normal values from pathology based on updated and contextually relevant information.

Unique differential features among racial groups in the ON head characteristics were found in various studies. These have led to theories regarding vulnerability to glaucoma. It has been particularly suggested that people of African ancestry tend to have large nerves and cup to

disc ratios (CDR) (4)and they may be at higher risk of developing glaucoma due to this large CDR (5,6) Variations in the structure of the optic nerve (ON) have been suggested an important factor in the more aggressive disease seen in at-risk and underserved population (7).

African race is diverse and studies in different areas of the African continent are paramount to providing more objective evidence related to this issue. There is no sufficient information about normative data of the ocular parameters, particularly the nerve head (ONH) structure and RNFL thickness for the population of Ethiopia. Therefore, this research was conducted with the purpose of determine normative value for RNFL thickness and optic disc parameters measured by cirrus HD OCT and their corresponding correlation with each other as well as with age, gender and axial length.

Subjects and Methods

Study subjects and setting

A hospital based cross sectional design study was conducted between September 2019 and January 2020 among adult population attending the eye department, St. Paul's Hospital Millennium Medical College (SPHMMC), Addis Ababa, Ethiopia. The eye center is giving clinical and academic services and almost all the population attending is black in ethnicity. Current study was focused on those populations who came to the eye center either for eye examination or as an attendant for their family or colleagues. Study subjects were recruited by simple random sampling based on their willingness to participate and hence, a total of 330 eyes of 165 subjects were included in the study. Inclusion criteria includes age 18 years or older, best corrected visual acuity of better than 20/40, refractive error less than 5 Diopter sphere and less than 3D cylinder, IOP <22 mmHg. We excluded all subjects with optic neuropathy, a history of intraocular surgery, media opacities obscuring the view of the optic disc (including cornea or vitreous opacity and cataract), pseudophakia or aphakia, the presence or known history of retinal pathology (artery or retinal vein occlusion, diabetic retinopathy etc) using full eye examination by slit lamp biomicrosoppe and dilated fundus examination.

Procedures

All study subjects underwent complete eye examinations for both eyes including dry refraction, slit lamp bio microscopy, and dilated fundus examination by 90D Volk lens stereoscopically to determine eligibility for the study. For those who fit inclusion criteria, optic disc and RNFL thickness were measured by Cirrus HD- OCT and axial length was determined by contact A scan biometer (Quantel medical, Couron, d'Auvergne, France). All participants were asked their age and gender and data was recorded on data extraction format by trained optometrists. Study subjects were selected by measuring visual acuity, intra ocular pressure and refraction by optometrists and slit lamp bio microscopy and dilated fundus examinations by ophthalmologists for all of them.

The ONH parameters were automatically generated by a Carl Zeiss Meditec analysis algorithm developed for Cirrus HD-OCT 5000, which does not involve user interactions. The HD-OCT scans were included if the signal strength was greater than 6 and there were no saccades in the enface image. Scans in which the line-scanning laser ophthalmoscope image did not have sharp uniform focus or had poor centration, non-uniform illumination, or vitreous or media artifacts were also excluded. Optometrist did ONH parameters measurements and A scan biometer, height and weight measurement.

Statistical analysis

Data was entered using Epi data version 3.1 and analysis was done using SPSS version 20. Age and sex of participants were summarized by frequency. Simple linear regression analysis was used to examine the relationship between age and average RNFL and between axial length and Average RNFL thickness. First, the model fitness for linear regression was checked by linear relationship by scatter between dependent and independent variables. Secondly, multivariable normality was checked with Q-Q plots and thirdly by one sample Kolmogorov-Smirnov tests for approximate normal distributions of variables. Multivariable adjusted linear regression analysis was done to determine the association of Average RNFL thickness and age, sex, axial length and optic disc parameters. The statistical significance was considered at 95% CI and p-value less than 0.05.

Results

A total of 330 eyes of 165 patients were included. The mean (SD) age

of the study subjects was 40.79 (± 11.0) years and ranged from 18 years to 69 years. More than one third of participants were between 41 and 50 years and female proportion was slightly above half of the total subjects 178 (53.9%) (Table 1).

Table 1: Demographic distribution of study participants among adults at St. Paul's 373 Hospital Millennium College eye departments, 2020

Variables	Frequency	Percentage
Age		
18-30	66	20.0
31-40	84	25.5
41-50	118	35.8
51-60	52	15.8
61-70	10	3.0
Sex		
Male	152	46.1
Female	178	53.9
Height(meters)		
Up to 1.60	88	26.7
1.61-1.65	72	21.8
1.66-1.72	96	29.1
1.73 and above	74	22.4

The mean of vertical disc diameter was 1.50mm and average CDR 0.48. Mean Disc area (DA) and neuro-retinal rim area (RA) measurements were 2.009mm² and 1.451mm² respectively (Table 2).

Table 2: Optic disc parameters measurements of study subjects among adults at St. Paul's Hospital Millennium College eye department, 2020

Optic disc parameters	Mean	Standard deviation	95%CI
Vertical Disc Diameter	1.50	0.15	(1.48, 1.52)
Average Cup disc ratio	0.48	0.15	(0.47, 0.50)
Vertical Cup disc ratio	0.46	0.19	(0.44, 0.47)
Disc Area	2.01	0.36	(1.97, 2.05)
Cup Volume	0.14	0.14	(0.13, 0.16)
Neuroretinal Rim Area	1.45	0.26	(1.43, 1.48)

The inferior RNFL was thickest (131.19 μ m), followed by superior (122.14 μ m), nasal (76.51 μ m) and temporal quadrants (65.42 μ m). The mean of the average RNFL was 98.54 μ m with SD of 11.933 (Table 3).

Table 3: Retinal nerve fiber layer thickness at different quadrant of study subjects among adults at St. Paul's Hospital Millennium College eye department, 2020

Retinal nerve fiber layer thickness	Mean	Standard deviation	95%CI
Average	98.54	11.933	(97.23, 99.77)
Superior	122.14	18.228	(120.03, 124.02)
Inferior	131.19	20.494	(129.16, 133.42)
Nasal	76.51	13.630	(75.06, 78.01)
Temporal	65.42	12.224	(64.15, 66.79)

The average RNFL thickness was inversely correlated with age for every 170 one decade, the increment of age decreased by 0.201 μ m (Figure 1).

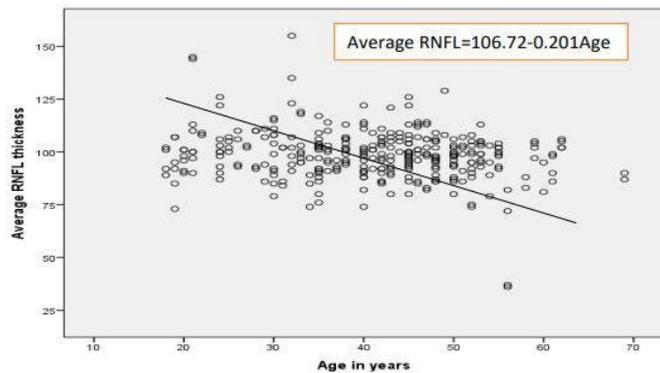


Figure 1: Relationship of average retinal nerve fiber layer thickness and age of study subjects among adults at St. Paul's Hospital Millennium College eye department, 2020

Average RNFL was also negatively correlated with axial length and for every one millimeter increment of axial length, RNFL thickness decreased by 2.17µm (Figure 2).

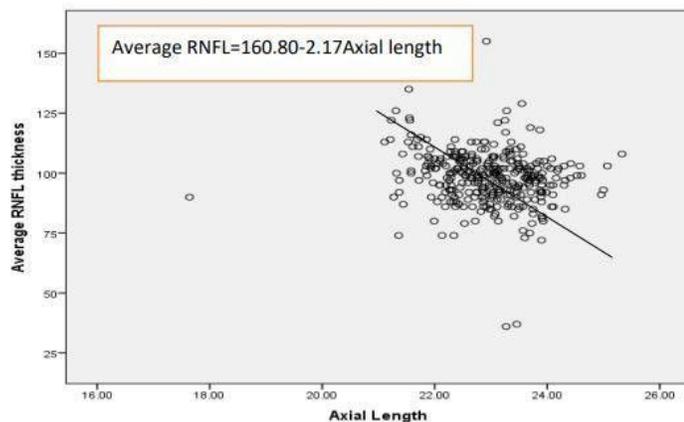


Figure 2: Relationship of average retinal nerve fiber layer thickness and axial length of study subjects among adults at St. Paul's Hospital Millennium Medical Tertiary Eye Center, 2020.

Average RNFL became thinner as age increased ($p=0.009$). The RNFL 175 thickness of all quadrants (superior, inferior, nasal and temporal) also 176 decreased as age increased. In terms of gender, the value of average RNFL 177 and all four quadrants were similar between males and females. The mean of 178 Average RNFL in males was 98.19µm and in females was 98.84µm. This was 179 not statistically different (Table 4).

Multivariate adjusted linear regression analysis revealed that age ($p=0.002$), axial length ($p=0.01$) and horizontal DD ($p<0.001$) were negatively associated with average RNFL thickness. Vertical DD ($p<0.001$) and RA ($p=0.025$) were positively associated with average RNFL thickness measured in µm, but disc area was not associated (Table 5).

Table 4: Variations of RNFL thickness in age groups and gender category of study subjects among adults at St. Paul's Hospital Millennium College eye department, 2020.

Variables	Measurement	Retinal nerve fiber layer thickness				
		Average	superior	Inferior	Nasal	Temporal
Age						
18-30	Mean	101.26	126.53	135.58	77.00	65.58
	SD	12.49	20.84	21.38	15.62	11.13
31-40	Mean	99.38	120.24	132.17	77.01	67.92
	SD	12.45	17.64	22.08	13.33	15.95
41-50	Mean	98.81	122.61	131.85	77.37	65.24
	SD	9.42	14.99	16.32	13.21	0.36
51-60	Mean	93.50	117.81	124.56	74.00	61.25
	SD	14.70	22.30	24.69	12.99	10.05
61-70	Mean	96.50	126.10	120.80	71.80	67.40
	SD	11.93	9.75	10.41	10.95	9.50
Sex						
Male	Mean	98.19	122.47	130.57	75.48	64.86
	SD	9.92	15.42	18.52	12.29	10.76
Female	Mean	98.84	121.86	131.72	77.38	65.91
	SD	11.93	18.23	20.49	13.63	12.22

Table 5: Multivariate adjusted linear regression result of Average RNFL thickness with demographic and optic disc parameters of study subjects among adults at St. Paul's Hospital Millennium College eye department, 2020

Variable	Regression coefficient	Standard error	P-value	95%CI
Age per decade	-0.182	0.058	0.002	(-0.311, -0.084)
Sex	-0.052	1.365	0.191	(-3.935, 1.436)
Axial length	-0.159	0.839	0.010	(-3.941, -0.639)
Vertical DD	0.142	1.621	<0.001	(0.371, 6.752)
Horizontal DD	-0.017	1.973	<0.001	(-0.882, -0.002)
Average CDR	-0.026	1.912	0.710	(-4.381, 3.142)
Vertical CDR	-0.109	1.783	0.096	(-6.128, 0.886)
Disc area	0.046	3.445	0.963	(-3.968, 9.587)
Cup volume	-0.036	1.860	0.090	(-4.538, 2.780)
RA	0.103	1.553	0.025	(0.0954, 1.529)

Discussion

Knowledge of ONH and RNFL measurements of a particular population is essential to compare pathologic conditions with normative values installed in most OCT machines. To the best of our knowledge, this is the first study to assess these variables from Ethiopia. The mean global RNFL of our participants was $98.54 \pm 11.93 \mu\text{m}$. This is slightly thinner than finding from studies done in African populations in Ghana (9) and Nigeria (10) that reported averages of RNFL 102.37 ± 7.45 and $104.2 \pm 10.7 \mu\text{m}$, respectively using Cirrus HD OCT. Similar measurement among African Americans RNFL values ($99.2 \pm 10.2 \mu\text{m}$) has been

reported using Spectral OCT (11). An average RNFL of $110 \pm 7.4 \mu\text{m}$ has been reported from a study among black population in South Africa using iVue100SD-OCT (Optovue Inc. Fremont, CA, USA) (12).

However, our RNFL finding is thicker than the normative database in the Cirrus HD- OCT measured among both the African descent samples ($93.9 \pm 1.2 \mu\text{m}$) and the total average for all races ($94.0 \pm 0.6 \mu\text{m}$) (12). These show that interpretation of abnormal RNFL measurements should be made with caution and that there might be wide variations of normal RNFL measurements among the black populations. We found no significant difference between males ($98.19\mu\text{m}$) and female ($98.84\mu\text{m}$) on the mean RNFL thickness. This is similar to other studies (9,11,14,15). Average RNFL thickness was inversely correlated with age, and for every decade of higher age, RNFL was thinner by $2.01\mu\text{m}$. We also found that this decline with age is observed in all quadrants.

The age related decline in RNFL thickness is well described in the literature. A similar amount of RNFL thickness declined by $0.19 \mu\text{m}/\text{year}$ (13). and $2.0 \mu\text{m}$ decline in RNFL thickness per a decade of age has been reported using stratus OCT (16). A $0.25 \mu\text{m}$ decreases in RNFL thickness per yearly increase in age was reported from the study in Ghana (9). The current study also showed that as AL the mean RNFL decreases; for every one millimeter increment of axial length RNFL thickness decreases by $2.17\mu\text{m}$. This is similar to what has been reported in other studies (12,13,17). Inferior RNFL thickness was the greatest ($131.19\mu\text{m}$), followed by superior ($122.14\mu\text{m}$), nasal ($76.51\mu\text{m}$) and then the temporal quadrant ($65.42\mu\text{m}$). This pattern of RNFL reduction from Inferior to temporal quadrant is well described the literature as well and sometimes referred to as the ISNT rule.

Regarding the ONH parameters, the current study found mean disc area of 2.009mm^2 , rim area 1.451mm^2 , average CDR of 0.482 , vertical CDR of 0.456 and 222 cup volume of 0.139mm^2 . There is a great degree of variation due to race in disc area amongst imaging modalities in normal subjects, while RA is generally not as dependent on race in OCT or HRT technologies (13).¹The Ghanaian study using Cirrus OCT (8) found the DA to be similar (2.0mm^2) with that of ours while Tariq et al reported $1.98 \pm 0.38\text{mm}^2$ (18). In the Cirrus OCT Normative Database Study Group, the average DA was 1.81mm^2 while those of the African descent had 1.93mm^2 as compared with European descent (1.68mm^2) and Hispanics (1.86mm^2) (13). Other studies have shown that DA was significantly smaller in individuals of European descent than in individuals of African descent and Hispanic (19). Our finding of

average disc area in Ethiopians demonstrates a much smaller disc area than that of the African Descent and Glaucoma Evaluation Study, in which DA was 2.47mm^2 among the African Descent.

Similarly, a larger DA (2.49mm^2) was reported among individuals of African descent as compared with those of European descent (2.17mm^2) and Hispanic individuals (2.33mm^2) (20). These findings suggest that the normative findings of Africans may not be similar to those of the African descent living in the west. The mean RA found in our study (1.45mm^2) is smaller than the reported value of 1.32mm^2 using the Cirrus OCT among the African Descent group (13), while it is similar to the value reported from Ghana (1.48mm^2) (9). The findings of average CDR (0.48mm) and vertical CDR (0.46mm) in our study are similar to those reported from Ghana (8) 0.50mm and 0.47mm respectively and those among Africans¹² 0.53mm and 0.51mm respectively. Though the current study was pioneering in Ethiopia, there were certain limitations. It was studied in hospital based and only considered adult population with age 18 and above years old. It couldn't also consider the ethnic variation for Ethiopian population rather it considered all people as black African.

Conclusion

This study reports the normative values for RNFL thickness and ONH parameters measured using Cirrus HD-OCT 5000 in healthy Ethiopian adults. The average RNFL thickness was $98.54 \pm 11.93 \mu\text{m}$. The RNFL was thickest inferiorly, followed by superior, nasal, and temporal quadrants. Age and axial length correlated strongly with the RNFL thickness. It will be good to conduct such study in the community with larger sample size which involves all age group of populations with different ethnic background.

Declarations

Ethical statement

This study was conducted according to Declaration of Helsinki and approved by ethical review board of SPHMMC. Written Informed consent was obtained from all study subjects after clearly explaining the procedures and purposes of the study. All subjects' data was handled anonymously without using personal identifiers.

Conflict of Interests

All authors assured that there is no any competing interest with regard to this study.

Author's Contributions

GW and AS contribution were study idea conceptualization, proposal writing and granting funding data collection, and reviewing report writing. DH contributions include data collection, data analysis and report write up and manuscript preparation. All authors reviewed final report and manuscript and approved it.

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Data availability

All information related this study is included in the manuscript and the main data is available and can be accessed up on request.

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