Reviving the Role of Optical Coherence Tomography and Visual Field Analysis as Investigative Tools for Diagnosis of Primary Open-Angle Glaucoma in Rural Tertiary Care Centre

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Abstract

Background: Glaucoma is the second most common cause of blindness globally and is characterised by raised intraocular pressure, optic disc cupping, and visual field defects. However, advanced imaging modalities such as optical coherence tomography (OCT) can pick up early changes. Our study aims to examine the role of OCT for the early diagnosis of primary open-angle glaucoma (POAG), its correlation with standard automated perimetry, and the diagnostic efficiency of both in POAG patients at a rural tertiary care centre in the Chengelpet District. **Materials and Methods:** This was a prospective observational study comparing the quantitative measurement of RNFL using OCT with functional loss analysed using the Automated Perimetry Humphrey Visual Field Analyzer in patients with POAG visiting the tertiary health centre in the Chengelpet district in Tamil Nadu. The study was conducted in 92 eyes of 50 patients diagnosed with POAG for 15 months from March 2022 to May 2023. **Results:** Of the 92 eyes of 50 patients, 26 were male patients and 24 were female patients. In total, 21 eyes had no demonstrable visual field defect, 49 eyes had single hemifield defect and 22 eyes had both hemifield defect. The area under the receiver operator characteristic curve for OCT RNFL layer measurement in patients diagnosed with visually confirmed ONH changes was 1.00, which was highly significant (P value = 0.01) and correlated well with the type of visual field defect with Humphrey's automated perimetry, suggesting significant correlation between the two. OCT–RNFL measurements are better diagnostic tests than standard automated perimetry for the early detection of glaucoma. **Conclusion:** Both OCT RNFL and Humphrey's automated visual field analysis play a most crucial role as an investigative modality for early diagnosis of POAG; however, OCT has an added advantage of detecting early glaucoma changes even without visible field changes and hence useful for very early detection of POAG in a tertiary care centre.

Keywords: OCT-RNFL, primary open-angle glaucoma (POAG), visual fields

Introduction

Glaucoma is defined as optic neuropathy characterised by programmed retinal ganglion cell apoptosis resulting in structural changes in the form of thinning of the neuroretinal rim causing circumferential enlargement of the cup or notching and functional changes in the form of visual field defects. Glaucoma has become the second most common cause of bilateral blindness[1] worldwide with more than three million people getting blind from primary open-angle glaucoma and two million developing POAG every year. Glaucoma contributes to 13% of blindness in India.[2] Glaucoma can be open-angle or closed-angle type, which may be primary or secondary, of which primary open-angle glaucoma (POAG) is common and often undiagnosed as it is generally asymptomatic and often undetected and can cause permanent loss of vision. To date, a POAG has high prevalence (2.4%) worldwide, affecting 68.56 million adult people of age above 40 years.[3]

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Population-based data suggest that 4% of the population is affected by glaucoma,[4,5] and based on previous studies,[6-8] it was found that there is a higher incidence of POAG in rural areas due to a lack of awareness in the community. Robin *et al.,*[9] in his study, found there was underutilisation of eye care services in patients with glaucoma in rural areas of southern India and there is a need for effective strategies to improve the uptake of services to reduce the burden of blindness due to glaucoma. Additionally, the asymptomatic nature of the disease, lack of follow-up and compliance with treatment may add to glaucoma prevalence in rural areas.

Hence, the need for effective screening of patients for glaucoma especially POAG is essential and early diagnosis by optic disc imaging, gonioscopy and visual field analysis by perimetry plays a crucial role in effective and successful treatment. Although clinical examination of the optic nerve head is a sensitive test for glaucoma detection, evidence suggests that the examination of the retinal nerve fibre layer (RNFL) may provide important diagnostic information[10] as RNFL loss occurs before detectable visual field defects can be measured,[11] which can be detected precisely by optical coherence tomography (OCT). With the advent of OCT, which is a non-invasive, non-contact method that allows cross-sectional, *in vivo* imaging of the intraretinal layer and also quantitatively assess the RNFL thickness,[12,13] we can assess the pre-existing damage in the early stages so that progression can be halted. This is an added advantage, especially for people residing in rural areas for much early detection of POAG. Our purpose of the study is to quantitatively assess the RNFL using OCT and correlate it with standard automated perimetry in eyes with POAG and their role as a diagnostic modality in identifying POAG in the rural areas of the Chengelpet District in Tamil Nadu.

Materials and Methods

This was a prospective study to quantitatively measure the peripapillary RNFL using OCT and compare it with standard automated perimetry using the Humphrey Visual Field Analyzer in patients with POAG. The study was undertaken at Shri Satya Sai Medical College and Research Institute, Ammapettai, Chengelpet district, Tamil Nadu. The sample size was calculated using the OenEpi online software, based on the previous study[14] The total sample size was 92 in the current study. The study was conducted for 15 months from March 2022 to May 2023, during which 92 eyes of 50 patients were studied and analysed. Ethical committee approval from the Institute obtained on 22-9-2022.

Both male and female patients between 40 and 70 years of age, patients with clear media where OCT–RNFL analysis was possible those who could cooperate enough to perform automated perimetry were included in the study. We excluded patients with absolute glaucoma, neuro-ophthalmic field defects, non-dilating pupils, central nervous system or spinal problems that could interfere with test performance.

All patients were subjected to a complete ophthalmological examination, which included refraction, slit-lamp examination, gonioscopy, dilated +90 D examination, ONH photographs, intraocular pressure measurement using the Goldmann applanation tonometry and pachymetry.

The glaucomatous disc was identified based on neuro-retinal rim (NRR) thinning,[15] which can be generalised (diffuse) loss or focal loss of NRR (notching) and the sequence of loss is usually first in the inferotemporal and superotemporal disc regions in early glaucoma, temporal part of the horizontal disc for moderate glaucoma, and rim remnants mainly in the nasal sector in advance glaucoma, presence of disc hemorrhage, excavation and asymmetry of vertical cup disc ratio of greater than 0.2 between two eyes with evidence of open angles on gonioscopy. All patients in the study were subjected to field examination using Humphrey perimeter and OCT-RNFL analysis. Diagnosis of POAG was established based on the above findings by two independent investigators and both were not shown field defects and OCT-RNFL data to avoid bias.

Standard automated perimetry was conducted using Humphrey's field analyzer (Zeiss model 750) using the 24-2 program with a Goldman size III (0.430) stimulus on a 31.5 apostilb background.

All tests were reliable (with false positives, false negatives ≤33% and fixation loss ≤20%), and diagnosis of glaucomatous visual field [Figure 1] was established based on Anderson's criteria.

a. A cluster of 3 or more adjacent non-edge points depressed found in less than 5% of the population (i.e., P <5%) concentrated more in the arcuate area.
b. Pattern standard deviation found in less than 5% of the population (i.e., P <5%).
c. Glaucoma hemifield test outside normal limits.

OCT was performed using the Stratus OCT III machine (Stratus OCT Model 3000 OCT III, Zeiss Co., Oberkochen, Germany), which used low coherence illumination (840 nM) with a tissue resolution of 10–15 µs. The OCT RNFL thickness was analysed based on colour coding [Figure 2] according to the age-related normal of the population. In all, 95% of the normal population falls in or below the green band and 90% falls within the green band, 5% of the normal population falls within or below the yellow band, 1% falls within the red band and is considered outside the normal limit. RNFL thickness measurements were outside normal limits [Figure 3] if they were thinner than 97.5% of normal values derived from healthy eyes in the normative database of our clinic.

Statistical analysis was performed using SPSS and STRATA software and descriptive statistics and analysis of variance (ANOVA) for comparison of means. A ROC curve also performed in the study with a 5% level of significance and 95% confidence interval.

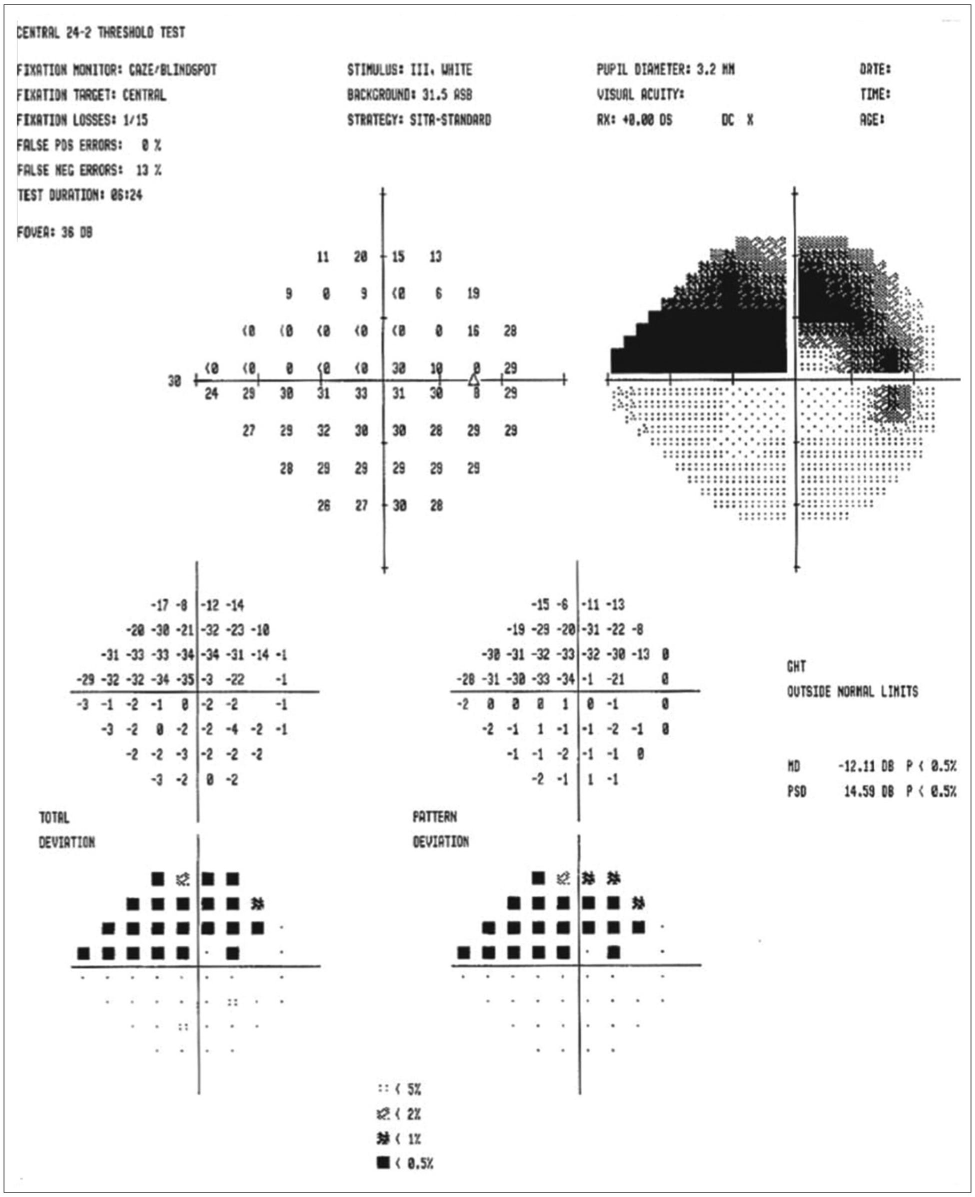

Figure 1: Glaucomatous field defect

Results

Of 92 eyes of 50 patients diagnosed with primary open-angle glaucoma, both eye examination was performed in 42 patients, and one eye examination was performed in 8 patients.

The other eye examination was excluded in 8 patients due to dense media opacity (cataract) in 5 patients, advanced glaucoma in 2 patients and phthisis bulbi in 1 patient.

The mean age of the patient was 61.07 ± 8.868 years [Table 1] with 50 eyes examined in males with and 42 eyes in females with gender ratio of 54.3% and 45.7% respectively [Table 2 and Figure 4].

Of the 92 eyes, 21 eyes had no demonstrable visual field defect, 22 eyes had field defect in both hemifields, and 49 eyes had defect in single hemifield [Table 3a and Figure 5]. The ANOVA for the mean deviation in these three groups of eyes (no visual field defect, single hemifield visual field defect and both

Table 1: Age distribution

	n	Minimum	Maximum	Mean	Std. deviation
Age in years	92	41	70	61.07	8.868

Table 2: Sex distribution

	Sex	Frequency	Percentage
Valid	Male	50	54.3
	Female	42	45.7
	Total	92	100.0

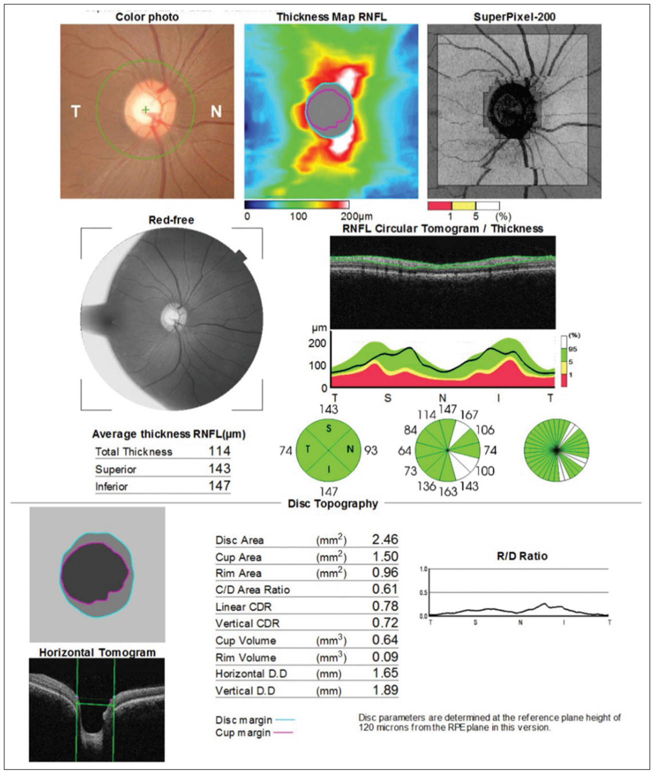

Figure 2: Normal OCT RNFL

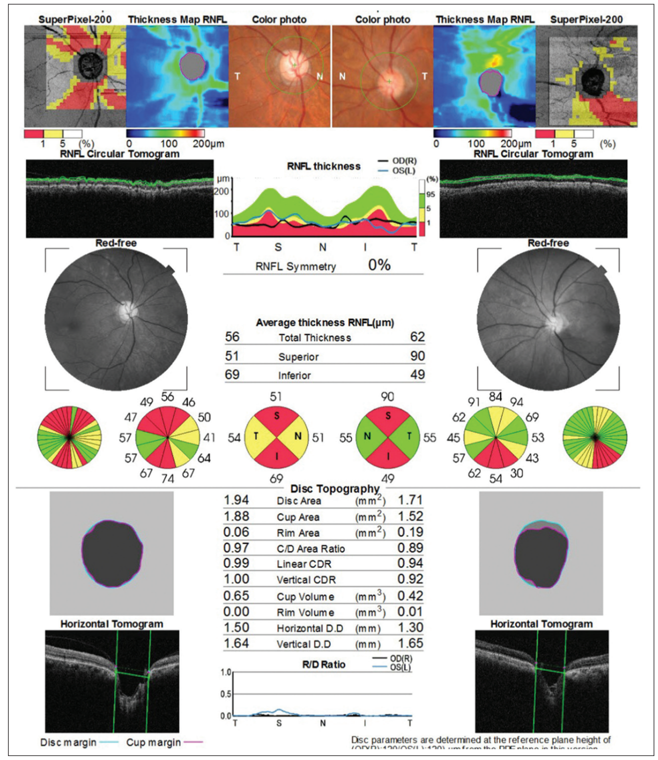

Figure 3: Glaucomatous RNFL defect

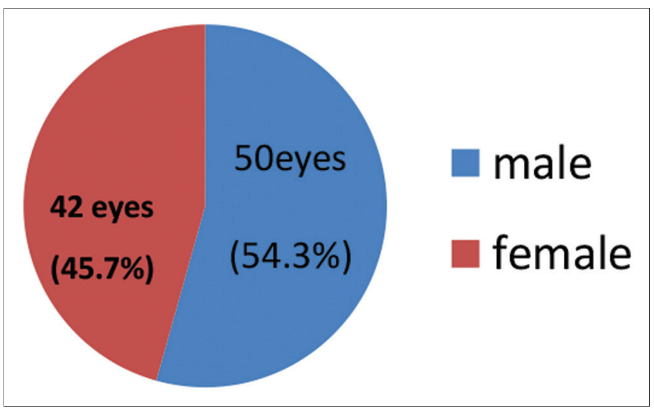

Figure 4: Sex distribution

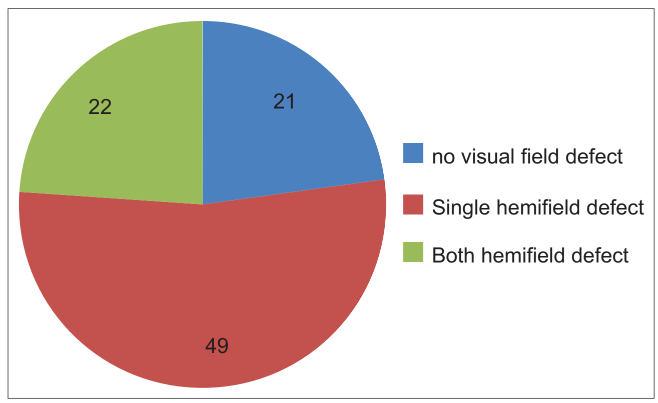

Figure 5: Distribution of field defects in 92 eyes

hemifield visual field defect) was significant (*P* value < 0.000) [Table 3a] and pattern deviation in these three groups (no visual field defect,single hemifield visual field defect and both hemifield visual field defect) was statistically insignificant (*P* value = 0.605) [Table 3b]. The average mean deviation for these eyes was −8.7735 [Table 3a] and the average pattern deviation was 10.23 [Table 3b].

The ROC curve was plotted using SPSS™ and STRATA software. For the entire study group, the area under the ROC curve (AUC) for OCT RNFL layer measurement in patients diagnosed with visually confirmed ONH changes was 1.00 [Chart 1], which was highly significant (*P* value = 0.01). OCT measurement correlated well with the type of visual field defects. Higher AUCs were found for areas that corresponded to the location of visual field defects (AUC = 0.949) [Chart 2]. Measurements of superior RNFL thickness were significant in predicting the presence of inferior visual field defects (AUC = 0.75) [Chart 3], and the measurement of inferior RNFL thickness was significant in predicting the presence of superior visual field defects (AUC = 0.645) [Chart 4]. However, when compared to superior RNFL measurements, inferior RNFL measurements appeared to be slightly less accurate in predicting visual field defects.

Test result variable (s): OCT

The AUC is highly significant to state that the test (OCT peripapillary NFL measurement) is accurate in diagnosing the disease (POAG).

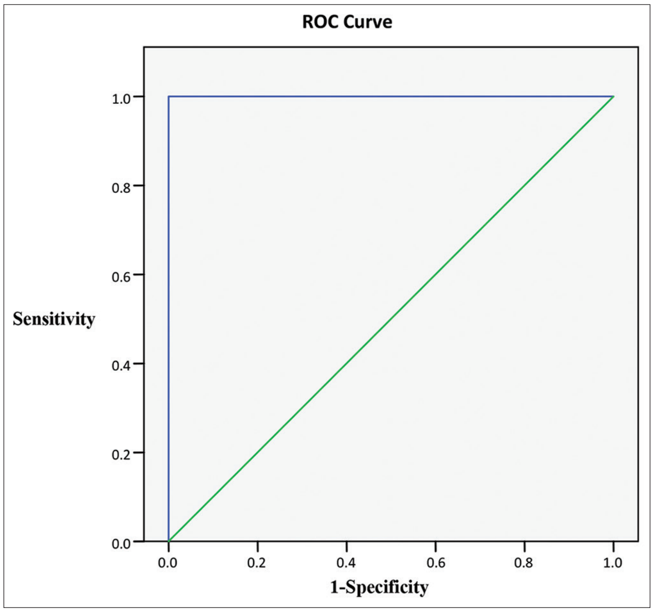

Chart 1: Area under the ROC curve for OCT peripapillary nerve fibre layer measurement ofeyes with POAG

Area	Std. Error (a)	Asymptotic Sig.(b)	Asymptotic 95% confidence interval	
			Lower bound	Upper bound
1.000	0.000	0.001	1.000	1.000

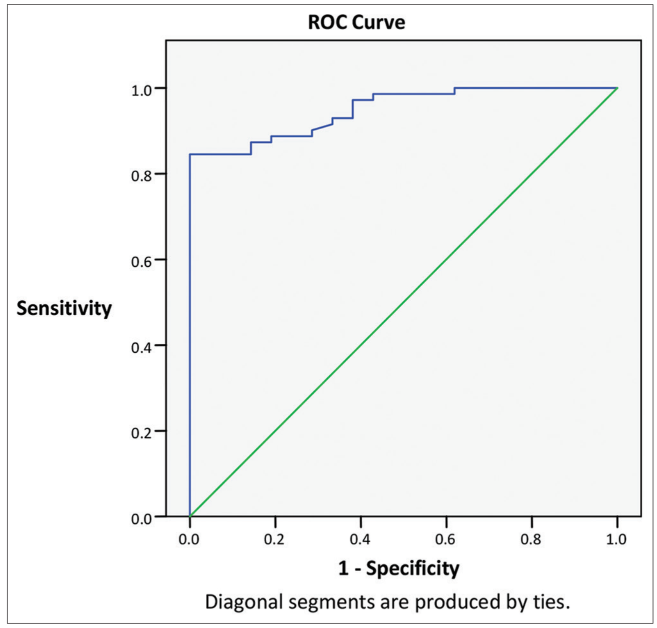

Chart 2: Area under the ROC curve for OCT peripapillary nerve fibre layer measurement in a patient with visual field defect by Humphrey's field analysis

Area	Std. Error (a)	Asymptotic Sig.(b)	Asymptotic 95% confidence interval	
			Lower bound	Upper bound
0.949	0.021	0.000	0.909	0.990

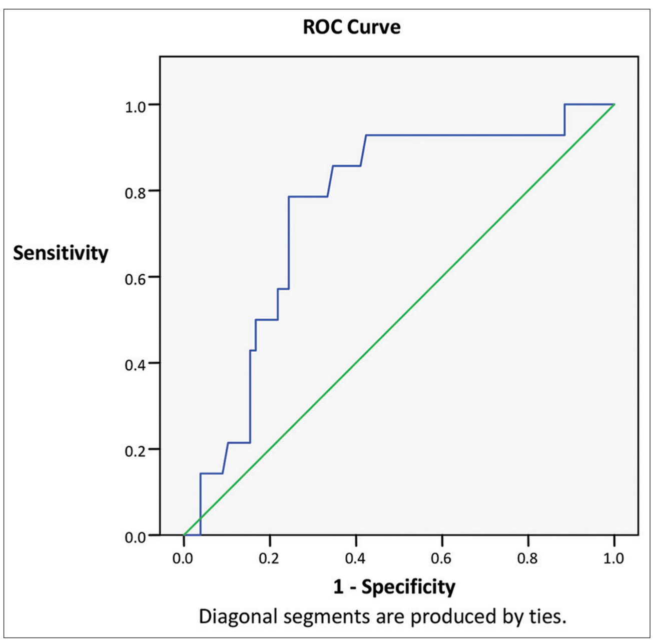

Chart 3: Area under the ROC curve for OCT superior peripapillary nerve fibre layer measurement in patients with inferior hemifield defects

Area	Std. Error (a)	Asymptotic Sig.(b)	Asymptotic 95% confidence interval	
			Lower bound	Upper bound
0.758	0.065	0.002	0.631	0.884

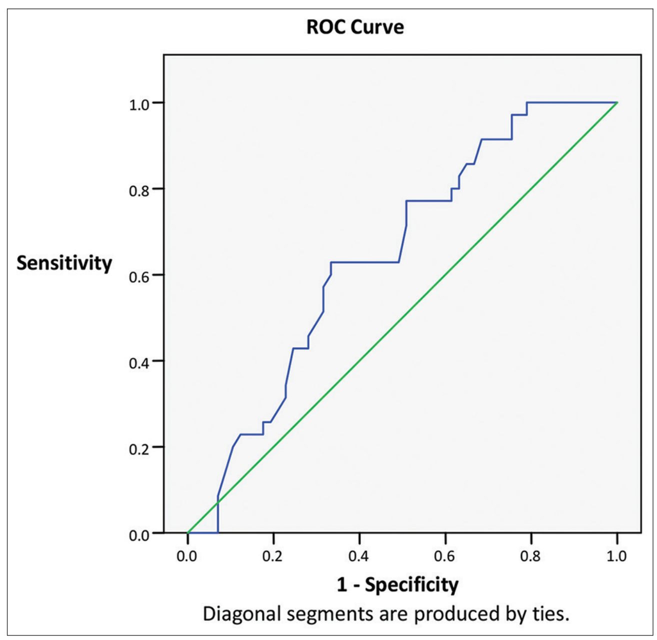

Chart 4: Area under the ROC for OCT inferior peripapillary nerve fibre layer measurement in patients with superior visual field defect

Area	Std. Error (a)	Asymptotic Sig.(b)	Asymptotic 95% confidence interval	
			Lower bound	Upper bound
0.645	0.057	0.020	0.533	0.757

Table 3a: Distribution of visual field defect

Mean deviation			
	N	Mean	Std. deviation
No visual field defect	21	−2.9471	3.17312
Single hemi field defect	49	−6.7045	4.80354
Both hemi field defect	22	−18.9432	10.27682
Total	92	−8.7735	8.59640

ANOVA-mean deviation					
	Sum of squares	Df	Mean square	*F*	Sig.
Between groups	3197.928	2	1598.964	40.350	0.000
Within groups	3526.801	89	39.627		
Total	6724.729	91			

Table 3b: Pattern deviation

	N	Mean	Std. deviation
No visual field defect	21	2.7886	1.95959
Single hemi field defect	49	14.5773	64.03855
Both hemi field defect	22	7.6550	2.49837
Total	92	10.2311	46.79716

ANOVA-pattern deviation					
	Sum of squares	Df	Mean square	*F*	Sig.
Between groups	2234.818	2	1117.409	0.505	0.605
Within groups	197052.800	89	2214.076		
Total	199287.618	91			

Test result variable (s): OCT

The AUC) is highly significant to state that the diagnostic modality being tested (OCT peripapillary nerve fibre measurement) is comparable with the standard diagnostic modality (standard automated perimetry-Humphrey's visual field analyzer) for diagnosing the disease (POAG).

Test result variable (s): Smax

The AUC is significant to state that the OCT superior peripapillary nerve fibre layer measurement corresponded well with the presence of an inferior field defect.

Test result variable (s): Imax

The AUC is significant to state that OCT inferior peripapillary nerve fibre layer measurement corresponds well with superior hemifield defect.

Discussion

This study was performed to emphasise the usefulness of OCT and automated perimetry in the diagnosis and management of POAG, especially in rural areas. The study evaluated the association between functional and structural damage of peripapillary RNFL thickness by automated perimetry and OCT. The current study showed a significant correlation between RNFL thinning measured by OCT and glaucomatous disc changes detected on fundus examination ($P = 0.01$). High AUC (1.00) was found in ROC for the peripapillary RNFL thickness in patients with POAG.

In a significant number of eyes, that is 21 eyes, RNFL thinning could be demonstrated by OCT even in the absence of glaucomatous visual field changes detected by the Humphrey perimeter. Hence, OCT could predict the onset of optic nerve head changes much before they became structurally visible and could be very useful for diagnosing pre-perimetric glaucoma in rural setups. The correlation of quantitative assessment of RNFL thickness with conventional measurement of optic nerve structure and function has been studied by several authors.[16-18] Bowd *et al.,*[17] in his study of 87 eyes, concluded that RNFL thickness was significantly thinner in glaucomatous eyes than in normal eyes in each quadrant. The study also mentioned that among all quadrants, the inferior quadrant measured NFL defects showed the closest relationship to glaucoma status, followed by the superior quadrant NFL defect.

When OCT was compared with current Humphrey's automated perimetry, the AUC was 0.949 for RNFL thickness in eyes with field defect, suggesting a significant correlation between the two, which correspondingly matches with the previous studies.[19,20]

In our study, we compared the RNFL thickness in superior and inferior poles (i.e., Smax and Imax respectively) as they are most related to glaucomatous visual field defect areas, and comparing them with corresponding visual field zones may provide more specific results of the correlation. Several authors[21,22] have concluded that the RNFL thinning is common in the inferior pole followed by the superior pole and we assessed these two specific areas.

The current study also showed a higher AUC for the ROC of OCT in optic nerve head changes (1.00) than the AUC for visual field defects (0.949), pointing to the fact that OCT–RNFL measurements are a better diagnostic test than standard automated perimetry, which is documented in earlier studies[23,24] and can be a boon for people residing in rural areas where recent diagnostic facilities are non-accessible. This is also supplemented by the fact that 21 eyes with normal automated perimetry showed significant RNFL thinning in OCT and hence, OCT should be considered in early glaucoma and glaucoma-suspected patients who may otherwise show normal visual fields by standard automated perimetry.

Glaucoma patients could suffer a loss (approximately 40%) of retinal ganglion cell axons before an automated perimetry visual field defect is evident.[10] Hence, an advanced imaging modality such as OCT is warranted in the early detection and appropriate treatment of eyes with POAG before valuable ganglion cells and visual fields are lost permanently.

The ROC curve for inferior hemifield defects with superior hemiretina NFL thinning showed a significant AUC (0.758); however, the AUC for superior hemifield with inferior hemiretinal

NFL thinning was (0.645), which is less sensitive compared to inferior hemifield defect. This is in contrast to previous studies that showed most sensitive NFL areas to be inferior and inferotemporal areas. This might be because of a smaller number of superior hemifield visual field defect cases, which artificially appear to decrease its diagnostic efficiency. Also, the study conducted by Choi *et al.*[25] conclude that a superior RNFL defect associated with inferior hemifield loss was wider than an inferior RNFL with superior hemifield loss, which could be a reason for slightly higher sensitivity in superior RNFL defects.

The limitation of this study is the lack of age-matched control from the normal population as it uses the pre-existing normative database of the machine in presenting the population of the clinic. The inclusion of glaucoma suspects and ocular hypertensive patients in subsequent trials of glaucoma diagnosis would make the use of OCT more rewarding and provide the glaucoma specialists with an invaluable weapon in the armamentarium in a rural setup.

Conclusion

The current study establishes the fact that OCT RNFL thickness measurement provides an accurate and sensitive tool for detecting POAG. Changes detected in OCT corresponded well with visual field defects detected by Humphrey's automated perimetry. Furthermore, the study proves that OCT–RNFL analysis is effective in diagnosing patients who have early disc changes suggestive of glaucoma even before apparent visible field changes. Hence, the use of OCT–RNFL in POAG and the Humphrey visual field analyzer should be considered to the patient's advantage, especially in rural areas as they reduce the burden of glaucoma prevalence in the community. However, regular follow-up with IOP assessment, repeat visual field and OCT peripapillary NFL examination are required to monitor the treatment response and arrest the progression as glaucoma patients need life-long follow-up.

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Conflicts of interest

There are no conflicts of interest.

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