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Original Research Article

Analysis of retinal thickness using spectral domain optical coherence tomography in hypertensives and normotensives: A comparative study

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ABSTRACT

Background: The change in the retinal thickness is the indicator of retinal disease. These changes can be measured with Spectral-domain optical coherence tomography (SD-OCT). This study was conducted to compare the central macular thickness (CMT), retinal nerve fiber layer (RNFL), and ganglion cell inner plexiform layers (GCIPL) thickness using SD-OCT in hypertensive and normotensives.

Materials and Methods: All patients with systemic hypertension above the age of 18 years were included in Group A and the age-matched normotensive patients in group B. A history of hypertension was obtained and blood pressure was measured. A standard eye examination and retinal imaging were performed using SD-OCT. The main parameters studied were CMT, RNFL, and GCIPL. An odds ratio and t-test were performed. A probability value of <0.05 is considered significant.

Results: There were 60 eyes in each group. The mean age in group A was 52.43±10.35 years. The mean standard deviation of the duration of hypertension in group A was 6.41±6.28 years. The mean standard deviation CMT was 251.03±18.25μm and 256.77±15.09μm in group A and B respectively. There was no statistically significant difference in CMT of hypertensive and normotensives. The hypertensive patients had significant thickening of RNFL in the nasal quadrant compared to normotensive individuals.

Conclusion: The present study supports the concept that CMT is less likely to be influenced by systemic HTN. RNFL thickness may increase in hypertensives compared to normotensives.

1. Introduction

Hypertension (HTN) is a multi system disease with the potential for profound effects on various organs of the body, including the eye. It is generally asymptomatic, but when it affects the eye, it can herald serious systemic effects. The most common manifestation of systemic HTN in the eye is hypertensive retinopathy (HTR).[1]

The hypertensive retinal vascular changes include generalized arteriolar narrowing, focal arteriolar narrowing, arteriovenous nicking, arterial wall opacification, micro aneurysms, blot and flame-shaped hemorrhages, cotton wool spots, hard exudates, and disc swelling. These are visualized by retinal examination, at various stages.[2]

Spectral domain optical coherence tomography (SD-OCT) is a non-invasive modality used to evaluate the various retinal layers and the optic disc. It is widely used as a diagnostic tool in glaucoma, diabetic retinopathy, and macular disorders.[3,4]

The change in the macular thickness measured with OCT is one of the indicators of macular disease and index for diagnosis and treatment of macular pathology. In addition to genetic factors, many other factors, including age, sex, axial length, fasting glucose, and ethnicity, have

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been suggested to affect macular thickness.[5–15] Studies using SD-OCT have revealed changes in Retinal Nerve Fiber Layer (RNFL) thickness, with the change in blood pressure.[15–17] Limited knowledge is available regarding the effect of high systemic blood pressure (BP) on macular and RNFL thickness.[18,19] Hence we conducted this study with the primary objective to compare the thickness of the central macula, RNFL, and Ganglion Cell Inner Plexiform Layers (GCIPL) using Spectral-domain Optical Coherence Tomography (SD-OCT) in hypertensive and normotensive adults. This may be indicative of vascular damage and also form the basis of new evidence in the interpretation of Central Macular thickness (CMT) and RNFL change in hypertensives.

2. Materials and Methods

This is a case control study done in a tertiary care hospital in south India. All necessary approval was taken from the institutional research and ethics committee. The study was carried out in accordance with the Declaration of Helsinki. Assuming the means as 98.31 and SD 7.01 in group A and mean as 102.51 and SD 8.72 in group B with significance as 5% and power 80% the sample size was 60 in each group.

2.1. Inclusion criteria

The patients attending the ophthalmology and general medicine outpatient department, who fulfilled the eligibility criteria were selected for the study. The written informed consent was obtained before participants were recruited for the study. All patients with systemic hypertension above18 years of age were included in Group A. Age-matched patients without hypertension (normotensives controls) were included in group B.

2.2. Exclusion criteria

Patients who had glaucoma, optic nerve disease, other retinal or macular disease, recent intraocular surgery, media haze which precludes a good scan, high myopia, secondary HTN, gestational HTN, and malignant HTN, were excluded from the study. The patient's demographic details were noted. A detailed history of hypertension was obtained including the duration of disease, treatment, and other comorbidities like diabetes, renal disease, coronary artery disease. Personal history about smoking, alcoholism, tobacco chewing was also recorded.

2.3. Methodology

General physical examination included systolic blood pressure (SBP) and diastolic blood pressure (DBP) measured manually using a sphygmomanometer. The patients were categorized into normotensive (SBP <130 and DBP<80), stage 1 HTN (SBP130-139 or DBP 80-89), stage 2 HTN (SBP 140 or higher or DBP 90 or higher), and hypertensive crisis (SBP >180 and/or DBP>120) based on American Heart Association classification. One or both eyes of a patient were included for the study as per inclusion criteria. A standard eye examination, including best-corrected visual acuity (using a Snellen chart), retinoscopy, intraocular pressure (using applanation tonometry), and slit-lamp microscopy were done. The pupils were dilated using tropicamide 1% eye drops and fundoscopy (using 90D lens) was performed. Retinopathy was graded by Keith Wagener classification. The retinal imaging was performed using NIDEK Retina Scan Duo 330 SD-OCT a non-invasive imaging modality. Two scans of each macula map and disc map were obtained both with a signal strength of more than 7/10 and with good centration. The details collected were documented in the case report form and the printout of the SD-OCT was attached to it and used for future reference. The main Parameters studied were CMT, RNFL, and GCIPL.

2.4. Statistical analysis

The data were analyzed with statistical package for the social sciences software (SPSS) version-21. Categorical data were expressed in terms of percentage. Continuous data were expressed as mean +/- Standard deviation. An odds ratio and t-test were performed. A probability value (p-value) of <0.05 is considered significant

3. Results

Group A consisted of 60 eyes of 35 with a male to female ratio of 20:15 females and group B consisted of 60 eyes of 34 patients with a male to female ratio of 21:13. The mean age in group A was 52.43±10.35 years and in group B was 51.47±10.27years. The mean ± SD duration of hypertension in group A was 6.41±6.28 years. In group A 18 patients had stage 1 HTN, 16 patients' stage 2 HTN, and one patient had a hypertensive crisis. In group A, two patients had a history of stroke and nine patients had a history of diabetes and in group B, one patient had a history of stroke and six patients had a history of diabetes. According to Keith-Wagener-Barker classification, a total of 14 patients had HTR in group A, out of which seven patients had grade 1 HTR, four patients had grade 2 HTR and three patients had grade 3 HTR. The CMT of cases was less than controls. However, there was no statistically significant difference in CMT (P = 0.1597) and subgroup analysis of macular thickness in all four quadrants in the outer and inner circle (Table 1).

There was a slight increase in the thickness of GCIPL of cases than controls in the inferior and superior quadrant. However, it was not statistically significant. The subgroup analysis of the thickness of GCIPL in all four quadrants was less for cases compared to controls, which were not

Table 1: Comparison of macular thickness between the cases and controls

Macular Thickness (mean+ SD in μm)	Cases	Controls	P value
Central Macular thickness	251.03 ± 18.25	256.77 ± 15.09	0.1597
Inner superior	313.95 ± 26.43	322.01 ± 21.89	0.1730
Inner temporal	309.74 ± 16.88	316.65 ± 15.49	0.0812
Inner inferior	325.01 ± 17.47	330.06 ± 14.84	0.2007
Inner nasal	323.09 ± 19.05	330.77 ± 16.46	0.0780
Outer superior	297.82 ± 14.48	296.73 ± 18.69	0.7870
Outer temporal	282.06 ± 14.02	283.47 ± 13.89	0.6761
Outer inferior	279.69 ± 15.60	281.30 ± 16.71	0.6803
Outer nasal	304.68 ± 17.26	306.51 ± 16.04	0.6499

Table 2: Comparison of GCIPL thickness between cases and control

GCIPL thickness (mean+SD in μm)	Cases	Control	P-value
GCIPL Superior	98.76 ± 9	97.61+ 7.75	0.5719
GCIPL Inferior	100.95 ± 8.65	100.07 ± 7.01	0.6445
Superotemporal	91.73 ± 9	95.11 ± 13.79	0.0795
Inferotemporal	106.98 ± 12.27	110.38 ± 10.29	0.2173
Inferonasal	109.54 ± 13.63	112.61 ± 11.65	0.3188
Superonasal	98.77 +16.09	101.60 ± 16.76	0.4767

GCIPL: Ganglion cell inner plexiform thickness

Table 3: Comparison of RNFL thickness between cases and controls

RNFL thickness (m ean+SD in μm)	Cases	Control	P-value
Inferior	129.19 ± 20.88	127.74 ± 16.12	0.7483
Superior	132.07 ± 24.51	125.39 ± 16.89	0.1932
Nasal	79.76 ±13.80	71.25 ± 14.93	0.0164*
Temporal	68.38 ± 11.37	67.69 ± 9.41	0.7848
Average	102.25 ± 12.81	98.04 ±10.61	0.1424

RNFL: Retinal Nerve Fiber Layer, *Nasal quadrant in cases had significant thickening of RNFL

Table 4: Comparison of duration of hypertension with CMT, GCIPL-S, GCIPL-I, RNFL

	Hypertension< 10years (mean±SD) (n=23)	Hypertension >10years (mean±SD) (n=12)	P value
CMT	253.1 ± 9.41	248.89 ± 15.16	0.3204
GCIPL – S	99.84 ± 9.23	96.26 ± 8.81	0.2880
GCIPL – I	102.18 ± 8.24	98.15 ± 9.28	0.2054
RNFL	102.75 ± 13.15	101.10 ± 12.23	0.7272

CMT: Central Macular Layer Thickness, GCIPL-S: Ganglion cell inner plexiform thickness-Superior, GCIPL-I: Ganglion cell inner plexiform thickness-Inferior, RNFL: Retinal Nerve Fiber Layer

Table 5: Change of retinal thickness with age

Age group (yrs.)	CMT	GCIPL – S	GCIPL – I	RNFL
30-40	257 ± 17.94	104.9 ± 4.90	107.2 +± 5.25	108.05 ± 10.31
41-50	251.69 ± 16.15	99.65 ± 7.14	101.76 ± 6.24	100.56 ± 11.88
51-60	259 ±17.11	96.16 ± 9.18	98.85 ± 7.97	97.42 ± 11.09
61-70	247.72 ± 14.19	91.72 ± 7.14	93.73 ±7.64	96.56 ± 12.13

CMT: Central Macular Layer Thickness, GCIPL-S: Ganglion cell inner plexiform thickness-Superior, GCIPL-I: Ganglion cell inner plexiform thickness-Inferior, RNFL: Retinal Nerve Fiber Layer

statistically significant. Comparison of RNFL thickness in all four quadrants and average RNFL thickness in both groups shows that there is an increase in thickness in cases compared to controls and the difference was statistically significant in the nasal quadrant ($P < 0.05$) (Table 3)

Group A patient with a duration of HTN of more than 10 years had less CMT, average RNFL thickness, inferior and superior GCIPL thickness compared to patients who had HTN for less than 10 years, which was not statistically significant (Table 4).

As age advanced there was a decrease in CMT, RNFL thickness, and GCIPL thickness in superior and inferior quadrants in both cases and controls (Table 5)

4. Discussion

The current study found no statistically significant difference in CMT of hypertensive and normotensives. However, on quadrant wise analyses of the macula map, there was relatively more thinning in the inner temporal and inner nasal quadrant in cases. GCIPL showed relatively more thinning in the supero-temporal quadrant in hypertensives compared to normotensives. RNFL thickness analysis revealed that hypertensive patients had significant thickening- in the nasal quadrant compared to normotensive individuals. In our study, the mean age for the Hypertensive group was 52.43±10.35 years. Other studies in the literature also suggest the high prevalence of HTN in this age group.[20,21] Males were more than females in the hypertensive group in our study with a male: female of 1.3: 1 and correlates with male gender as a risk factor of HTN.[19,22]

Lee SH et al. in his study found significant thinning of RNFL, macular, and GCIPL in chronic hypertensive (HTN > 10 years) patients than normotensive controls, and these retinal changes were more prominent in chronic hypertensives with retinopathy in the past.[18] In our series of cases too, macular thickness and GCIPL were found to be reduced in a hypertensive group compared to the normotensive group, but it was not statistically significant. This could be attributed to the average duration of HTN being comparatively less in our study (6.41±6.28 years). Further, Lee et al. also found that there was relatively more thinning in the supero- temporal quadrant in the GCIPL map which is similar to our results, and therefore it is possible that the thinning starts in this quadrant. Further, studies with long-term follow-up could confirm this finding. Our study also differed in that it showed relatively more thinning in the inner temporal (p=0.0812) and inner nasal (p=0.0780) quadrant on subgroup analysis of the macular map. This can be attributed to differences in study participants' characteristics. In our study, we have recruited all patients with HTN irrespective of the duration and most of the patients had a duration of HTN of less than 10 years, this might have influenced the results. Our patients had reduced macular thickness despite no evidence of exudative retinopathy (only three out of 14 patients with HTR had exudative changes) a feature also noted by Kong M et al., where they found, reduced macular thickness (except CMT) in eyes without exudative HTR. This can be explained by autoregulation of retinal blood vessels induced by increased blood pressure leading to vasoconstriction and ischemia. The normal thickness of the central subfield of the macula can be due to foveal avascularity and hence the absence of any auto regulation.[22] This could also be due to hypo perfusion resulting from ischemia due to over treatment. Most of the patients in the hypertensive group were on fair control with anti hypertensives, another possible reason for no significant thinning of macular and GCIPL thickness. The RNFL, is the axons of retinal ganglion cells, and hence we expect a decrease of RNFL thickness with decreased GCIPL thickness but, interestingly, we found increased RNFL thickness in all four quadrants in hypertensives when compared to normotensives. This difference was not statistically significant except in the nasal quadrant, which is in contradiction to a few other similar studies done in hypertensive patients.[18,19,23] Khawaja AP found no positive correlation between HTN and RNFL thickness. Increase in RNFL thickness in the present study, could be attributed to subclinical disc edema because of possible acute elevation of blood pressure due to abnormal fluctuation and absence of chronic compensatory mechanism. This could possibly be due to the comparatively shorter duration of HTN, in our study population.[24] Further studies are recommended to confirm this hypothesis. The average RNFL thickness in our study was comparable to the study done by Ramakrishnan R et al. They found that the thickness was more in the superior quadrant followed by inferior, nasal, and temporal quadrant which was similar to our results in group A.[25–27] CMT was found highest in the age group 51-60 years and lowest in the age group 61-70 years. Few other studies have also shown that there was no association between age and macular thickness.[28–30] GCIPL thickness was also found to decrease with age in our study in both cases and controls. This is supported by previous histological data, where the estimated loss of retinal ganglion cells for the age range studied was 7209 retinal ganglion cells/year.[20,31–33] RNFL, also showed decreased thickness with advancing age in both cases and controls, which is comparable with the other studies.[19,34–36] The decrease in RNFL thickness of 500 to 7000 axons per year was reported with increasing age in numerous histological studies also.[26,37] The macular, RNFL, and GCIPL thickness was reduced in patients who had HTN for more than 10 years compared to patients who had HTN for less than 10 years but it was not statistically significant. This can be attributable to hypertensive retinal ischemia. The majority of patients 65.71 % (23/35) in our study in group A had HTN for the duration of less than 10 years. Another study that included chronic hypertensive patients

with a duration of more than 10 years found significant macular, RNFL, and GCIPL thinning in the hypertensive group compared to the normotensive group.[18]We have used SD-OCT in our study which is a 3rd generation OCT, that facilitates unprecedented ultra-high-resolution, ultra-high-speed RNFL imaging, which makes our results more accurate and strengthens our study.[38] All patients were thoroughly evaluated by a physician who was also part of our study investigator team which ascertained that all patients were labeled hypertensive after proper evaluation by the medicine team at our institute. We had most hypertensive with a duration less than 10 years in our study which might have provided limited evidence for a causal association between HTN and macular thickness.

5. Conclusion

The present study supports the concept that CMT is less likely to be influenced by systemic HTN. Perifoveal macular thickness may be reduced. We recommend more studies including those with a longer duration of HTN.

RNFL thickness may increase in hypertensives compared to normotensives. We hypothesize that this could be due to possible acute rises in blood pressure and lesser duration of HTN in our study group. Aging is also found to reduce the GCIPL and RNFL and therefore it should be taken into consideration, along with those in HTN, while analyzing OCT parameters for glaucoma, neuro ophthalmological diseases, and other retinal conditions.

6. Ethical Approval

This study was done after taking approval from Institution ethics committee (IEC) approval number: RC/ 2018/97

7. Source of Funding

Nil.

8. Conflicts of Interest

Nil.

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