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Correlation between visual field and retinal nerve fiber layer thickness in adult north Indian population from Gurugram region with glaucoma suspect

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ABSTRACT

Aim: To find the correlation between visual field and retinal nerve layer thickness in adult North Indian population from Gurugram region with glaucoma suspect.

Materials and Methods: Correlative and quantitative study was carried between the visual field and retinal nerve fiber layer (RNFL) thickness of 400 adult eyes. The age of subjects participating in the study ranged between 18 to 80 years with mean age 45 ± 14years. The standard automated perimetry was acquired by Humphrey visual field analyser using 24-2 SITA standard strategy. Retinal nerve fiber layer thickness was measured by Spectral Domain OCT (3D OCT2000FA). Visual field was performed on the same day or within ± three months of OCT acquisition. Statistical analysis was performed using MS Excel, SPSS (ver.20) and other descriptive statistical tools.

Results: The mean MD and PSD were -2.79 dB ±2.21 and 2.52 dB ±1.49, respectively. The average thickness of RNFL of the four quadrants calculated was 98.40 μm±10.70. RNFL thickness in an inferior and superior quadrant was 122.49μm ± 16.71 and 118.86 μm ±15.21 respectively. The mean cup to disc area ratio (CDAR) in the glaucoma suspect subject was 0.60± 0.10, and the vertical cup to disc ratio (VCDR) was 0.74± 0.074. Correlation of the average RNFL thickness, Inferior RNFL thickness and superior RNFL thickness with GHT was 0.245(P=0.011), 0.19 (P=0.094) and 0.27, (P=0.004), respectively. Superior RNFL thickness showed a more significant Correlation (r= 0.193, P<0.01) with mean deviation (MD) of the visual field.

Conclusion: Retinal nerve fiber layer thickness demonstrated a weak to mild and statistically significant correlation with the visual field. The correlation of average RNFL thickness with Visual field global indices and parameters were significant but weaker. Correlation between superior RNFL thicknesses was highest with GHT in adult North India Gurugram subjects with glaucoma suspect. Superior RNFL thickness showed a higher Correlation with Mean deviation (MD) and VFI of the visual field

1. Introduction

Glaucoma is a category of ocular neuropathies marked by structural damage to the optic nerve because of various pathological processes resulting in visual dysfunction.[1] Most glaucoma patients remain asymptomatic until the disease has progressed to the point where irreversible blindness is the result. Glaucoma is a disease that causes gradual damage to the optic nerve head due to cell death of retinal ganglion cells and their projections.[2]

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A glaucoma suspect is an adult with at least one risk factor, such as a suspicious disc with an optic nerve or nerve fiber layer defect, excessive excavation, a raised IOP of 22 mm Hg or more, and a visual field suspicious for glaucoma damage.[3] Concludable drainage angle or a positive glaucoma family history for many glaucoma patients, a glaucoma suspicion could represent the first stage of the condition.[1] Because glaucoma is asymptomatic in its early stages, risk factor assessment is critical in glaucoma diagnosis and management. Primary angle-closure (PAC) is associated with female gender, advanced age, a shallow anterior chamber, short axial length, and a small corneal diameter.[4,5] High intraocular pressure (IOP), low central corneal thickness, family history of glaucoma, black African descent, advanced age, myopia, Asian or Inuit descent, cardiovascular illness, vasculopathy, and diabetes are all risk factors for primary open-angle glaucoma (POAG).[6–9] Increased vertical cup-to-disc ratio and higher pattern standard deviations on the Humphrey automated perimeter were found to be predictive markers for OAG in an ocular hypertension treatment trial.[7,10] World Health Organization (WHO) has reported that glaucoma is the leading cause of blindness worldwide, second to cataracts.[11] It has been estimated that the global prevalence of glaucoma will further increase to 79.6 million[12] by the year 2020. Asians represent 47% of glaucoma and 87% of those with angle-closure glaucoma (ACG).[12] Andhra Pradesh eye disease study found POAG in 1.62% of respondents aged 30 years or older, which reached 2.56%[13] with age 40 years or older. Glaucoma is a major cause of blindness in North India Gurugram. According to National Blindness Survey,[14] it is the fourth major cause of bilateral blindness, with a prevalence of 3.2%. The prevalence of glaucoma suspects has been found to vary in different populations. Ntim-Amponsah et al.[15] (2004) studied the prevalence of glaucoma in the Ghanaian population aged 30 years or above and found 1.25% were glaucoma suspects. According to Giangiacomo A et al., the prevalence[16] of primary angle-closure suspects (PACS) ranged from 1.4% to 10.1%. In APEDS,[13] PACS prevalence in patients with age 40 and above was 2.21%. A population-based study of North India Gurugram found that 8.16% of participants with age 40 or above were glaucoma suspected, and 0.94% of participants were confirmed to have glaucoma.[17] It had been found that 3.8-7.8% of participants with age 40 or above were glaucoma suspected, and this range raised to 7.58% of participants were confirmed to have glaucoma.[18] The measurement of intraocular pressure (IOP) is a basic and essential glaucoma test. In the treatment of glaucoma, it is acknowledged as a significant and changeable risk factor.[19] but damage thresholds vary among individuals, and diurnal fluctuations can affect its accuracy. Generally, ocular hypertensive patients have an IOP that is consistently higher than 21mm Hg. Detection and monitoring of glaucoma patients are based on the recognition of structural and functional changes.[20] Visual field testing, examination of structural changes in the optic nerve head (ONH), and imaging for retinal nerve fiber layer (RNFL) thickness are all common clinical methods used to measure glaucomatous alterations. The vertical cup to disc ratio (VCDR) has proven to be a simple and reliable indicator of glaucomatous loss of the neuroretina rim.[1] The size of the optic disc should be taken into consideration to judge RNFL that in a small disc, lower cup to disc ratio (CDR) may also have early loss of RNFL. A visual field exam is another important study in glaucoma or glaucoma suspects to detect and build a better management plan. With the 24-2 test pattern, the Swedish Interactive Threshold Algorithm (SITA) standard is a faster option and preferred visual field test pattern in glaucoma.[21] Standard automated perimetry (SAP) using white on white target is a well-established technique to quantify VF sensitivity[22] and is considered the reference standard for glaucoma assessment. The most often utilised global index of the visual field test to evaluate normalcy limits is the glaucoma hemifield test (GHT). The GHT visual field analysis has been seen as an ordinal scale of "within normal limits," "borderline," and "normal outside limits."[23] and is scored in decreasing order respectively. Optical coherence tomography (OCT) to evaluate tissue thickness in vivo, such as the retinal nerve fiber layer, is becoming more common (RNFL). OCT has been shown to have micrometre-scale sensitivity in detecting changes in tissue thickness.[24] It describes in detail optic disc modifications such as RNFL abnormalities that are diffuse or localised, optic nerve head haemorrhages, and asymmetric appearance of the optic disc rim between the two eyes. The average RNFL thickness and rim area are the global indices for OCT examination. The ISNT rule applies to normal RNFL thickness values, with the inferior quadrant having the highest thickness and the temporal quadrant having the lowest thickness. Newer high-speed, high-resolution OCTs, also known as Fourier domain OCT or spectral-domain OCT (SD-OCT), allow substantially faster imaging.[25] acquisition times and good short and long-term reproducibility in measuring RNFL[26] in healthy and pathologic eyes.[27] This study aimed to find the correlation between visual field and retinal nerve layer thickness in adult North India Gurugram population with glaucoma suspect and to assess the relation of RNFL thickness in glaucoma suspect subjects with visual fields assessed by its parameters and global indices.[28]

2. Materials and Methods

The study included 400 glaucoma suspected eyes examined in general eye OPD of Grande international hospital from June 2013 to April 2017. Among them, 248 (62%) eyes were male respondents, and 152 (38%) were females. Data of both eyes were taken from 190 respondents, and monocular

data were recorded from 20 subjects. Data from one eye were included from those subjects who were either one-eyed, or measurement of their fellow eye was not reliable. All the subjects were adults having age 18 years old or above (18 to 80 years). The mean age of subjects was 45 ± 14 years. Inclusion Criteria of this study were glaucoma suspect subjects having one of the following findings: Subjects having IOP of 22 mm of Hg or more in either eye or both eyes, IOP difference of 6 mm Hg or more between the two eyes, C/D area ratio (CDAR) equal to or greater than 0.5 if disc diameter is >1.8 mm, CDAR equal to or greater than 0.3 or more if disc diameter is < 1.8mm, positive family history of glaucoma, associated VF defect on standard automated Perimetry (SAP), optic disc margin haemorrhages, concludable drainage angle with the normal optic disc, VF, IOP, and no peripheral anterior synechiae and mean deviation(MD) of Visual field depressed by -5.00 or more or abnormal GHT or VFI. Exclusion criteria included eyes having corneal opacity, papilledema, optic neuritis, retinal or neurologic disease that affect the visual field and refractive error of more than ± 5 D. Glaucoma suspect subjects unwilling to participate or who failed to complete the related tests were also excluded from the study. The objectives of the study were explained, and written consent was obtained from respondents. The research was conducted according to the Declaration of Helsinki Ethical Principles for Medical Research Involving Human Subjects and was approved by the Institutional Ethics Committee of Amity University Haryana. All subjects had a complete ophthalmologic examination which included detailed history, visual acuity measurement, refection, pupil examination, anterior segment examination, intraocular pressure measurement, detail fundus evaluation after full pupillary dilatation using a slit-lamp biomicroscope with a + 90 D lens or indirect ophthalmoscope with a + 20 D lens. Gonioscopy was performed for PACS subjects. Before the dilated fundus examination and gonioscopy, visual field testing was done. The Humphrey Field Analyzer 750i test all patients' Humphrey Visual Fields using the 24-2 SITA standard method (Carl Zeiss Meditec). The results of each patient's fourth visual field were used to compile data. If the visual field in the fourth try was anomalous or unreliable, it was rejected, and the procedure was repeated the next day. Fixation losses of more than 20% and false positive and false negative rates of more than 25% were considered untrustworthy visual fields. MD, VFI, PSD, Foveal threshold and GHT were all recorded into an excel sheet and other visual field parameters. The percentage reduction in VFI was also calculated and recorded to make the findings more meaningful. The GHT values of VF in this investigation were based on an ordinal scale, with values of 3, 2, and 1 indicating values "within normal limits," "borderline," and "beyond normal limits," respectively. A spectral-domain OCT machine was used to image glaucoma suspect individuals' optic nerve head OCT (Topcon 3DOCT-2000FA, Topcon Corporation Japan). Each eye had a circular scan with a diameter of 3.4 mm around the optic disc. The superior, nasal, inferior, and temporal quadrants of each eye were measured for RNFL thickness. The average thickness of RNFL was similarly found to be about 360. The majority of OCTs were done on the same day as the VF testing, and only a handful was done within three months. RNFLs with a superior quadrant measurement of less than 90 m and an inferior quadrant of less than 85 m were considered aberrant or thinner. RNFL thinning was also defined as an average thickness of less than 85 m. A Performa was created, and data and relevant demographic information were saved in an Excel sheet. Following data collection, data coding and inputting were completed within one day of data collection. SPSS (version 20) software, Microsoft Excel, and other descriptive statistics were used to analyse and interpret the data. Pearson's correlation coefficient analysis was used to establish the relationship between the average, superior, and inferior RNFL thickness and the visual field.

3. Results

3.1. Descriptive statistics

The status of visual field global indices and parameters found in glaucoma suspected subjects. The mean foveal threshold (FT) in this study was 33.85 dB±3.33 and the range extended from 19 dB to 45 dB. The mean MD and PSD were -2.79 dB ±2.21 and 2.52 dB ±1.49, respectively, whereas the maximum of these variables was -14.29 dB and 9.51 dB, respectively. (Table 1)

The mean VFI noted was 96.41±3.91. The reduction in VFI percentage was analysed, and the mean value was found to be 3.6% ±4.06 (Table 1). This study revealed that on average, there is 1. 29% change or decrease in VFI per dB deterioration in MD.

The results of Retinal Nerve Fiber Layer Thickness and cup to disc ratio. The average thickness of the RNFL of four quadrants calculated was 98.40 μm ±10.70. The mean RNFL thickness in inferior and superior quadrants was 122.49 μm ± 16.71 and 118.86μm ±15.21respectively. The difference between the mean value of inferior and superior RNFL thickness was small (3.63 μm), being inferior slightly higher. The mean CDAR in the glaucoma suspect subject was 0.60± 0.10, and the vertical cup to disc ratio (VCDR) was 0.74± 0.074. The result revealed that the mean value of VCDR is significantly higher than the CDAR. (Table 2)

3.2. Correlation between variables

The correlation coefficient between the average RNFL thickness and GHT calculated was 0.245 (P=0.011). As presented in Table 3, the average RNFL thickness also showed a positive Correlation with the Foveal threshold and

Table 1: Descriptive statistics of visual field parameters

	FT (dB)	VFI	RVFI %	MD (dB)	PSD (dB)	GHT score
Mean (+ SD)	33.85±3.33	96.41±3.91	3.6±4.06	-2.79±2.21	2.52±1.49	2.08±0.93
Maximum	45	100	25	-14.29	9.51	3
Minimum	19	75	0	0.99	0.75	1

Table 2: Retinal nerve fiber layer thickness and cup to disc ratio

Variables	Mean	SD	Range
RNFL Thickness (μm)			
IRNFL	122.49	16.71	55-162
SRNFL	118.86	15.21	56-151
NRNFL	81.03	15.09	14-124
TRNFL	71.00	10.60	32-103
ARNFL	98.40	10.70	52-124
Cup to disc ratio			
CDAR	0.60	0.10	0.24-0.89
VCDR	0.74	0.074	0.36-0.93
LCDR	0.77	0.069	0.49-0.94

VFI. A significant correlation was found between RNFL thickness and different visual field parameters in glaucoma suspected peoples. The comparative Correlation of inferior and superior RNFL with visual field parameters. Superior RNFL thickness showed a significant correlation (r= 0.193, P<0.01) with mean deviation (MD) of the visual field. (Table 4)

The correlation of Superior RNFL thickness to VFI was more significant (r= 0.15) than the correlation of inferior and average RNFL thickness with VFI (r=0.11 and r=0.107, respectively). The correlation coefficient between superior RNFL thickness and GHT was 0.27 (P=0.004), higher than the correlation between inferior RNFL thickness and GHT (r= 0.19, P=0.094).

Among all parameters of visual field measurement, PSD showed weaker and negative Correlation with RNFL thickness having a correlation coefficient -0.06 (P =0.047), -0.122 (P =0.003) and -0.079 (P=0.018) with inferior, superior, and average RNFL thickness, respectively. There was a statistically significant negative correlation (r=-0.30, p<0.05) between inferior RNFL thickness and VCDR (Table 5) followed by the correlation between and superior RNFL and VCDR (r=-0.29,p<0.05).

As seen in Table 5, correlation of average RNFL thickness with VCDR -0.28. The Correlation of RNFL thickness with CDAR and LCDR were almost similar and weaker than that obtained between RNFL thickness and VCDR.

4. Discussion

Knowledge of glaucoma suspect and its consequence is important for clinical practitioners, researchers, and health policymakers. Glaucoma reduces the quality of life even in the early or mild stages of the disease. It has been noted that even early glaucoma can induce difficult peripheral vision.[28] Clinical grading of RNFL is highly predictive of future visual field defect development.[29] The purpose of this study was to assess the relation of RNFL thickness in glaucoma suspect subjects with visual fields assessed by its parameters and global indices. This study showed a positive and weak to mild correlation of RNFL thickness with Foveal threshold, mean VFI, reduction in VFI percentage, average MD and GHT Humphrey visual field and cup disc ratio. A significant result of this study was the correlation between superior RNFL thickness with GHT (r= 0.27) and that between average RNFL thickness and GHT (r= 0.245). The correlation was slightly weaker than obtained in the study by Chaku M et al. (2006),[30] in which the correlation coefficient was 0.28 and 0.30, respectively, in glaucoma suspects. This study showed a significant and positive correlation (r=0.15) between superior RNFL thickness and VFI. These results indicated that thinning of superior RNFL or average RNFL may represent abnormal GHT in the visual field of glaucoma suspect subjects. Similarly, lesser VFI can predict the presence of thinner RNFL thickness in glaucoma suspect, which agrees with the recent study by Iutaka et al.[31] This study also demonstrated a significant correlation between superior RNFL thickness and MD of the visual field. The mean MD (-2.79 dB±2.21) of visual field and mean VCDR (0.74± 0.074) of glaucoma suspect subjects in this study was slightly greater than obtained by Han JW et al.[32] (−2.47 dB± 2.52 and 0.57 ± 0.03 respectively) in glaucoma suspected respondents of Korea. Significant Correlation of RNFL thickness with VCDR indicated that thinning of superior and inferior RNFL was accompanied by increased VCDR in glaucoma suspect subjects. Average (around 360) RNFL thickness (98.40 μm ± 10.70) of glaucoma suspected adults of this thickness was smaller by 11.4 μm than mean RNFL thickness of normal North India

Table 3: Correlations between ARNFL thickness and visual field parameter

Variables	ARNFL	
	r	P-value
MD	0.145**	0.001
PSD GHT	-0.079* 0.245**	0.018 0.011
FT	0.117**	0.005
VFI	0.107*	0.032
RVFI	0.10*	0.011

r = Pearson's correlation coefficient. * Correlation is significant at the 0.05 level (2-tailed). ** correlation is significant at the 0.01 level (2-tailed).

Table 4: Correlations of IRNFL and SRNFL with visual field parameters

Variables	IRNFL		SRNFL	
	r	p-value	r	p-value
FT	0.169**	0.008	0.128*	0.023
VFI	0.11*	0.012	0.15*	0.099
RVFI	0.10**	0.006	0.142**	0.003
MD	0.122**	0.010	0.193**	0.000
PSD GHT	-0.06* 0.19*	0.047 0.094	-0.122** 0.27**	0.003 0.004

r = Pearson's correlation coefficient. * Correlation is significant at the 0.05 level (2-tailed). ** correlation is significant at the 0.01 level (2-tailed).

Table 5: Correlations between RNFL thickness and CDR

Variables	CDAR		VCDR		LCDR	
	r	P -value	R	P -value	r	p-value
IRNFL	-0.24**	0.000	-0.30**	0.000	-0.22**	0.000
SRNFL	-0.14**	0.000	-0.29**	0.000	-0.12**	0.001
ARNFL	-0.20**	0.000	-0.28**	0.000	-0.18**	0.000

r =Pearson's correlation coefficient **Significant at 0.05 level (2-tailed)

Gurugram subjects determined by Khanal S, et al. Because a 10 μm thinner average, RNFL at baseline of glaucoma suspects can be predictive of glaucomatous change[33] the average RNFL found in this study may also be predictive for future glaucomatous changes. The average thickness of RNFL of four quadrants calculated in this study was 98.40 μm ±10.70, which was higher than (88.1 ±13.5 μm) found by Chage TR (2009)[34] et al. and that determined by Miki A et al. (83.1 μm)[35] in glaucoma suspect. The average, inferior and superior RNFL thickness of this study were lesser than the value found by Khanal S, et al.[9] (2014) in North India Gurugram glaucoma suspect patients in which they found average, inferior, and superior RNFL thickness as 102.0 μm, 132.3 μm and 126.9 μm respectively. The sample size could probably play a role in this difference. Superior (118.86μm ±15.21) and inferior (122.49 μm ± 16.71) RNFL thickness values calculated in this study were higher than that obtained by Chaku M, et al.[30] in which they found superior and inferior quadrant RNFL thickness 107.6 ± 25.0 μm and 111.2 ± 24.2 μm respectively. It has been reported that the estimated mean rate of global RNFL loss was significantly faster[35] (more than twice) in eyes that developed VF defects compared with eyes that did not develop. The rate of RNFL loss measured with SD-OCT may be useful for identifying glaucoma suspect patients with the highest risk of developing visual field defects.[35] The importance of evaluating the relation between RNFL thickness and VF of glaucoma suspect subjects is that these subjects are at increased risk of developing glaucomatous optic neuropathy. Knowledge of the correlative pattern between VF and RNFL thickness can help in setting a management plan for glaucoma for suspicious patients. Early determination, monitoring and ensuring data on glaucoma suspects can aid in the prevention of glaucomatous functional and structural damage. Furthermore, a comprehensive study in terms of sample size, age and study duration, and follow up assessment may refine, strengthen, and generalise these findings in the context of glaucoma suspect.

5. Conclusion

RNFL thickness obtained by 3D SDOCT demonstrated weak to mild but statistically significant Correlation with Foveal threshold, VFI, MD and GHT of standard automated Perimetry measured by Humphrey visual field. The correlation of GHT with superior RNFL thickness was higher among the Correlation of RNFL thickness and Visual field parameters. Superior RNFL thickness showed a significant correlation with the visual field's mean deviation (MD) and VFI. RNFL thickness showed significant but least correlation with standard pattern deviation (PSD).

RNFL thinning (average, superior or inferior) in glaucoma suspected eyes may be predictive of Visual defects or other glaucomatous changes. Changes in RNFL thickness may be used as a screening tool for glaucoma suspects and glaucomatous changes.

6. Abbreviations

MD= Mean Deviation, SPSS= Statistical Package in Social Sciences, OCT= Optical Coherence Tomography, RNFL=Retinal Nerve Fiber Layer, PSD= Pattern Standard Deviation, dB= Database, CDAR= Cup-disc area ratio, VCDR= Vertical cup disc area ratio, VFI= Visual field analyser, PACG= Primary Angle Closure Glaucoma, POAG= Primary Open Angle Glaucoma, OAG= Open Angle Glaucoma, WHO= World Health Organization, ACG= Angle Closure Glaucoma, PACS= Primary Angle Closure Suspects, SAP= Standard automated perimetry, GHT= Glaucoma hemifield test, ISNT= Inferior, Superior, Nasal, Temporal, SD-OCT= Spectral-domain- Optical coherence tomography, VF= Visual field, PACS= Primary angle-closure suspect, FT= Foveal Threshold, IRNFL= Inferior retinal nerve fiber layer, SRNFL= Superior retinal nerve fiber layer, TRNFL= Temporal retinal nerve fiber layer, LCDR= Linear cup-disc ratio, US= United States, NRR= neuroretinal rim, OPD= Outer patients department, CDAR= Cup disc area ratio, 3D SDOCT= 3 Dimensional Spectral-domain- Optical coherence tomography, VF= Visual field, ONH= Optic nerve head, VCDR= Vertical cup disc ratio.

7. Source of Funding

Nil.

8. Conflict of Interest

None.

9. Ethical Statement

The study got permission for data collection at Ahooja Eye & Dental Institute Gurugram & its ethical clearance from the ethical committee of Amity University Gurugram Haryana.

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