STUDY OF RETINAL NERVE FIBER LAYER THICKNESS BY OPTICAL COHERENCE TOMOGRAPHY IN PRIMARY OPEN ANGLE GLAUCOMA, GLAUCOMA SUSPECT AND NORMAL NEPALESE POPULATION

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ABSTRACT

The measurement of retinal nerve fiber layer thickness can help significantly in the early diagnosis of glaucoma and monitoring of its progression. The objective of this study was to compare the retinal nerve fiber layer (RNFL) thickness by optical coherence tomography in primary open angle glaucoma, glaucoma suspects and normal Nepalese population. This was a hospital based cross-sectional study conducted in the Ophthalmology Out Patient Department of Manipal Teaching Hospital, Pokhara. Total 100 numbers of subjects (40 primary open angle glaucoma, 30 glaucoma suspects and 30 normal people) were evaluated. Complete ophthalmological examinations including tonometry, gonioscopy, optical coherence tomography, perimetry were performed. Statistical analysis was carried out using Epi-info 7. The result showed that the average retinal nerve fiber layer (RNFL) thickness was 70.22±12.07μm in right eye and 69.42±11.53μm in left eye in primary open angle glaucoma (POAG), 88.87±10.39μm in right eye and 88.73±9.59μm in left eye in glaucoma suspects (GS) and 94.40±9.21μm in right eye and 94.73±6.76μm in left eye in normal group respectively. The mean RNFL thickness was statistically significant in all three comparison groups except in nasal quadrant. The mean RNFL thickness was statistically significant in two comparison groups except in GS-Normal (nasal and temporal quadrant), GS-POAG (left nasal quadrant) and Normal-POAG (left nasal quadrant). The study concluded that the RNFL thickness is lower in POAG as compared to glaucoma suspects and normal group in the Nepalese population.

KEYWORDS

Glaucoma suspect, optical coherence tomography, primary open angle glaucoma, retinal nerve fiber

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INTRODUCTION

Glaucoma is defined by a characteristic optic neuropathy that is consistent with remodeling of the connective tissue elements of the optic nerve head and with loss of neural tissue associated with the eventual development of the distinctive patterns of visual dysfunction.[1] Glaucoma affects more than 70 million worldwide with approximately 10% being bilaterally blind. There are 60.5 million people affected by primary open angle glaucoma which is expected to rise to 79.6 million by 2020.[2] The first nationwide epidemiological survey done in Nepal reported 0.84% prevalence of blindness in Nepal and found 3.2% cases were blind due to glaucoma.[3]

Glaucoma is one of the main causes of irreversible legal blindness worldwide and the second cause of loss of vision in patient over 40 years of age in the developed countries,[4] with an important impact on quality of life.[5-7] Early diagnosis and treatment of glaucoma has been shown to reduce the rate of disease progression and improve patient's quality of life.[8]

Optical coherence tomography (OCT) developed in 1991, is an imaging technology that performs high- resolution, cross- sectional imaging of the optic nerve head, retinal nerve fiber layer and macula.[9] Retinal nerve fiber loss precedes measurable optic nerve head and visual field damage and is observed in 60% of eyes approximately six years before any detectable visual field defect in glaucoma.[10] OCT is used for the detection of early structural glaucomatous nerve alternations that precede optic disc and visual field damage.[11] Retinal nerve fiber layer analysis is the most commonly used scanning protocol for glaucoma diagnosis.[12-14]

The objective of the study was to compare the retinal nerve fiber layer thickness by optical coherence tomography in primary open angle glaucoma (POAG), glaucoma suspects (GS) and the normal Nepalese population.

MATERIALS AND METHODS

This was a hospital based cross-sectional study conducted in OPD of the Department of Ophthalmology, Manipal Teaching Hospital, Pokhara, Nepal for one year (from April 2019 to March 2020). Ethical approval was taken from the Institutional Review Committee of the Manipal College of Medical Sciences, Pokhara before the start of the study. The total of 100 patients aged 40 years and older were enrolled for the study (40 patients of POAG, 30 patients of GS and 30 normal samples) after taking informed consent. The patients with opacity in cornea, lens or vitreous, refractive error more than +/- 5.0 Dsph or 2.0 Dcyl or those with optic nerve pathology other than glaucoma or any other neurological damage were excluded from the study. Patients with hypertensive and diabetic retinopathy or history of prior intraocular surgery or trauma were also excluded from the study.

Relevant history and detailed ocular examination was performed including refraction, anterior segment evaluation by slit lamp and fundus evaluation after full dilatation using +90D Volk lens and +20D lens. Intra ocular pressure was measured with applanation tonometer, gonioscopy with Volk Three - Mirror Gonio lens, visual field examination with Humphrey SITA Standard, 24-2 Static threshold perimeter (Model no. Humphrey field Analyser II – i series Ziess company), central corneal thickness with optical coherence tomography and optic disc cube 200x200 and retinal nerve fiber thickness measurement by using Carl Zeiss Spectral Domain OCT V3.

Primary open angle glaucoma (POAG) is defined by following three criteria:

1. An intraocular pressure (IOP) consistently above 21 mmHg in at least one eye
2. An open, normal appearing anterior chamber angle with no apparent ocular or systemic abnormalities that might account for the elevated IOP
3. Optic nerve head damaged with typical glaucomatous visual field changes.

Criteria for glaucoma suspect: Subjects with raised intraocular pressure or glaucomatous optic disc changes or visual field abnormalities in isolation.

Criteria for normal: Subjects with no history of ocular disease. Intraocular pressure should be less than or equal to 21 mmHg, normal optic disc appearance and normal perimetry.

The statistical tests used were mean, chi-square and analysis of variance (ANOVA). Data entry and analysis was done in Epi-info version 7. The p-value less than 0.05 was considered significant in this study.

RESULTS

A total of 100 patients were included in the study. The mean age ±standard deviation was 62.03±13.39 years in POAG group, 56.03±12.61 years in GS group and 50.57±9.01years in normal group. The mean age difference

between the three groups was statistically significant. There was statistical significance in gender of the participants, but not in their place of residence (Table1).

Table 2 shows the comparison of the mean retinal nerve fiber layer thickness in POAG, GS and normal groups. The mean was statistically significant in average RNFL as well as in

Table 1: Variables of study participants

Variables		POAG (n=40)	GS (n=30)	Normal (n=30)	Chi –square	p-value
Mean Age ±SD (in years)		62.03 (±13.39)	56.03 (±12.61)	50.57 (±9.01)		0.0007
Gender	Female	18	24	23	11.79	0.0027
	Male	22	6	7		
Residence	Urban	25	22	21	1.0034	0.6055
	Rural	15	8	9		

Table 2: Comparison of mean retinal nerve fiber layer thickness between the study groups.

RNFL thickness (in µm)		POAG	GS	Normal	p-value
Average	Right eye	70.22(±12.07)	88.87(±10.39)	94.40(±9.21)	0.0000
	Left eye	69.42(±11.53)	88.73(±9.59)	94.73(±6.76)	0.0000
Superior quadrant	Right eye	91.05(±20.88)	110.20(±15.11)	121.10(±14.80)	0.0000
	Left eye	89.32(±23.42)	114.26(±16.13)	124.90(±12.64)	0.0000
Nasal quadrant	Right eye	61.87(±7.47)	67.73(±10.70)	67.56(±11.63)	0.0192
	Left eye	60.17(±8.50)	65.00(±10.81)	64.06(±11.06)	0.1026
Inferior quadrant	Right eye	76.12(±31.58)	117.06(±16.38)	128.30(±17.50)	0.0000
	Left eye	76.50(±28.07)	114.16(±13.58)	126.80(±15.13)	0.0000
Temporal quadrant	Right eye	50.52(±11.58)	60.30(±8.87)	62.16(±5.88)	0.0000
	Left eye	52.45(±9.47)	61.33(±13.11)	61.00(±6.96)	0.0003

Table 3: Comparison of mean retinal nerve fiber layer thickness between two study groups.

RNFL thickness (in µm)		GS-POAG (p-value)	GS-Normal (p-value)	Normal-POAG (p-value)
Average	Right eye	0.0000	0.0332	0.0000
	Left eye	0.0000	0.0069	0.0000
Superior quadrant	Right eye	0.0000	0.0065	0.0000
	Left eye	0.0000	0.0062	0.0000
Nasal quadrant	Right eye	0.0192	0.9541	0.0153
	Left eye	0.1026	0.7422	0.1005
Inferior quadrant	Right eye	0.0000	0.0129	0.0000
	Left eye	0.0000	0.0012	0.0000
Temporal quadrant	Right eye	0.0000	0.3411	0.0000
	Left eye	0.0003	0.9026	0.0001

superior, inferior and temporal quadrant in both right and left eyes, except in nasal quadrant.

Table 3 shows the comparison of the mean retinal nerve fiber layer thickness between the two groups. The mean RNFL thickness was statistically significant between two comparison groups except in GS-Normal (nasal and temporal quadrant), GS-POAG (left nasal quadrant) and Normal-POAG (left nasal quadrant).

DISCUSSION

Glaucoma is the second leading cause of blindness worldwide. The main goal of glaucoma management is to diagnose when patients are asymptomatic. Visual field testing is important in the diagnosis and monitoring of glaucoma, however, standard perimetry alone cannot detect visual field defects until 20%-40% of ganglion cells have been lost.[15,16] Retinal nerve fiber layer defects have been detected earlier than visual field defects with Optical coherence tomography. Measuring RNFL thickness by OCT helps in quantitative assessment of glaucomatous structural loss.[17]

In our study the mean age (±SD) was 62.03 years (±13.39 years) in POAG group, 56.03years (±12.61 years) in GS group and 50.57 years (±9.01years) in normal group and was statistically significant. A study in India noted that the mean age ±SD was 57.4±10.4 years in glaucomatous eyes, 51.6±10.5 years in eyes with ocular hypertension and 51.1±12.9 years in normal eyes and was significantly higher in patients with glaucoma compared with normal patients and patients with ocular hypertension.[18] Our results were similar to a study in Greece where mean age for normal group was 58.03±15.62 years and for glaucomatous 62.57±14.5 years.[19] A study in Nepal, however, observed no statistically significant difference in age.[20]

There was significant difference regarding gender between the three groups in this study. This is different from the studies done in India,[18] Nepal[20] and USA[21] which showed no statistically significant difference.

There was significant thinning of RNFL in POAG compared with GS and normal group. In the RNFL thickness measurement in different quadrants, we observed that it was thickest in the inferior followed by superior, nasal and temporal quadrant. Similar results was seen in a study conducted at Nepal, where the mean RNFL thickness was 109.8±8.32µm in normal eyes, 102.0±9.37µm in GS and 64.30±14.45µm in eyes with POAG.[20] Similar study in China observed the mean RNFL thickness was significantly higher in the inferior sector (131.4±20.6µm) followed by superior sector (126.1±19.1µm), temporal sector (79.8±12.2µm) and nasal sector (75.1±12.6µm).[22] The RNFL thickness distribution in normal eyes was such that the inferior quadrant was the thickest followed by superior, nasal and temporal quadrant. This follows the convection that is often referred to as ISNT rule in glaucoma.[23] Mean RNFL thickness was statistically significantly less in glaucomatous eyes (56.9±21.5µm) than in eyes with ocular hypertension (83.7±16.6µm) and normal eyes (90.9±14.2µm) in a study from USA. RNFL thickness was greater in normal than in ocular hypertensive eyes but it wasn't statistically significant.[21] A study by Mansoori *et al*[18] noted that mean RNFL thickness was 112.5±6.5µm in normal eyes, 110.1±10.9µm in eyes with ocular hypertension and 93.4±16.9µm in glaucomatous eyes. Mean RNFL thickness showed a significant difference between glaucomatous eyes, normal eyes and eyes with ocular hypertension. Mean RNFL thickness between normal eyes with ocular hypertension wasn't statistically significant.

Our study was different from the study done in Greece which noted superior quadrant RNFL was thickest (136.7±18) followed by inferior (134.5±18.1), nasal (107.2±17.8) and temporal (79.5±15.3).[19]

Anton *et al*[24] reported that mean RNFL thickness around the disc and superior and inferior RNFL thickness was significantly thinner in glaucomatous eyes than in eyes with ocular hypertension or normal eyes. They found no significant difference in RNFL parameters between eyes with ocular hypertension and normal eyes. Most studies using Stratus OCT have identified the average and inferior average RNFL thickness as the best discrimination between normal and glaucomatous eyes.[25] Our study also found inferior quadrant RNFL thickness to be the best parameter to differentiate between normal and glaucoma.

In our study, the RNFL thickness difference was statistically significant in all the quadrants except nasal between the study groups. However, only the superior and inferior RNFL was thinned significantly between normal and GS eyes. It may be due to the fact that the superior and inferior poles of the optic nerve head are more vulnerable to glaucomatous damage. A significant difference in quadrantic RNFL thickness across all comparison groups except Normal vs GS in which nasal and temporal

RNFL thickness did not differ significantly as reported from a study by Khanal *et al.*[20] Guedes *et al*[26] reported that mean RNFL was the only parameter in which a statistically significant difference was observed between the normal and GS groups.

In conclusion, this study showed that there was statistical significance in RNFL thickness in POAG group as compared to GS and normal groups. RNFL thickness measurement by OCT can be used as an early tool to differentiate between normal, glaucoma suspect and glaucomatous eyes. This could help in early diagnosis and proper management of glaucoma patients. It would also help in the follow up of these patients.

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