Correlation Among Optic Nerve Head Changes, Visual Field Changes and Retinal Nerve Fiber Layer Thickness in Primary Open Angle Glaucoma

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Original Research Article

ABSTRACT

A prospective cross-sectional non interventional type of study was conducted among cases of primary open glaucoma (POAG).The purpose of the study was to understand correlation among optic nerve head changes, visual field changes and retinal nerve fiber layer thickness in cases of primary open angle glaucoma. This study, conducted among 72 patients with 138 eyes, established a positive correlation between mean vertical CDR (r 0.5726) as compared with mean RNFL thickness and a negative and weak positive correlation between mean vertical CDR compared to visual field parameter mean defect MD (r -0.2364) and PSD (r 0.3516) respectively. The p value between CDR and RNFL thickness was 0.00001, which was statistically significant.

KEY WORDS: optic nerve head (ONH), primary open angle glaucoma (POAG), retinal nerve fiber layer (RNFL), visual field (VF)

INTRODUCTION:

Primary open angle glaucoma (POAG) is the most common type of glaucoma. POAG can be considered chronic progressive optic neuropathy which is accompanied by a characteristic cupping and atrophy of the optic disc, visual field (VF) loss, open angles and no obvious ocular or systemic reason. The disease is characterized by progressive loss of retinal ganglion cells and their axons associated with tissue remodelling in the optic nerve head (ONH). The concepts and definitions of glaucoma have evolved in the past 100 years[1]and still they remain imprecise and subject to technical qualifications. Glaucoma is a leading cause of irreversible blindness throughout the world. World Health Organization statistics, published in 1995, indicate that glaucoma accounts for blindness in 5.1 million persons, or 13.5% of global blindness (behind only cataracts and trachoma at 15.8 million persons, or 41.8% of global blindness, and 5.9 million, or 15.5%, respectively) [2]. Worldwide, it has become the second most common cause of bilateral blindness. Open-angle glaucoma and angle-closure glaucoma were estimated to affect approximately 66.8 million persons by the year 2000, with 6.7 million experiencing bilateral blindness[3]. The word glaucoma originally meant 'clouded' in Greek; as such, it may have referred either to a mature cataract or to corneal edema that might result from chronic elevated pressure. Today the term does not refer to a single disease entity, but rather to a group of diseases that differ in their clinical presentation, pathophysiology, and treatment. These diseases are grouped together because they share certain features, including cupping and atrophy of the optic nerve head, which has attendant visual field loss and is frequently related to the level of intraocular pressure (IOP).

Whether manifesting as POAG, primary angle-closure, or congenital disease, glaucoma is the second leading cause of blindness worldwide, with a disproportional morbidity among women and Asians [4-7]. The major mechanism of visual loss in glaucoma is retinal ganglion cell apoptosis, leading to thinning of the inner nuclear and nerve fiber layers of the retina and axonal loss in the optic nerve. The optic disc becomes atrophic, with enlargement of the optic cup. Diagnosing POAG requires evaluation of IOP, the anterior chamber angle (by gonioscopy), optic disc, and visual field. In glaucoma, there may be concentric enlargement of the optic cup or preferential superior and inferior cupping with focal notching of the rim of the optic disc. As cupping develops, the retinal vessels on the disc are displaced nasally (Figure1). Typical

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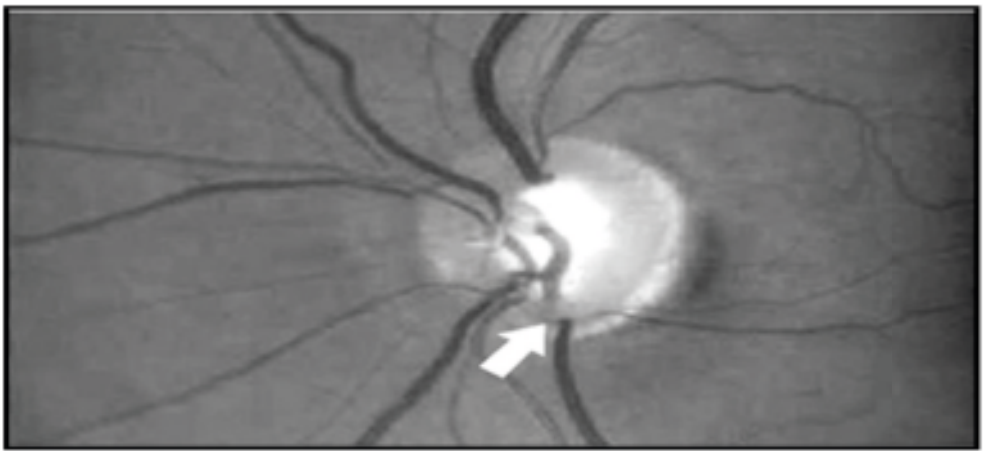


Figure 1: Early glaucoma showing inferior focal notching of the neuroretinal rim (arrow).

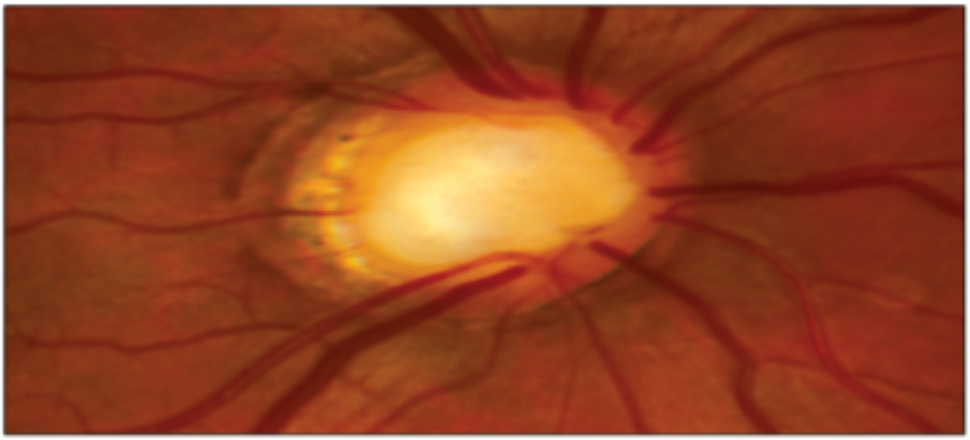


Figure 2: Typical glaucomatous cupping in right eye.

glaucomatous cupping in right eye (Figure 2).

Glaucomatous field loss involves mainly the central 30 degrees of field (Figure 2,3). The earliest change is baring of the blind spot. Contiguous extension into Bjerrum's area of the visual field at 15 degrees from fixation-produces a Bjerrum scotoma and then an arcuate scotoma. Focal areas of more pronounced loss within Bjerrum's area are known as Seidel scotomas. Double arcuate scotomas above and below the horizontal meridian are often accompanied by a nasal step (of Roenne) because of differences in size of the two arcuate defects. Peripheral field loss tends to start in the nasal periphery as a constriction of the isopters. Subsequently, there may be connection to an arcuate defect, producing peripheral breakthrough. The temporal peripheral field and the central 5-10 degrees are affected late in the disease.

***Optical Coherence Tomography (OCT) findings in POAG*:**

Optic Nerve Head Changes: The *optic nerve head,* or *optic disc,* is usually round or slightly oval in shape and contains a central *cup.* The tissue between the cup and the disc margin is called the *neural rim* or *neuroretinal rim.* In normal individuals, the rim has a relatively uniform width and a color that ranges from orange to pink.

Retinal Nerve Fiber Layer (RNFL) thickness: RNFL thinning is a sensitive indicator of the extent of glaucomatous damage and that RNFL loss precedes measurable ONH and VF damage approximately six years before any detectable VF defects. Thus, the possibility of detecting these defects in areas of physiological decreased visibility is enhanced, when OCT is used. Accurate and objective methods of detecting disc and RNFL abnormalities, and their progression, would facilitate the diagnosis and monitoring of glaucomatous optic neuropathy.

MATERIALS & METHODS:

Total 72 patients (6 patients, uniocular) were included in this study which was conducted in

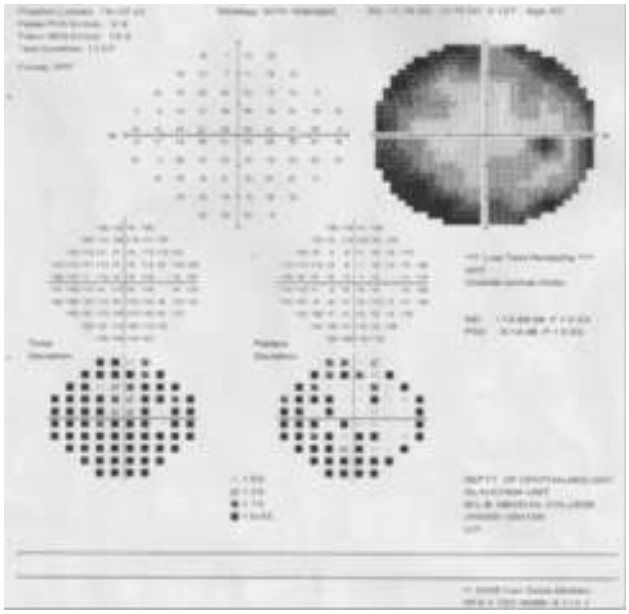


Figure 3: Perimetry report of patient's Right eye.

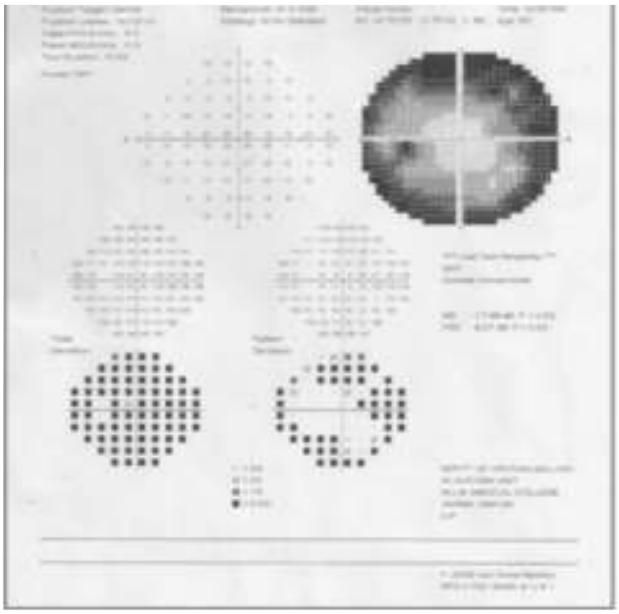


Figure 4: Perimetry report of patient's left eye.

Department of Ophthalmology, MLB medical college, Jhansi, India over a period of 18 months (i.e. April 2018 to September 2019). All procedures were followed according to Helsinki Declaration of 1975, as revised in 2000. The necessary permission from the Ethical and Research Committee was obtained for the study.

The POAG patients were included if the following inclusion criteria was satisfied: (a) Age ≥40 years; (b) Known/ newly diagnosed patient with unilateral or bilateral primary open angle glaucoma with either (i) Visual acuity or Best corrected visual acuity 6/24; or (ii) Elevated intraocular pressure (IOP) (greater than 21mm Hg) on at least two separate visits; or (iii) Glaucomatous optic disc appearance; (c) Wide and open angle on gonioscopy with goldmann gonio lens[Grade 3 and above by Shaffer, classification]; and (d) Those who were physically fit for perimetry and OCT evaluation.

The criteria for exclusion were: (a) Age < 40years; (b) Patients with diabetes, hypertension or any other chronic disorders like uveitis, retinal detachment or retinal vascular disorders; (c) Other forms of glaucoma like acute angle closure glaucoma, steroid induced glaucoma etc (all forms of secondary glaucoma); (d) History of ocular trauma and Recent ocular surgery (<6 months); (e) Patients with very high refractive error more than [± 5.0 D]; (f) Pregnancy or Lactation.

All the patients reported in Out Patient Department of Ophthalmology were evaluated, as per inclusion and exclusion criteria of the study, for diagnosis of primary open angle glaucoma. The status of each patient was evaluated by Slit lamp examination, Visual Acuity, Best Corrected Visual Acuity (BCVA), Intra Ocular Pressure by Non Contact Tonometer, Fundus examination (clinical vertical CDR), OCT(VCDR and RNFL Thickness (Retinal nerve fiber layer Thickness),and Perimetry (Visual field parameters i.e. Mean Deviation (MD), Pattern Standard Deviation (PSD). Quantitative data as mean and qualitative variables were expressed using percentage. The Student's paired 't" test for equal or unequal variances was used. The p-value of < 0.05 for one - tailed hypothesis was considered statistically significant to reject the 'null hypothesis', if the t test value or the observed difference between two means is greater than 2 times of standard error of difference (SED), the 5% level of significance. All statistical calculation/descriptive analyses were made with the help of data analyses tool of Microsoft Excel 2016 as shown below: Calculation of total sum, mean/average & standard deviation (SD) of each data group. Obtaining p value between study parameter by student's paired t-test of two independent mean. Scatter diagram also made for showing correlation in VCDR and RNFL Thickness, VCDR and MD (Visual field parameter) VCDR and PSD (Visual field parameter). Calculation of correlation coefficient(r) of both eyes data by Pearson's Correlation Coefficient formula. The Pearson's coefficient (r) can take range of values from +1 to -1.

The patient's protocols were recorded in data collection form and all values were taken from raw

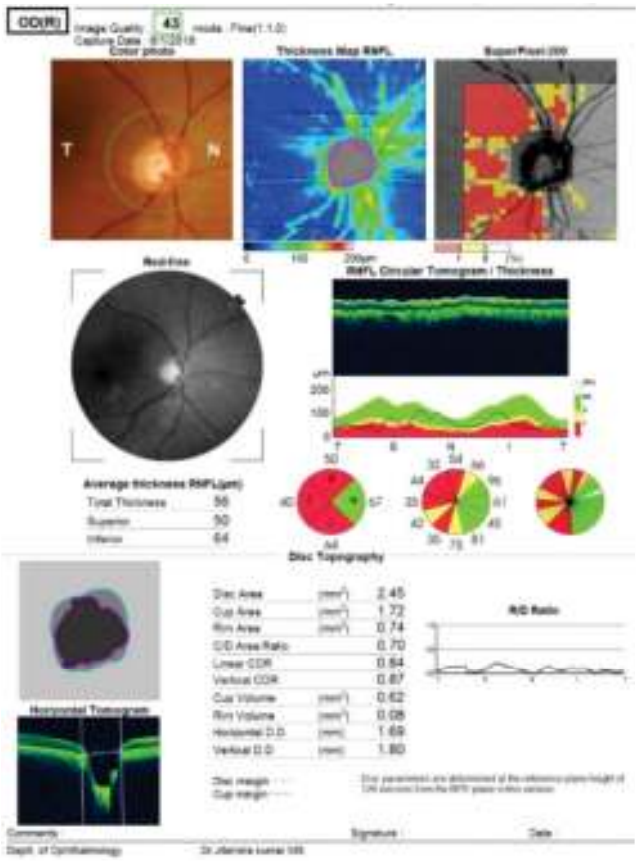


Figure 5. OCT –Inferior ,superiorand temporal thinning (right Eye).

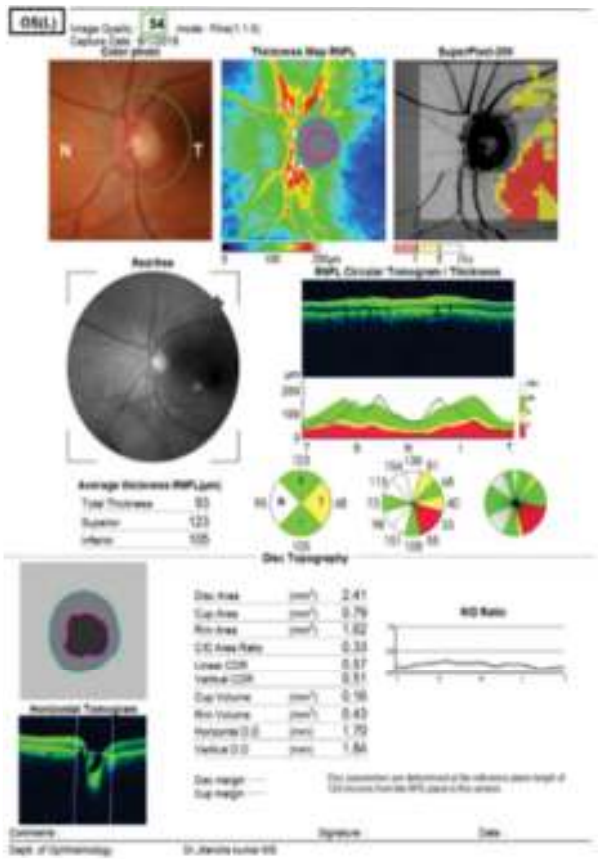


Figure 6.OCT - RNFL thinning in inferior(left eye)

data of the total patients.

RESULTS:

Seventy Two patients with primary open angle glaucoma fulfilled the inclusion and exclusion criteria of this study. The mean age in years was 59.44 ±11.64 (Range 42to 89 years) of total patients. The majority of POAG patients were age group above 50 year (73.6%). Sex wise distribution shows, 42 (58.33%) male and 30(41.67%) female. The male female ratio was 1.4:1.

The mean vertical CDR was 0.54 (±0.145) in right eye and 0.54 (±0.106) in left eye compared with Mean RNFL (µm) of 93.87(±24.71) in right eye and 93.35(±24.12) in left eye of all the patients. The "p value" was 0.00001. indicating that there was statistically significant difference in VCDR and RFNL thickness changes of right eyes of patients. The Pearson's correlation coefficient value of right eye was 0.5726, suggestive of moderate positive correlation between VCDR and RNFL thickness changes in right eye.With the "p value" was 0.1169, indicating that there was no statistically significant difference in VCDR and RFNL thickness changes of left eyes of patients. The Pearson's correlation coefficient value of left eye was 0.1864, suggestive that weak positive correlation between VCDR and RNFL thickness changes in left eye.

The Mean Deviation (MD) of -4.29 (±2.767) in right eye and -4.40 (±02.807) in left eye of all the patients. The 'p value' was 0.025382, indicating that there was statistically significant difference in CDR and visual field parameter Mean Deviation (MD) changes of right eyes of patients. The correlation coefficient (r) value of right eye was -0.2634, suggesting a weak negative correlation between CDR and MD in right eye. The 'p value' was 0.00093, indicating that there was statistically significant difference in CDR and MD changes of left eyes of patients. The correlation coefficient (r) value of left eye was -0.38, suggesting a weak negative correlation between CDR and MD changes in left eye.

The Pattern Standard Deviation (PSD) of +3.77(±3.05) in right eye and +3.29(±2.21) in left eye of all the patients. The "p value" was 0.0024, indicating that there was statistically significant difference in CDR and visual field parameter Pattern

Table 1: Age wise distribution of patients.

S. No	Age group (in years)	Total number of patients	Percentage (%)
1.	40-44	9	12.5
2.	45-49	10	13.9
3.	50-54	10	13.9
4.	55-59	8	11.1
5.	60-64	9	12.5
6.	65-69	11	15.3
7.	70 and above	15	20.8
Total	59.44 ± 11.64	72	100%

Table 2: Gender wise distribution of patients.

Gender	Male	Female	Total
No of patients	42	30	72
Percentage	58.33 %	41.67 %	100 %

Table 3: Mean CDR (Cup: Disc ratio) of total patients on OCT.

CD (OCT)	Total patients		t test score	p value
	Right eye	Left eye		
Mean	0.54	0.54	0.2098	0.4170
SD	±0.145	±0.106		

Table 4: Mean Retinal Nerve Fiber (RNFL in µm) thickness of patients.

RNFL thickness (µm) in OCT	Total patients			
	Right eye	Left eye	t test score	p value
Mean	93.87	93.35	0.3624	0.3587
SD	±24.71	±24.12		

Standard Deviation (PSD) changes of right eyes of patients. The correlation coefficient (r) value of right eye was 0.3516, suggesting a weak positive correlation between CDR and MD in right eye. The "p value" was 0.7154, indicating that there was not statistically significant difference in CDR and visual field parameter Pattern Standard Deviation (PSD) changes of left eye of patients. The correlation coefficient (r) value of left eye was 0.0437, suggesting a very weak positive correlation between CDR and PSD in left eye.

DISCUSSION:

In our study, we have analyzed technique of quantifying disc changes. Vertical CDR (Optic nerve head changes) correlates better with RNFL thickness and visual field changes in Glaucoma patients. Glaucoma is major public health problem, a leading cause of irreversible blindness throughout the world and the second leading cause of world blindness. It accounts for 15% of global blindness. The regional burden of blindness (RBB) is highest for India (23.5% of global blindness) [8]. With such prevalence rates, it is imperative to find measures to detect the disease in early stages before it starts to cause visual morbidity. By 2020, the number of glaucoma patients is expected to be 76 million and by 2040 this number will increase to 112 million. [9,10,11]

Table 5:Visual field mean deviation (VFMD) in perimetry of patients.

	Total Patients		t test score	p value
Visual field test Parameter	Right eye	Left eye		
Mean Deviation (MD)	-4.29	-4.40	0.2248	0.4112
SD	±2.76	±2.80		

Table 6: Visual field parameter mean defect in both eye of total patients.

	Total patients		t test score	p value
Visual field test Parameter	Right eye	Left eye	1.085	0.1398
Pattern Standard Deviation (PSD)	+3.77	+3.09		
SD	±3.050	±2.217		

Another study [12] found that men were 1.37 times more likely to have open angle glaucoma than women, although gender wise prevalence of POAG has always been controversial. Majority of our subjects (55%) were from low socio-economic strata which resonates with the study conducted for assessment of the rates of blindness and of partial sight registration in glaucoma patients [13] inferring that low socio-economic background was indeed a risk factor for development of glaucoma despite universal health care. A study published in journal of Ophthalmology [14] aimed to compare SD-OCT evaluation of RNFL thickness in normal controls and POAG of various stages and found that normal patients had the thickest RNFL thickness when compared with patients. Moreover, increased glaucoma severity was associated with thinner RNFL. In a study conducted for correlation of average thickness using the SRRATUS OCT with the

Table 7: Correlation between VCDR and RNFL Thickness.

Total patients	VCDR (µm) in OCT (Mean ± SD)	RNFL (µm)	Correlation (r)	p value
Right eye	0.54 ± 0.145	93.87 ± 24.716	0.5726	0.00001
Left eye	0.54 ± 0.106	93.35 ± 24.125	0.1864	0.1169

Graph 1: Scatter diagram between VCDR changes and RNFL thickness changes

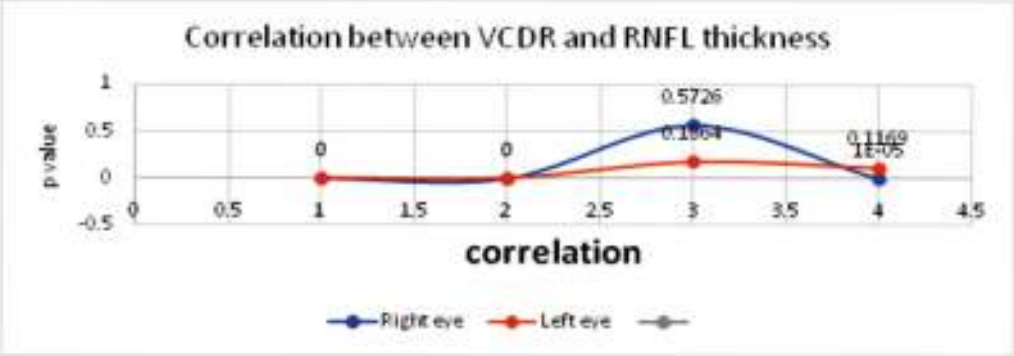
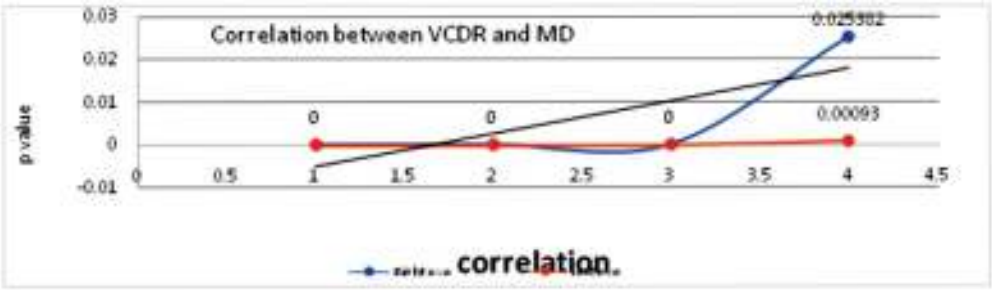


Table 8: Correlation between CDR and Mean Deviation (MD).

Total patients	CDR (µm) in OCT (Mean ± SD)	MD (dB) (Mean ± SD)	Correlation (r)	p value
Right eye	0.54 ± 0.145	-4.29 ± 2.767	-0.2634	0.025382
Left eye	0.54 ± 0.106	-4.40 ± 2.807	-0.38	0.00093

Graph 2*:* Scatter diagram between CDR changes and Visual field parameter (MD changes.



perimetric staging of glaucoma demonstrated that NRR area correlates more strongly with field damage than C/D ratio or cup volume [15]. However, the correlation between VCDR and RNFL thickness in the present study is more strongly than visual field parameter (MD, PSD) due to small sample size studied over short span of time. Since our study included less advanced glaucoma cases, it could be expected that it would not reveal such high correlation between RNFL thickness and visual field parameters (MD ,PSD).

In subjects with early glaucoma, evaluation of the RNFL is important for evaluating glaucomatous ganglion cell loss. Kanamori et al. [22] showed that the RNFL decreased in glaucomatous eyes, with or without early visual field defects. This study comprising total 72 patients with 138 eyes, established a positive correlation between mean vertical CDR (r 0.5726) compared with mean RNFL thickness and a negative and weak positive correlation between mean vertical CDR compared to visual field parameter mean defect MD (r -0.2364) and PSD (r 0.3516) respectively. The p value between CDR and RNFL thickness was 0.00001, which was statistically significant.

Each 1 mmHg rise in IOP during a median follow-up time of 5.3 years has been shown to be

Table 9: Correlation between CDR and PSD.

Total patients	CDR (μm) in OCT (Mean ± SD)	PSD (dB) (Mean ± SD)	Correlation (r)	p value
Right eye	0.54 ± 0.145	+3.77 ± 3.050	0.3516	0.0024
Left eye	0.54 ± 0.106	+3.29 ± 2.217	0.0437	0.7154

Graph 3: Scatter diagram between CDR (OCT) and visual field parameter (PSD).

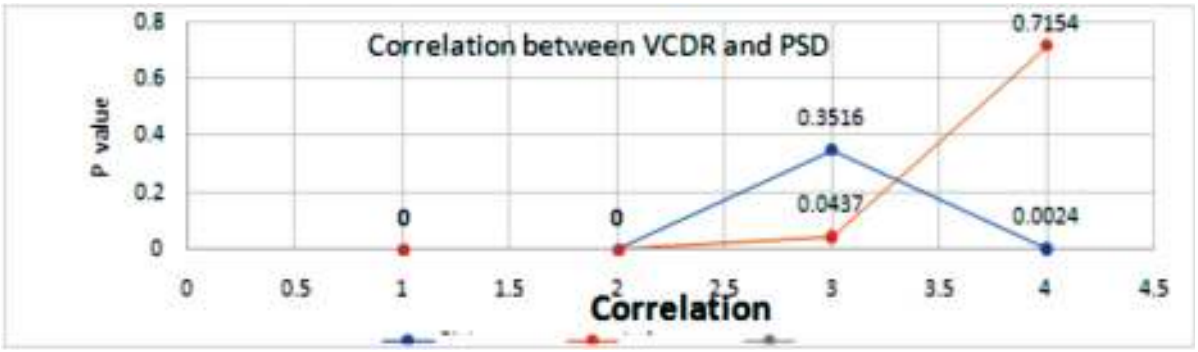


Table 10: Strength of correlation between different parameters.

Study variables	p value	Pearson's coefficient (r)
VCDR and RNFL Thickness	0.00001	0.5726
VCDR and MD	-0.2538	-02364
VCDR and PSD	0.0024	0.3516

Table 11: Summary of P values showing difference between correlation.

Study variables	p value	Pearson's correlation coefficient (r)	Statistical significance
VCDR and RNFL Thickness	0.00001	0.5726	Significance at 5% significance level
VCDR and MD	0.025382	-0.2364	Significance at 5% significance level
VCDR and PSD	0.0024	0.3516	Significance at 5% significance level

Table 12: Correlations between RNFL thickness and Visual field parameter (MD).

Study	Correlation coefficient between RNFL and MD
Sihota R et al. 2006 [16]	0.626 (p<0.001)
Ajtony C et al. 2007 [17]	0.718 (P=0.01)
Horn FK et al. 2009 [18]	0.75 (p<0.001)
Cvenkel et al. 2011 [19]	0.549 (p<0.001)
Kaushik S et al. 2011 [20]	0.560 (P=0.005)

**The present study is in agreement with the study of Bobrow, who also found a negative correlation (-0.68) between DDLS or Vertical CDR and MD [21]*

associated with a 19% increased risk of visual field progression[23]. This can explain why the present study observed vague correlation between OCT and Visual Field changes. Nevertheless, progression of visual field disorder in glaucoma is usually slow. The result of this study demonstrates that functional loss in glaucoma relates well with OCT measurement of peripapillary RNFL. Our knowledge concerning the functional/ structural relationship in glaucoma is progressively increasing. So, we can also diagnose a case of POAG by OCT before visual field changes in perimetry (Pre- perimetric glaucoma) because RNFL defects proceed the development of datable optic disc and visual field changes[24,25,26].About 40% of retinal ganglion cells will be damaged by the time the VF changes are first manifested[27,28,29.30].

CONCLUSION:

Ophthalmologists still have to fight a grim battle with the problem of glaucoma. Most frequently involved topographically corresponding sector of VF

(Supero-nasal and Inferonasal) and peripapillary RNFL (Inferotemporal and Supero-temporal) may represent common investigation aimed at exploring the diagnostic ability of the combination of functional and structural test, which has already been proved to be highly promising for more accurate detection of early glaucoma. However, long term studies are needed to be conducted involving considerations for visual field parameter changes in Perimetry and optic nerve changes in Optical Coherence Tomography.

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