RESEARCH ARTICLE

Effect of refractive errors/axial length on peripapillary retinal nerve fibre layer thickness (RNFL) measured by Topcon SD-OCT

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Abstract

Objectives: To evaluate the effect of refractive error and axial length on peripapillary retinal nerve fibre layer thickness in myopic, hypermetropic and emmetropic eyes by Topcon spectral domain optical coherence tomography.

Methods: This cross-sectional study was conducted at the ophthalmology clinic of Shifa Foundation Falahee Clinic, Islamabad, Pakistan, from January to December 2016, and comprised eye patients including emmetropes, hypermetropes and myopes. All participants underwent detailed ophthalmic examination including axial lengths measurements, auto refraction andretinal nerve fibre layer thickness analysis. Retinal nerve fibre layer thickness was obtained from the peripapillary quadrants: temporal, superior, nasal and inferior and 12 sub-quadrants using Topcon spectral domain optical coherence tomography. Pearson correlation coefficients (r) were calculated to evaluate relationships between the retinal nerve fibre layer thickness and axial length before and after adjustment for ocular magnification by using Littmann's formula.

Results: Of the total 93 eyes of as many patients, 46(49.5%) were right eyes and 47(51.5%) left eyes. There were 35(37.6%) myopes, 29(31.2%) hypermetropes and 29(31.2%) emmetropes. Mean age was 30.45±7.86years. Mean axial length was 23.40±1.25mm.Mean retinal nerve fibre layer thickness after correction of magnification effect was 100.59±9.25 µm. Correlation analyses showed that the average retinal nerve fibre layer thickness and mean thickness of major superior and nasal quadrants and also in nasal, upper nasal, superonasal, inferior and inferonasal sub-quadrants had negative correlation with axial length. However, correction of the magnification effect by applying Littmann's formula eliminated the relationship between the two.

Conclusions: Retinal nerve fibre layer thickness measurements were found to vary with refractive status and axial length of the eye. Ocular magnification significantly affected the retinal nerve fibre layer thickness, and it should be considered in diagnosing glaucoma.

Keywords: Optical coherence tomography, Refractive errors, Axial length, Glaucoma, Retinal ganglion cells.
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Introduction

Glaucoma is the second leading cause of blindness in the world.[1] Glaucoma results in progressive damage to the retinal ganglion cells resulting in changes in the optic disc structure as well as thinning of the retinal nerve fibre layer (RNFL).[2] The changes in RNFL precede changes in visual field and the extent is proportional to severity of functional loss in the visual field.[3] Thus, RNFL assessment may be more valuable than optic disc assessment in these subjects.

Various methods are being used to assess and image the RNFL, including fundus photography, scanning laser polarimetry, Heidelberger retinal tomography(HRT) and optical coherence tomography (OCT).[4] The OCT is a modern non-invasive imaging device which measures the peripapillary RNFL thickness in all quadrants in non-contact manner.[5] The latest spectral domain optical coherence tomography (SD-OCT) provides high axial scanning resolution (<10µm) which makes RNFL measurements reliable and reproducible.

Age, gender, ethnicity, axial length, size of the optic disc and refractive status of the eye are different factors which have been reported to affect the RNFL thickness.[6]

The relationship of the RNFL thickness with axial length and refractive error has been extensively investigated in adults[7,8] and in children[9,10] in other countries. Different studies have shown racial differences in RNFL thickness.[6] Results of these studies cannot be applied to Pakistani population as no such study has been conducted here as yet. It is therefore important to investigate whether any correlation exists between RNFL measurements and the axial length/refractive error in our population. The current study was planned to determine the relationship between refractive error and axial length and the RNFL

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thickness measured by Topcon SD 1-maestro OCT in our clinical setting.

Material and Methods

Patients were recruited for this cross-sectional study from the eye clinic of Shifa Foundation Falahee Clinic, Islamabad, Pakistan, from January to December 2016, using convenience sampling technique. Approval for the study was given by the institutional review board and ethics committee. Eye patients, including emmetropes, hypermetropes and myopes, older than 18 years of age, both males and females and having best corrected vision 6/6 were included in the study. Those with astigmatism >2.00 dioptre, amblyopia, retinal and optic disc diseases, corneal disorders, strabismus, glaucoma, ocular hypertension and a previous history of ophthalmic surgery, both intraocular and refractive surgeries or ocular trauma were excluded. Verbal informed consent was taken from all the patients. Detailed history was taken and complete examination of both eyes, including visual acuity, auto refraction, applanation tonometry, slit lamp examination of anterior and posterior segment, was done.

Refractive errors were measured by spherical equivalent (SE) via auto refraction. Axial lengths were noted using a-scan (quantal medical axis-11). An average of 3 measurements were taken for both. All OCT examinations were performed by single examiner. RNFL thickness and various disc parameters (e.g. Cup-to-disc ratio etc.) were observed from OCT analysis report. RNFL thickness was obtained from all peripapillary sections: temporal, superior, nasal and inferior and also in 12 sub-quadrants i.e. temporal (T), upper temporal (UT), lower, temporal (LT), nasal (N), upper nasal (UN), lower nasal (LN), superior (S), superotemporal (ST), superonasal (SN), inferior (I), inferotemporal (IT), inferonasal (IN). We used Littmann's formula,[11,12] to correct the effect of ocular magnification induced by refractive error. All the data was entered in a predesigned proforma.

Statistical analysis was done using SPSS 20.0. Frequency and percentages were calculated for qualitative variables like gender and ethnicity, and were compared by chi square test. All variables were checked with the Kolmogorov-Smirnov test for normal distribution. Mean±SD was calculated for age, SE, axial length and RNFL thickness. Levene's test was used to assess the homogeneity of the variances. One-way analysis of variance (ANOVA) was used to compare the variables among the three groups. $P<0.05$ was taken as statistically significant. Pearson correlation coefficients (r) were calculated to evaluate relationships between the RNFL thickness and axial length.

Results

Of the total 93 eyes of as many patients, 46(49.5%) were right eyes and 47(51.5%) left eyes. There were 35(37.6%) myopes, 29(31.2%) hypermetropes and 29(31.2%) emmetropes. There were 48(51.6%) males and 45(48.4%) females. There were 8(8.6%) Baltis, 2(2.2%) Hindkus, 15(16.2%) Pathans and 68(73.1%) Punjabis (Table-1).

Mean age of the subjects was 30.45±7.86 years (range: 17-47years). Mean axial length was 23.40±1.25mm. Mean cup-to-disc ratio was 0.30±0.17. Mean intraocular pressure (IOP) was12.15±1.51mm of Hg. IOP in myopes was 12.40±1.44mm of Hg, in hypemetropes 11.93±1.73mm of Hg and in emmetropes 12.07±1.36mmHg. The difference in IOP between the groups was not statistically significant (p=0.443). Mean RNFL thickness of study population after correction of magnification effect was 100.59±9.25 µm. The mean age in the emmetropic group was significantly younger than the other 2 groups. There was no significant age difference between the myopic and hypermetropic group (p=0.716). SE and axial length were significantly different among the three groups (p=0.000 for both). The axial length was the longest in the myopic group (24.41±0.89), followed by the emmetropic (23.17±0.65) and hypermetropic groups (22.42±1.21).

There was no statistically significant difference in average RNFL thickness with age (p=0.770). There was also no statistically significant difference in average RNFL thickness with gender (p= 0.451).

The quadrantic assessment of RNFL thickness in the different groups followed Inferior >Superior >Nasal >Temporal (ISNT) rule with inferior quadrant being the thickest followed by the superior, nasal and temporal quadrants.

The mean average RNFL thickness and thickness values in 3 major quadrants were significantly different among the three groups except temporal quadrant (p<0.05). While comparing the sub-quadrants statistically significant

Table-1: Descriptive and clinical parameters of the groups (mean±SD).

Characteristic	Myopic eyes (n=35)	Hypermetropic eyes (n=29)	Emmetropic eyes (n=29)
Mean age (years)	31.54±6.73 (22-47)	32.31±10.0 (17-46)	27.28±5.7 (17-35)
Gender			
Male 48 (51.6%)	45.7%(n=16)	34.5%(n=10)	75.9%(n=22)
Female 45 (48.4%)	54.3%(n=19)	65.5%(n=19)	24.1%(n=07)
SE (dioptres)	-3.59±1.76	2.79±2.39	-0.17±0.23
Axial length (mm)	24.41±0.89	22.42±1.21	23.17±0.65

SE: Spherical equivalent.

Table-2: The mean values of the peripapillary retinal nerve fibre layer parameters of the groups (mean±SD) (microns) (before applying Littmann's formula).

Quadrant/ sub-quadrant	Myopia (n=35)	Hyperopia (n=29)	Emmetropia (n=29)	p-value
Average	94.54±8.50	104.79±7.6	103.69±7.87	0.000
Temporal quadrant	70.14±12.77	72.38±13.35	75.89±14.39	0.239
Superior quadrant	111.82±17.20	120.48±13.23	120.89±12.59	0.022
Nasal quadrant	78.42±17.67	92.65±14.24	87.69±13.69	0.001
Inferior quadrant	117.14±13.63	132.69±12.70	130.24±12.73	0.000
T	61.94±16.93	63.89±17.70	66.79±18.4	0.551
UT	76.25±16.20	81.20±15.69	83.82±14.98	0.149
LT	71.36±20.26	67.67±15.73	67.72±16.28	0.803
N	70.02±23.29	81.62±19.6	77.41±16.19	0.070
UN	90.85±16.71	108.55±20.21	109.65±15.61	0.000
LN	78.30±18.92	82.66±21.02	81.79±16.54	0.045
S	115.48±19.94	121.44±20.40	123.07±12.69	0.213
ST	116.71±17.77	121.79±21.44	122.65±20.47	0.428
SN	107.94±18.34	118.51±19.73	117.17±19.49	0.057
I	129.80±20.45	143.68±19.01	147.37±21.69	0.002
IT	118.57±20.31	129.03±29.24	126.06±23.37	0.209
IN	103.34±23.63	125.31±24.12	117.17±19.97	0.001

T= temporal. UT= upper temporal LT= lower temporal
N= nasal UN= upper nasal LN= lower nasal
S= superior ST= superotemporal SN= superonasal
I= inferior IT= inferotemporal IN= inferonasal

Table-3: The mean values of the peripapillary retinal nerve fibre layer parameters of the groups (mean±SD) (microns) (after applying Litmann's formula).

Quadrant/ sub-quadrant	Myopia (n=35)	Hyperopia (n=29)	Emmetropia (n=29)	p-value
Average	97.53±8.80	98.53±7.92	101.15±7.90	0.197
Temporal quadrant	72.27±12.25	68.21±13.69	74.02±13.97	0.234
Superior quadrant	115.46±18.60	113.41±13.82	117.95±12.52	0.536
Nasal quadrant	80.74±17.66	87.08±13.11	85.57±13.60	0.215
Inferior quadrant	120.91±14.69	124.51±9.03	127.01±12.30	0.147
T	63.76±16.44	60.39±18.52	65.11±18.00	0.575
UT	78.69±16.70	76.59±16.03	81.80±14.86	0.459
LT	71.36±20.62	67.67±15.75	67.72±16.28	0.634
N	72.19±23.91	76.46±17.44	75.48±15.54	0.657
UN	93.54±16.10	101.86±17.58	107.06±15.99	0.006
LN	78.30±18.92	82.66±21.02	81.79±16.3	0.615
S	119.33±21.81	114.14±19.25	120.05±12.42	0.411
ST	120.63±19.94	114.86±21.87	119.75±20.47	0.510
SN	107.94±18.34	118.51±19.73	117.17±19.49	0.801
I	133.97±21.52	121.05±25.83	123.09±23.55	0.113
IT	122.52±22.41	121.05±25.83	123.09±23.55	0.945
IN	106.53±24.42	117.60±21.36	114.20±18.96	0.120

T= temporal UT= upper temporal LT= lower temporal
N= nasal UN= upper nasal LN= lower nasal
S= superior ST= superotemporal SN= superonasal
I= inferior IT= inferotemporal IN= inferonasal

difference was found in mean thickness in UN, LN, SN, IN, and I sub-quadrant ($p<0.05$) (Table-2).

All the thickness values were found to be thinner in the myopic eyes than in the hypermetropic and emmetropic eyes for all, excluding the LT sub-quadrant.

On the other hand, after correction of the magnification effect by applying Littmann's formula, the statistically significant differences among the three groups

Table-4: Correlations between retinal nerve fibre layer thickness and axial length in study subjects before and after applying Litmann's formula.

Quadrant / sub-quadrant	Axial length Correlation coefficient r (p-value) Before Litmann's formula	After Litmann's formula
Average	-0.497 (0.000)	0.164 (0.116)
Temporal quadrant	-0.133 (0.205)	0.185 (0.076)
Superior quadrant	-0.201 (0.053)	0.241 (0.020)
Nasal quadrant	-0.396 (0.000)	-0.098 (0.352)
Inferior quadrant	-0.523 (0.000)	-0.004 (0.969)
T	-0.068 (0.515)	0.141 (0.179)
UT	-0.082 (0.432)	0.212 (0.041)
LT	-0.162 (0.120)	0.077 (0.463)
N	-0.321 (0.002)	-0.096 (0.360)
UN	-0.453 (0.000)	-0.165 (0.115)
LN	-0.154 (0.141)	0.084 (0.425)
S	-0.153 (0.143)	0.229 (0.027)
ST	0.024 (0.819)	0.357 (0.000)
SN	-0.242 (0.019)	0.092 (0.380)
I	-0.378 (0.000)	0.009 (0.936)
IT	-0.184 (0.077)	0.134 (0.201)
IN	-0.422 (0.000)	-0.151 (0.148)

T= temporal UT= upper temporal LT= lower temporal
N= nasal UN= upper nasal LN= lower nasal
S= superior ST= superotemporal SN= superonasal
I= inferior IT= inferotemporal IN= inferonasal

disappeared in all quadrants and sub-quadrants except for the UN sub-quadrant (Table-3).

Mean thickness of major superior and nasal quadrants had negative correlation with axial length (Table-4). Also in N, UN, SN, I and IN sub-quadrants negative correlation was observed between two variables. However, correction of the magnification effect by applying Littmann's formula eliminated the relationship both between RNFL thickness and axial length in each quadrant and sub-quadrants (Table-4).

The average RNFL thickness when compared with the normative database (provided in Topcon SD-OCT) in 4 major quadrants showed that 75(80.6%) of the eyes were within normal limit and rest of them were borderline (1-2 quadrants). While looking at 12 sub-quadrants, 36(39%) of the total eyes were below 99%. Of these eyes, 9(10%) (3 or more sub-quadrants) were identified as outside normal limits and 27(29%) (1-2 sub-quadrants) as borderline.

Discussion

In the present study, RNFL measurements were compared in a healthy non-glaucomatous group of Pakistani population and mean average RNFL was 100.59 ± 9.25µm after correction for ocular magnification. This value is consistent with values documented in other studies.[6,13]

Mean average thickness of our myopic population was 97.53±8.80µm after correction for magnification effect (mean SE-3.59±1.76DS). Similar results were reported in another study with Korean subjects where mean average RNFL thickness after adjustment for ocular magnification was 99.54 ± 8.69µm (mean SE -2.52 ± 2.30 DS).[14]

Other studies documented a higher value of average RNFL thickness in myopic patients. The average RNFL thickness (mean SE -3.9±1.5) was 107.49±12.74µm in another study with Chinese population.[15] In another study the average global RNFL was 105±9 µm. The myopic SE was -1.48±1.13 D and -2.42±2.22 D for black and Indian participants respectively.[16] In a study the mean RNFL thickness was 81.4±13.7µm (mean SE -7.7 D).[17] The differences in RNFL thickness in these studies may be due to ethnic variation and difference in mean SE. Also differences in study sample sizes and OCT device used could also account for the variation observed.

In the present study while looking at the quadrantic variation the RNFL thickness followed ISNT rule with inferior quadrant being thickest followed by the superior, nasal and temporal quadrants. This finding is in agreement with previous studies which documented similar results in their study.[6,7,16,18]

We found that the axial length was longest in the myopic group, followed by the emmetropic and hypermetropic groups. This is in agreement with other studies.[7,9,19,20]

We found significant negative correlation of RNFL thickness with axial length in the present study which disappeared after applying Littmann's formula. The 3 studies quoted below used Littmann's formula and found results similar to our study.

A researcher analysed 98 adult subjects divided into three groups 35 myopic, 30 emmetropic and 33 hyperopic patients using RTVue SD-OCT and found that the average peripapillary RNFL thickness (r= -0.741, p<0.001) as well as RNFL thicknesses in all quadrants and sectors had significant negative correlations with axial length.[19]

Another researcher compared peripapillary RNFL thicknesses of short, medium and long eyes using Cirrus HD OCT and they displayed that average 360° RNFL (r=-0.69, p<0.001) and RNFL of all quadrants become thinner as axial length increased.[21]

In another study using Stratus OCT documented similar results. r = -0.763 p< 0.001 and r = -0.266 p < 0.05 for myopic and hypermetropic patient respectively.[22] However, in all of the above mentioned three studies, correction of magnification effect by applying Littmann's formula eliminated the relationship between RNFL thickness and axial length.

A study was conducted on 162 Japanese normal subjects 20 to 83 years of age and compared parameters measured by stratus OCT and HRT and found similar correlation. According to their findings both RNFL thickness and disc area measured with OCT were inversely correlated with axial length.[8] Similar results were documented in another research.[13] (r= -0.391, P=0.001).

A researcher conducted a study using TOPCON SD-OCT similar to that used by us and got results consistent with our study. 300 eyes of 150 individuals (aged 20-40 years) were analysed and it was found that the RNFL thickness decreased with increasing axial length and this was statistically significant (p<0.001).[7] One study showed that with increase in axial length, mean RNFL thickness measured by stratus OCT became thinner.[6] One research analysed 485 eyes and documented that as the axial length increased average 360° RNFL thickness decreased (r=-0.244 p<0.001).[23]

Two similar studies in children found that average RNFL thicknesses had significant negative correlations with axial length (r=-0.460 p<0.001 and r= -0.4, P<0.0001 respectively for both studies).[9,20]

Previous studies using OCT have found a relationship between age and RNFL thickness in adults.[24] However, in our study there was no statistically significant difference (p=0.770).

Also no statistically significant difference in average RNFL thickness with gender (p=0.451) was found in our study. This is in agreement with some other studies.[16,18,25]

Different OCT models differ in technical specifications, imaging protocols and retinal segmentation software that lead to significantly different results. Recent studies have shown that values obtained from different OCT devices differ significantly and therefore cannot be interchanged.[26] As a result, we believe that our study will be helpful for those ophthalmologists who are using Topcon OCT device worldwide.

All the modern OCT devices have built-in software to correct the effect of refractive error and axial length. This should be taken into account to enhance the diagnostic accuracy of SD-OCT while measuring the RNFL thickness. Also our study will provide a database for emmetropic, hypermetropic and myopic eyes in Pakistani population which may assist in identifying changes in RNFL thickness in glaucoma and other diseases.

The strengths of our study include the use of a high-resolution SD-OCT, standardised examination techniques and a relatively uniform sample. Possible limitations include relatively small sample size and the limited range of SE considered. However, the study provides baseline data on RNFL thickness measurements in Pakistani population. Therefore, it is recommended that studies with larger sample size and with a wider range of SE can be conducted in future.

Conclusion

In myopic, hypermetropic and emmetropic eyes peripapillary RNFL thickness decreased with increase in axial length as measured by Topcon SD-OCT. However, this influence appeared to be due to the ocular magnification effects associated with refractive error and can be corrected by taking into account refractive status and axial length while measuring RNFL thickness.

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