

Correlation of Retinal Nerve Fibre Layer by Optical Coherence Tomography and Humphrey field Analysis in Primary open Angle Glaucoma

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Abstract:

Objective: To quantitatively assess the sensitivity and specificity of retinal nerve fiber layer thickness by Optical Coherence Tomography and Humphrey Field Analysis in primary open angle glaucoma and evaluate and correlate their efficacy in diagnosing primary open angle glaucoma.

Materials and methods: A total of 52 cases and 104 eyes diagnosed with POAG in the age group 40 years of age and above were included in the study. The diagnosis was made based on history, findings on slit lamp examination, gonioscopy, Goldmann's applanation tonometry, direct and indirect ophthalmoscopy, RNFL Optical Coherence Tomography and automated perimetry (Humphrey's visual field analyzer). The correlations between OCT RNFL and mean deviation with HFA were calculated. Receiver operating characteristic curve (ROC curve) and area under the curve (AUC) were evaluated.

Results: When OCT RNFL was compared with standard automated perimetry which is HFA, the AUC was 0.793 for RNFL thickness in eyes with visual field defects, suggesting significant difference between the two ($p < 0.001$). The current study also demonstrates that the OCT RNFL performs better as a diagnostic test to establish POAG than the conventional automated perimetry.

Conclusion: The current study demonstrates that OCT RNFL thickness measurements are a reliable and sensitive diagnostic modality for early detection of primary open angle glaucoma. Thus, it implies that RNFL thinning determined by OCT stands superior to the HFA in the individuals with early glaucoma and glaucoma suspects who exhibit normal visual fields (HFA) by routine automated perimetry.

Keyword: Primary open angle glaucoma, OCT RNFL, Humphrey field analysis, RNFL thinning, visual field defect.

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Introduction

Glaucoma is one of the major cause of irreversible blindness in the developing world and significant health issue in the developed world [1]. Glaucoma is defined as group of disorders characterized by chronic progressive optic neuropathy that causes distinctive morphological alterations at the optic nerve head and in the retinal nerve fibre layer, manifesting characteristic visual field loss. Rise in intraocular pressure may or may not be associated with it [2]. Glaucoma is a silent thief of sight because it is an asymptomatic disease and it slowly damages the eyes and cause irreparable harm before any significant vision loss.

Glaucoma continues to be a worldwide burden despite recent improvements in diagnostic and therapeutic approaches. Undiagnosed glaucoma affects a sizeable fraction of the population which is

a troublesome yet consistent finding throughout population-based studies. Glaucoma is responsible for 10.7% of blindness globally and 12.8% of blindness in India [3]. According to a study by Tham et al., the prevalence of glaucoma is 3.54 percent worldwide, with Africa having the highest prevalence. By 2040, there will be 111.8 million glaucoma patients globally (aged 40 to 80), up from 64.3 million in 2013, disproportionately affecting people living in Asia and Africa [4]. These figures are anticipated to rise significantly due to the ageing and growth of the global population. These data highlight the need of identifying and closely monitoring people who are at risk of developing glaucoma.

Slowing the pace of progression in order to maintain visual function and associated quality of life at a

reasonable cost throughout the patient's life is the goal of treatment of glaucoma. The patient is unaware of the glaucoma in early stages. Approximately 25-35% of retinal ganglion cell axons must be destroyed for standard automated perimetry to detect visual field abnormalities [5]. Visible cupping and significant axonal damage may occur before visual field abnormalities [6]. Therefore, earlier glaucoma detection is essential for preventing permanent vision loss, and more specific and sensitive diagnostic techniques should be used for this purpose.

Optical coherence tomography (OCT) has evolved to become an essential tool in ophthalmology over the past two and a half decades. OCT is a non-invasive, non-contact technique which enables cross-sectional, in vivo imaging of the intraretinal layers. Based on the various reflectivity properties of the different layers of the retina, anatomic layers inside the retina can be scanned and quantitative assessment of retinal nerve fibre layer (RNFL) thickness can be carried out. Additionally, studies have shown that the OCT RNFL thickness is lower in glaucomatous eyes than in healthy eyes [7]. Structure-based techniques must finally be compared to automated perimetry, which is now the gold standard.

The goal of this study is to observe the correlation between the structural alterations detected by OCT and functional changes detected by Humphrey field analysis.

Materials and methods

A cross sectional observational study was conducted on patients with primary open angle glaucoma (POAG) to quantitatively evaluate the retinal nerve fibre layer using optical coherence tomography and compare it to standard automated perimetry using the Humphrey visual field analyser.

Sample size was calculated using the formula:

$$\frac{2\sigma^2 (Z_{\beta} + Z_{\alpha/2})^2}{d^2}$$

To observe minimum of 5 points between normal and glaucoma eyes with pooled SD 9, a total 52 samples will be required to detect 80% power at 5 % level of significance.

Z beta = power

Z alpha = level of significance.

This study consisted of 52 patients and 104 eyes diagnosed with POAG in the age group 40 years and above presenting in Department of Ophthalmology, Silchar Medical College, Assam. The diagnosis was made based on eliciting detailed history, slit lamp examination, gonioscopy, Goldmann's applanation tonometry, direct and indirect ophthalmoscopy,

automated perimetry (Humphrey's visual field analyzer) and RNFL Optical Coherence Tomography. Duration of the study is 1 year, that is from June 2021 to May 2022.

Inclusion Criteria

- Patients aged 40 years and above diagnosed with POAG at the time of evaluation attending Eye department, SMCH during the study period.
- BCVA of at least 3/60 or better
- IOP >21mmHg (by Goldmann's applanation tonometry) with visual field defects or optic nerve head changes
- Open angle of anterior chamber on gonioscopy
- Patients who consented for visual field analysis and OCT

Exclusion Criteria

- Age < 40 years of age
- Closed angles by Gonioscopy
- Media opacities, advanced diabetic retinopathy, age related macular degeneration, retinitis pigmentosa, maculopathy, vitreous haemorrhage, various optic neuropathies, secondary glaucoma, post-operative and drug induced glaucoma.

The procedure and investigation were explained to the patient and informed consent taken. Each case was thoroughly investigated, critical analysis done and conclusions drawn.

Standard automated perimetry was conducted by using the Humphrey Field Analyzer II and 30-2 visual field charting was done. The total and pattern deviation plots as well as the global indices were calculated. STATPAC was used to calculate the mean deviation and pattern standard deviation for SITA.

The Topcon 3D OCT-1 Maestro 2 was used for this study. The thickness of the retinal nerve fibre layer is measured and analysed by the OCT software. The thickness of the nerve fibre layer is colour coded in accordance with the population's age-related average. 90% of the average population lies within the green band and 95% falls in or below green band. 5% of the general population is contained by or below the yellow band. 1% of the sample falls within the red band and is regarded as abnormal. Measurements of the thickness of the retinal nerve fibre layer were deemed abnormal if they were thinner than 97.5% of normal values generated from healthy eyes in the normative database.

Results

A total of 52 patients with 104 POAG cases who fulfilled the criteria were taken into consideration. The results and observations of the study are presented as follows:

Age Distribution

From the study it showed that maximum were from the age group >70 years (44.2%) and least from the

age group 40-49 years (13.5%). It is also seen that the incidence of POAG increases with age and with a maximum of above 70 years (Chart 1)

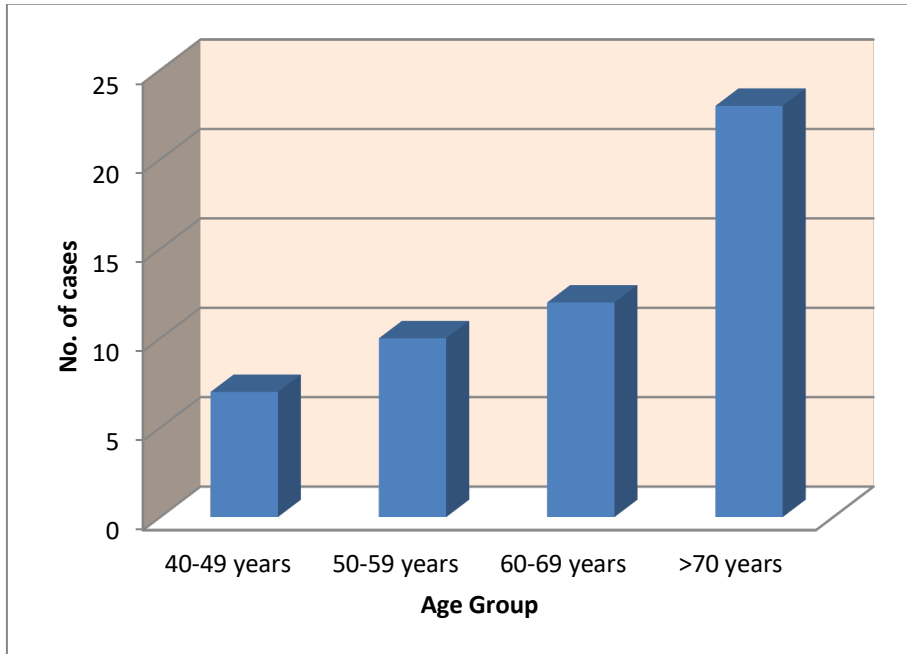


Figure 1: A bar diagram showing age distribution.

Sex Distribution

There were 32 males and 20 females in the study. Prevalence of POAG is more in males than females. (Chart 2)

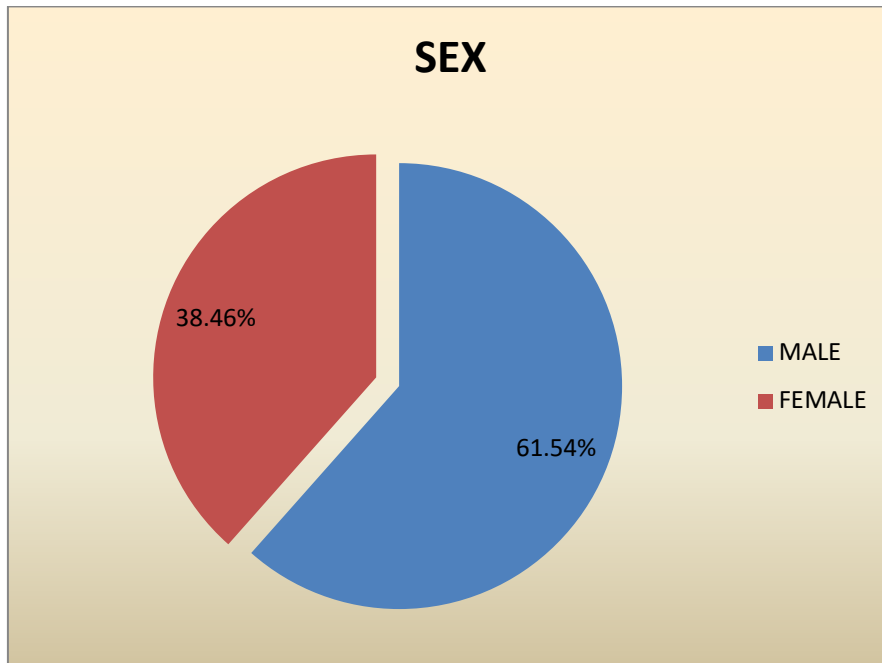


Figure 2: Pie chart showing sex distribution

Glaucomatous Field Defect

From the study 26 eyes (25%) showed no field defect, 55 eyes (52.9%) showed early glaucomatous field defect, 20 eyes (19.2%) showed moderate glaucomatous field defect and 3 eyes (2.9%) showed advanced glaucomatous field defect. (Chart 3)

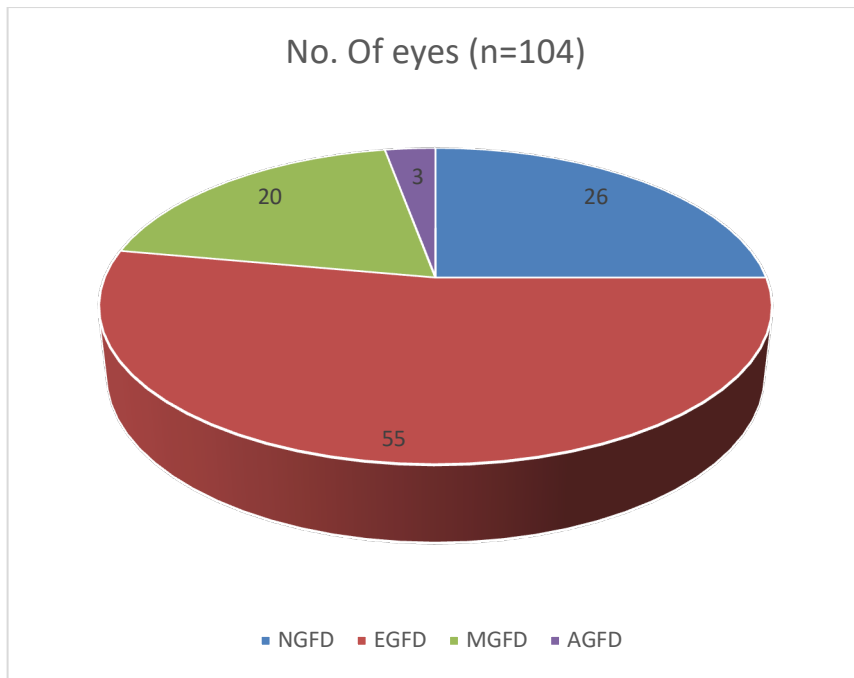


Figure 3: Pie chart showing glaucomatous field defect (GFD)
 *N= Normal *E= Early *M= Moderate *A= Advanced

Various Levels Of Iop Affecting The Visual Field Defects

From the study 63.3% of eyes with IOP in between 20-25mmHg showed VFD, 84.4% of eyes with IOP in between 25.1-30 mmHg showed VFD, 83.3% of eyes with IOP between 30.1-35 mmHg showed VFD, 100% of eyes with IOP more than 35 mmHg showed VFD. Mean IOP was 25.44±2.66 mmHg. (Table 1, Chart 4)

Table 1: Showing various levels of IOP affecting the visual field defects (VFD)

IOP	No. of eyes (n=104)	Eyes with VFD	Percentage of VFD with increasing IOP
20-25	49	31	63.3%
25.1-30	46	39	84.4%
30.1-35	6	5	83.3%
>35.1	3	3	100.0%

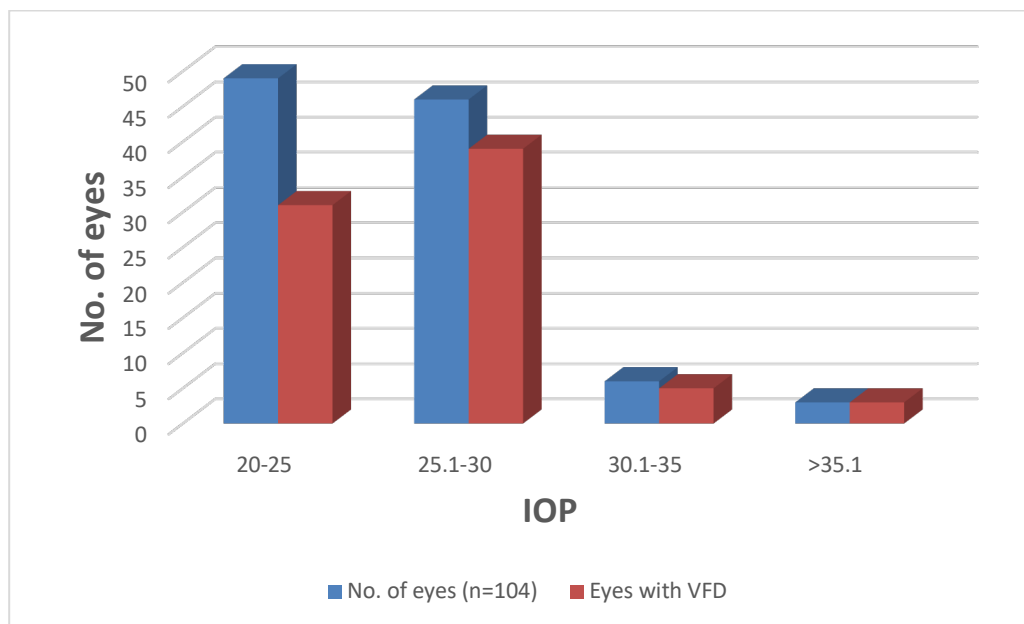


Figure 4: Bar diagram showing various levels of IOP affecting the visual field defects

Optic Nerve Head Changes

In our study we have found that 17 eyes (16.35%) showed no changes, 35 eyes (33.65%) showed atrophy of retinal nerve fibre layer, 3 eyes (2.88%) showed splinter haemorrhage, 19 eyes (18.26%) showed bayonetting sign, 12 eyes (11.54%) showed nasal shifting of the vessels, 15 eyes (14.42%) showed NRR thinning and 3 eyes (2.88%) showed lamellar dot sign. (Chart 5)

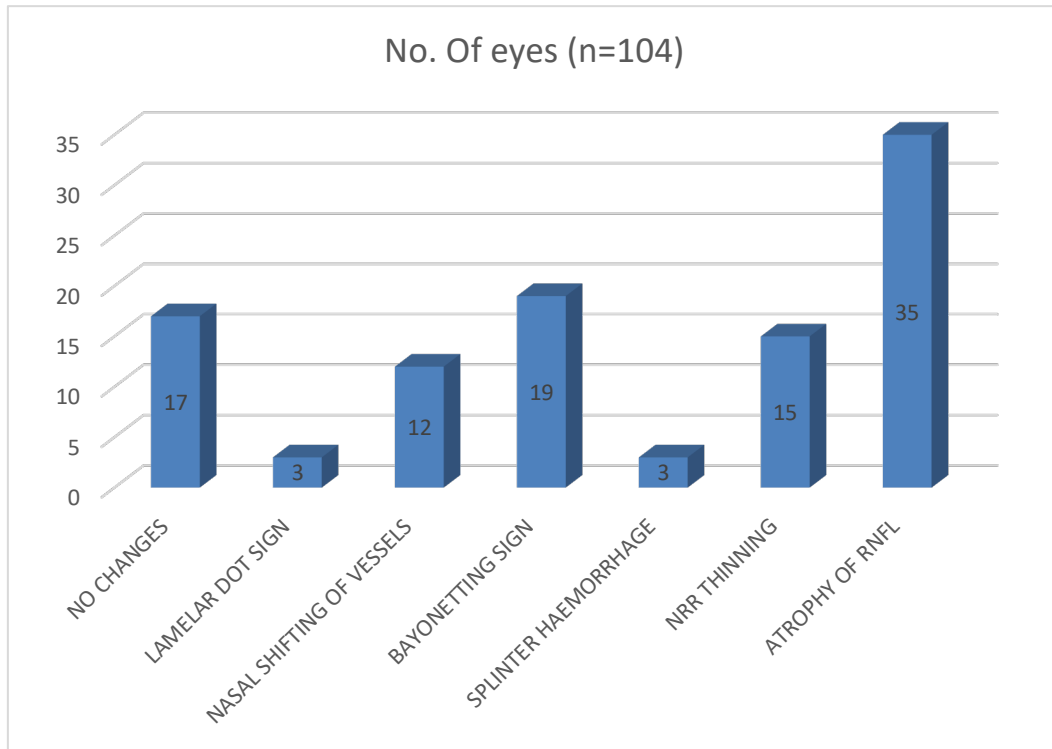


Figure 5: Bar diagram showing optic nerve head changes

DISTRIBUTION SHOWING THE RELATIONSHIP BETWEEN CUP DISC RATIO AND PERCENTAGE OF FIELD DEFECT

From the study we have seen that eyes with cup disc ratio of 0.4 or less showed no visual field defect. There was gradual increase in visual field defect with increase in cup disc size. There was 100% visual field defect when the cup disc ratio is 0.8 or more. (Table 2,3 and Chart 6)

Table 2. Showing distribution between cup disc ratio and percentage of field defect

CUP DISC RATIO	NO OF EYES N=104	EYES WITH VFD	PERCENTAGE
0.4	4	0	0.0%
0.5	16	3	18.8%
0.6	16	10	62.5%
0.7	33	30	90.9%
0.8	23	23	100.0%
0.9	12	12	100.0%

Table 3. Mean cup disc ratio (CDR) with field defect

VFD	Mean CDR	SD	p- value
NORMAL	0.53	0.09	<0.001
EGFD	0.69	0.08	
MGFD	0.83	0.06	
AGFD	0.90	0.00	
Total	0.69	0.13	

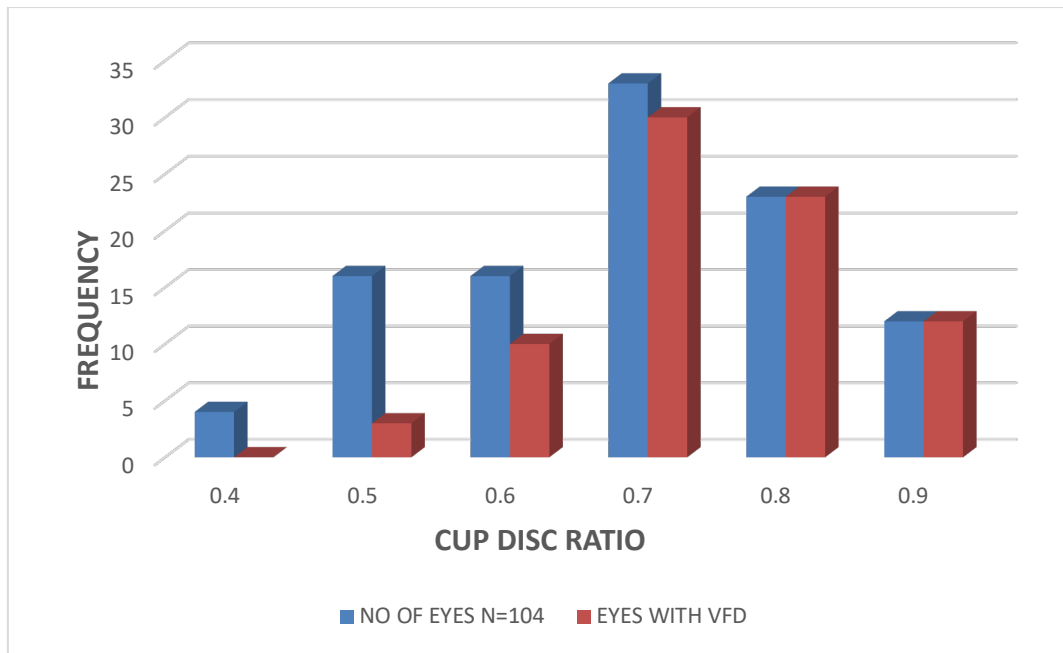


Figure 6: Bar diagram showing eyes with visual field defect

Distribution Showing Relation Of Retinal Nerve Fibre Layer With Visual Field Defects

From this table we have seen that mean RNFL thickness is 65.45 ± 12.79 and was correlated with the visual field defect in various stages of glaucoma which showed that with decrease in thickness, the visual field defect was more severe and it was statistically significant with p-value < 0.001 . (Table 4 and Chart 7)

Table 4: Showing correlation of retinal nerve fibre layer with visual field defects

VFD	Mean RNFL	SD	p-value
NORMAL	74.00	14.51	< 0.001
EGFD	65.29	8.97	
MGFD	55.70	13.01	
AGFD	59.33	7.50	
Total	65.45	12.79	

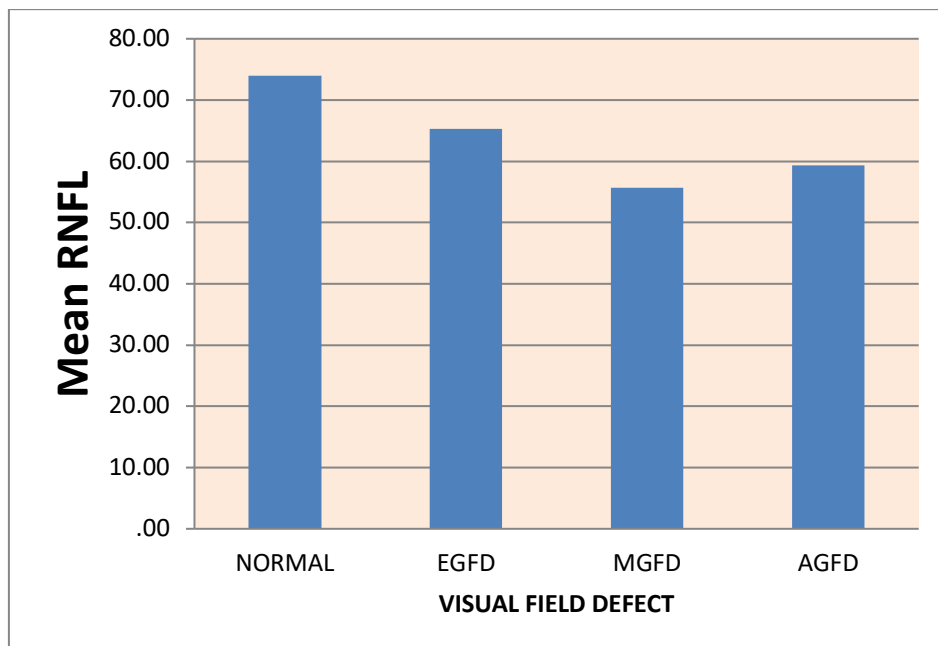


Figure 7: Bar diagram showing relation of mean RNFL with visual field defect.

Correlation Between RNFL and Mean Deviation

The RNFL thickness was correlated with the mean deviation from visual field defect in various stages of glaucoma. The relationship between RNFL thickness and mean deviation was calculated using linear regression analysis with X axis = mean RNFL and Y axis= mean deviation. The correlation coefficient was 0.443 and p-value < 0.001 which is statistically significant. (Chart 8)

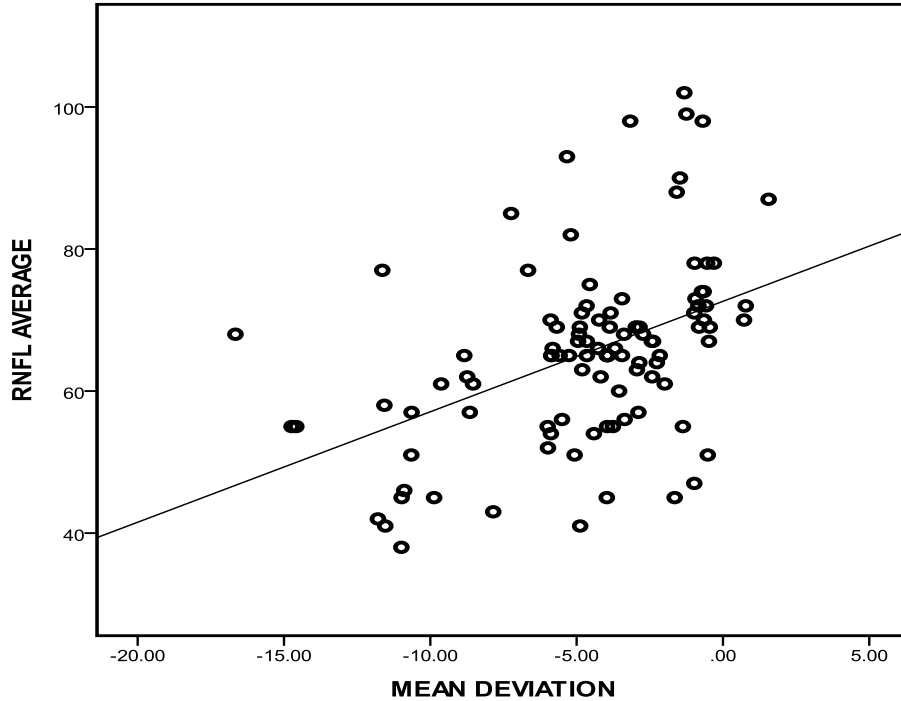
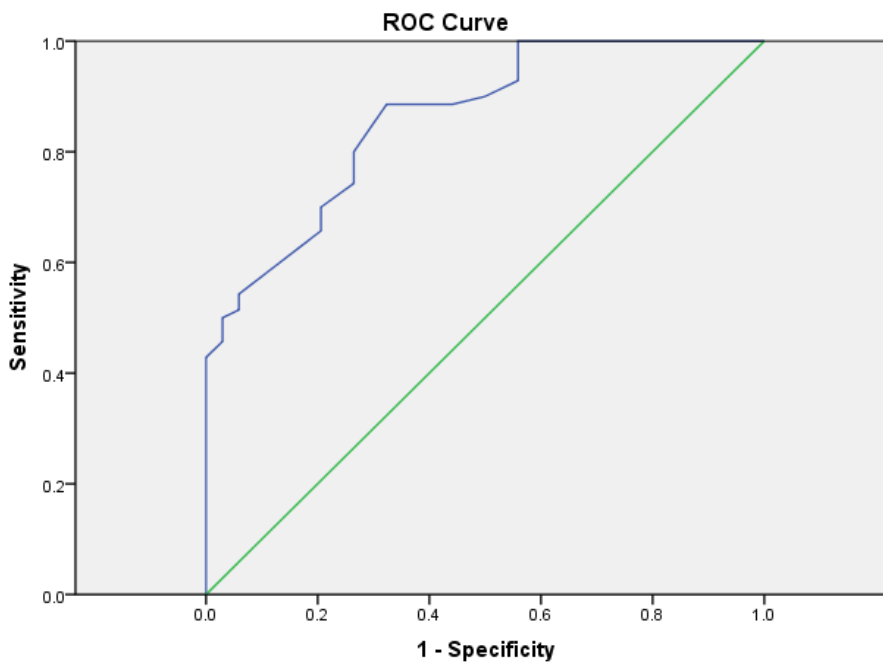


Figure 8: Linear correlation analysis between RNFL and mean deviation

Receiver Operating Characteristic Curve

CURVE 1: Area under the receiver operator characteristic curve for optical coherence tomography RNFL measurements for eyes with primary open angle glaucoma.



Diagonal segments are produced by ties.

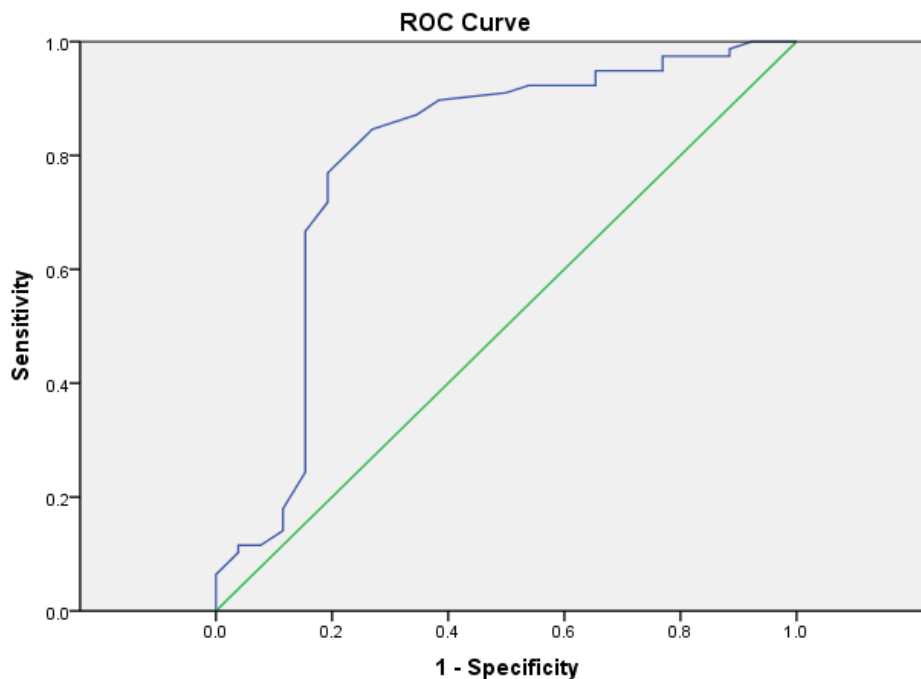
Table 5: Table showing sensitivity and specificity

Area Under the Curve				
Test Result Variable(s): RNFL Average				
Area	Std. Error	p- value	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
0.860	0.037	<0.001	0.788	0.931

Optimal Cut Of	Sensitivity	Specificty
69.5	88.60%	67.60%

The area under curve (AUC) for OCT RNFL measurements in patients with visually confirmed optic nerve head changes was 0.86 for the entire study group (Curve 1) which was both high and significant ($p < 0.001$). It showed a sensitivity of 88.60 % and specificity of 67.60%.

CURVE 2: Area under the receiver operator characteristic curves for OCT RNFL measurements in patients with Visual Field Defects by Humphrey’s field analysis.



Diagonal segments are produced by ties.

Table 6: Table showing sensitivity and specificity

Area Under the Curve				
Test Result Variable(s): RNFL Average				
Area	Std. Error	P-value	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
0.793	0.061	<0.001	0.674	0.912

Optimal Cutoff	Sensitivity	Specificty
68.5	76.90%	80.80%

The AUC for CURVE 2 is 0.793 which was also significant ($p < 0.001$). The AUC is significant enough to state that the diagnostic modality being tested (OCT RNFL measurement) is comparable with the standard diagnostic modality for diagnosing the disease (Standard automated perimetry - Humphrey’s visual field analyser). It showed a sensitivity of 76.90% and specificity of 80.80 %.

Discussion

Early detection of primary open angle glaucoma remains a challenge because the disease is absolutely asymptomatic in early stage. The assessment of the optic disc is an essential part of the evaluation of glaucoma because in most of the cases, the alterations to the optic disc begins before the loss of visual field. Therefore, early glaucoma diagnosis

is very much necessary before vision field impairments occurs.

In our study, data's have been analysed in tabular and diagrammatic form. The results of this series are now examined in the context of the available data, information, and observations compared with other researchers as well. In this study 104 eyes of 52 patients were examined and observed as per the methodology of this study.

When the age distribution was examined, we have found that the prevalence of POAG increased with age, with maximum above 70 years of age. The age of the study group had a range from 42-82 years and the mean age was 63.9 ± 10.92 years. L. Vijaya et al [8] in her study of 4800 subjects with diagnosed 132 individuals as POAG, found out that the prevalence of POAG increases with age and the mean age was 58.4 ± 11.3 years.

The relationship between gender and glaucoma has not always been as straight as one might anticipate. Results from various prevalence studies have not been conclusive in demonstrating gender predominance, with some research reporting a male POAG prevalence that is twice as high as a female prevalence or vice versa, while other studies claim no such association. In our study, we have found that the overall prevalence was higher among males (61.54%) than females (38.46%). Although the exact reason remains unclear probability that men have longer axial length [9] and deeper anterior chamber [10]. Such anatomical differences could be one of the causes of the gender difference observed in POAG.

In our study, visual field defect was measured in every case and 78 eyes showed detectable field changes and 26 eyes showed no changes in visual field at all. Over the past decade, technical and analytical advances have given us more quick and versatile approaches to evaluate visual function in glaucoma. Abnormalities in the visual field are preceded by the loss of retinal ganglion cells.

The most important risk factor for POAG is still the intraocular pressure, which is also the sole risk factor that is currently modifiable. The mean IOP of 104 eyes of 52 patients in the present study was found to be 25.44 ± 2.66 mmHg. Pankaj Soni et al [11] in their study of 114 eyes of 60 patients found mean IOP to be 27 ± 3.23 mmHg which is similar to our study. R vogel et al [12] in their study found that the visual field becomes worse with increase IOP with correlates with our study. Sommer et al [13] confirmed that IOP is an important risk factor in glaucoma in a population-based study in Baltimore Eye Survey. Lowering intraocular pressure (IOP) is the only proven way to slow or stop disease progression in people at high risk of developing glaucoma as well as those with early, moderate, or advanced glaucoma.

In our study we have found that significant number of eyes showed atrophy of nerve fibre layer. M li [14] found that RNFL atrophy was highly sensitive to glaucoma in POAG eyes with visual field loss which corresponds with our study. Clinically, it will be manifested when nearly half of the thickness of RNFL is lost. RNFL atrophy can be regarded as an important indicator in the diagnosis of glaucoma due to its high sensitivity and specificity.

The present study showed that cup disc ratio of 0.4 or less showed no visual field defect. There was a gradual increase in visual field defect with increase in cup disc size and when the cup disc ratio (CDR) is 0.8 or more, it showed 100% visual field defect. The mean cup disc ratio in 104 eyes of 52 patients was 0.69 ± 0.13 and with increase in CDR the field defect was more and statistically significant ($p < 0.001$). Pankaj Soni et al [11] in their study of 114 eyes found the mean cup disc ratio to be 0.64 ± 0.12 which is similar to our study.

The mean RNFL thickness in our study was found to be 65.45 ± 12.79 and correlated with the mean deviation from visual field defect in various stages of glaucoma. With decrease in RNFL thickness, the visual field defect increases. The relationship between RNFL thickness and mean deviation was calculated using linear regression analysis. The correlation coefficient was 0.443 and p value < 0.001 which was statistically significant. Soliman and associates [15] reported correlation coefficient 0.557 ($P < 0.001$) between average RNFL thickness and mean deviation which correlates with our study.

SPSSTM software were used to plot the receiver operator characteristic curves. In our study, we have found that the current investigation demonstrates a strong correlation between the detection of glaucomatous optic nerve head alterations by fundus evaluation and RNFL thinning determined by OCT ($p < 0.001$). OCT was able to show RNFL thinning even in cases where the existence of POAG could not be determined by visual field changes. This implies that OCT could detect early glaucoma.

When OCT RNFL was compared with standard automated perimetry, Humphrey field analysis. The area under curve was 0.793 for RNFL thickness in eyes with visual field defects, suggesting significant correlation between the two ($p < 0.001$). According to earlier research [16], the RNFL as evaluated by OCT was markedly thinned in regions that coincided with areas of visual field loss. The current study also demonstrated that the OCT RNFL measures perform better as a diagnostic test than the conventional automated perimetry, with an area under curve (AUC) for the receiver operator characteristic (ROC) curve of OCT RNFL in optic nerve head changes was 0.860 which was greater than the AUC for the ROC curve of OCT in visual field abnormalities was 0.793. Many recent studies have

used the Receiver Operator Characteristic curve to demonstrate the accuracy of the diagnostic test, and the figures for the area under the curve are similar. Budenz DL et al [17] in his study of 109 normal and 63 glaucoma subjects found that the mean RNFL thickness alone has a sensitivity of 84% and a specificity of 98% whereas in our study we found a sensitivity of 88.60 % and specificity of 67.60%. William ZY et al [18] in his study determine ROC curves are being utilised to see if OCT measures of RNFL thickness may be used to predict the existence of visual field abnormalities in glaucoma. Patients with visual field defects had an RNFL Area under the curve of 0.73, which was determined to be significant. We have found a similar result with AUC of 0.793 and was significant.

Conclusion

The current study demonstrated that OCT RNFL thickness measurements are a reliable and sensitive diagnostic modality for early detection of primary open angle glaucoma. In our study we have found that the OCT RNFL measures perform better as a diagnostic test than the conventional automated perimetry (Humphrey Field Analysis), with an AUC for the ROC of OCT in optic nerve head changes is 0.860 which is greater than the AUC for the ROC of OCT in visual field abnormalities is 0.793. It is useful in diagnosing patients who have early optic nerve head changes in comparison to Humphrey's visual field analysis. The fact that many patients with normal automated perimetry showed notable RNFL thinning by OCT which gives light to the early diagnosis and prognostic factors. Thus, it implies that RNFL thinning determined by OCT is comparatively superior to the HFA in the individuals with early primary open angle glaucoma and glaucoma suspects who generally exhibit normal visual fields (HFA) by routine automated perimetry. OCT in POAG should therefore be taken into consideration for early detection even before visual field changes manifest. The drawback of the study is that OCT is a costly machine and is not available in all the centres, the study group was small and for a short duration so it did not represent an adequate population.

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