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# Optical coherence tomography features and correlation of functional and structural parameters in patients of idiopathic intracranial hypertension

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**Purpose:** To determine the correlation between functional parameters and optical coherence tomography (OCT) features in patients of idiopathic intracranial hypertension (IIH). **Methods:** A prospective observational study in early and established cases of papilledema in IIH presenting from December 2017 to February 2019. Functional parameters (visual acuity, contrast sensitivity, mean deviation, VER, and MfERG) and structural parameters (RNFL, GCL-IPL, and optic disc height) were measured at baseline and every 6 weeks for 6 months. **Results:** At baseline, average RNFL had a moderate negative correlation with mean deviation (r = −0.45; *P* = 0.0007) and a positive correlation with logMAR visual acuity (r = 0.18; *P* = 0.17). On the contrary, baseline GCL and logMAR visual acuity had a negative correlation (r = −0.4, *P* = 0.02). Optic disc height (ODH) had a negative correlation with visual field mean deviation (r = −0.046; *P* = 0.0005). At 6 months, ODH and GCL-IPL complex had a statistically significant correlation with functional parameters. However, RNFL values did not show any significant correlation with any of the functional parameters. Baseline GCL-IPL and optic disc height values had a moderate and significant correlation with final functional parameters. However, RNFL did not show any correlation with final functional parameters. Correlation between GCL-IPL thickness at 6 weeks and final functional parameters were stronger than that with baseline GCL values. **Conclusion:** In the setting of severe papilledema, RNFL can misguide the prognosis. GCL-IPL can be a valuable tool for an objective evaluation of the integrity of the optic nerve in IIH and ODH may be used as an alternative or in combination with GCL-IPL in these cases.

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Optical coherence tomography (OCT) is a noninvasive, noncontact transpupillary imaging technology providing high-resolution, cross-sectional images of ocular and biological structures to visualize and measure anatomic layers of the retina. It is a useful investigation to diagnose and monitor cases of papilledema.[1,2]

Serial monitoring of the peripapillary retinal nerve fiber layer (RNFL) thickness may provide a quantitative, objective, and sensitive measurement of changes in papilledema,[3] especially when the patient is seen by different care providers. A reduction in peripapillary RNFL thickness can be a result of the improvement in papilledema *per se* or due to worsening axonal loss from disease progression. Combining the macular ganglion cell layer-inner plexiform layer thickness (GCL-IPL) with the peripapillary RNFL thickness allows one to evaluate optic nerve injury in the presence of papilledema.[4] Successful treatment with the protection of neuroaxonal structure will cause a reduction in the peripapillary RNFL thickness with a preserved macular GCL-IPL thickness. However, a concordant reduction in the RNFL thickness and macular GCL-IPL thickness indicates optic nerve injury and could be an indication of treatment failure.[5]

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This study aims to determine the correlation between functional parameters and OCT features in patients of idiopathic intracranial hypertension (IIH), which can further help to prognosticate these patients.

## Methods

The study was a prospective observational study done in a tertiary eye-care center from December 2017 to February 2019. The patients were recruited from the ophthalmology and neurology outpatient department and neuro-ophthalmology clinic.

Institutional ethics committee approval was obtained (IECPG-311/07.09.2017). The research was conducted by adhering to the tenets of the Declaration of Helsinki and informed consent was taken from the patients. The inclusion criteria were age ≥18 years, diagnosed cases of early and established cases of IIH based on modified Dandy criteria.[6]

Patients with evidence of hydrocephalus, space-occupying lesion on magnetic resonance imaging (MRI) of brain and



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orbit, structural or vascular lesion, venous sinus thrombosis on magnetic resonance venography (MRV), preexisting optic neuropathies including glaucoma and glaucoma suspects, dense media opacification (e.g., cataract) precluding precise ocular and OCT examinations, patients with chronic and atrophic papilledema, and patients not willing to give consent were excluded from the study.

Details regarding the onset, progression, duration of symptoms, and presence of preexisting comorbidities were recorded.

Best-corrected visual acuity was recorded with the Early Treatment Diabetic Retinopathy Study (ETDRS) chart. Slit-lamp anterior segment examination and posterior segment examination were performed using 90-D slit-lamp bio-microscopy. Magnetic resonance Imaging with contrast was performed to rule out any space-occupying lesion. Optic nerve function tests were performed, which included color vision (Ishihara pseudo isochromatic plates1997 version; Kanehara & Co., Ltd., Tokyo, Japan), contrast sensitivity (Pelli–Robson chart), and visual field charting (30-2 SITA Standard, Humphrey, San Leandro, CA). Pattern-reversal visual evoked response (VER) and multifocal electroretinogram (Metrovision Monpack, Pierenchies, France) were also performed.

Spectral-domain OCT (Cirrus HD-OCT Model 4000; Carl Zeiss Meditec Inc., Dublin, CA) was performed in all cases. Retinal nerve fiber layer thickness was measured with the RNFL scan centered on the optic disc (optic disc cube 200 × 200 volume scans). Average RNFL values of the four quadrants were used for calculating the final correlation. Macular ganglion cell layer-inner plexiform layer thickness (GCL-IPL) was evaluated with the help of the automated algorithm of Cirrus HD-OCT Model 4000 (Carl Zeiss Meditec Inc., Dublin, CA) centered on the fovea (512 × 128 volume scans). For optic disc height (ODH) measurement, a 5-line raster scan with 5 horizontally oriented lines of length 9 mm separated by 0.5 mm spreading across the entire surface of the optic disc was used. At the level of each raster line, a vertical line was manually placed, connecting the RPE layer to the maximum height of the optic nerve head. The average value of the 5 lines was considered to be the mean optic disc height.[7] All scans had a signal strength of a minimum of 6 and scans were repeated if any motion artifact was noted [Fig. 1].

Patients were advised treatment in the form of weight loss, acetazolamide ranging from 750 mg/day to 1.5 g/day as per response, and topiramate (25 mg once daily) as advised by the neurologist.

A control group of 40 patients (80 eyes) were included from the normal population (age group of 18–50 years) with no ocular diseases that may affect optic nerve function tests and OCT parameters, no neurological diseases that may affect OCT like multiple sclerosis, Alzheimer's disease, Parkinsonism. Functional parameters (visual acuity, contrast sensitivity, color vision, mean deviation, VER, and multifocal electroretinogram) and structural parameters (RNFL, GCL-IPL, and ODH) were measured at baseline.

The ocular parameters were measured at baseline and every 6 weeks for 6 months.

Correlation analysis was done at baseline and final visit to observe the relationship between the structural and functional

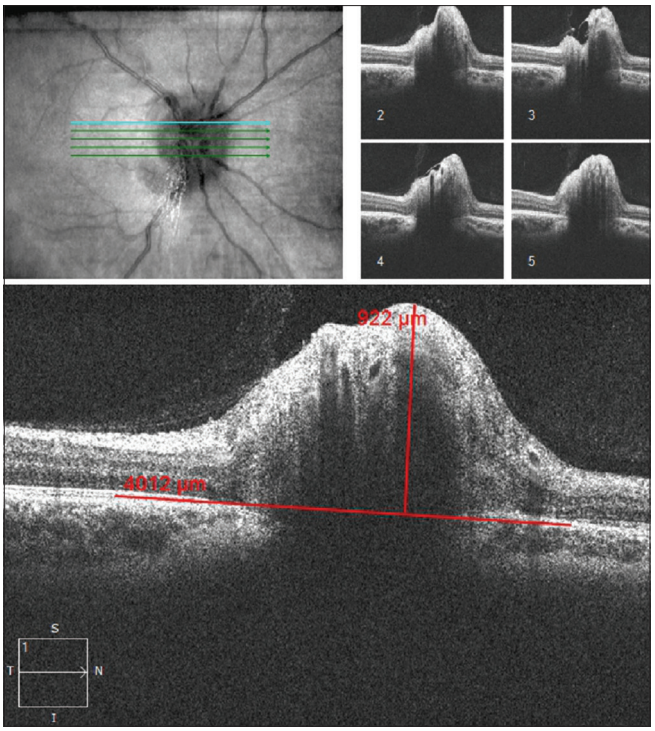


**Figure 1:** The 5-line raster scan for optic disc height measurement with 5 horizontally oriented lines of length 9 mm, separated by 0.5 mm spreading across the entire surface of the optic disc. At the level of each raster line, a vertical line is manually placed, connecting the RPE layer to the maximum height of the optic nerve head. The figure depicts a height of 922 µm at the level of one of the raster-line

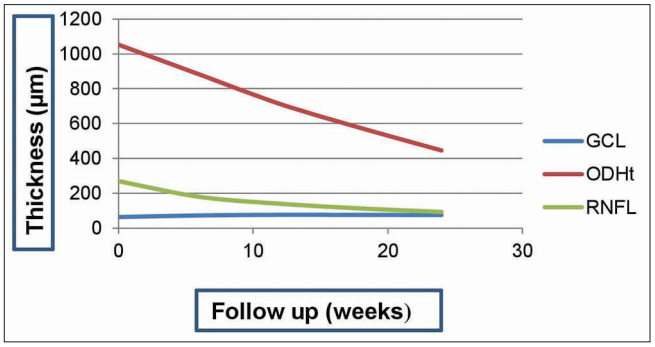


**Figure 2:** Trend of structural parameters over 6 months

parameters. We correlated the structural parameters at the baseline with the final visual outcome at 6 months to understand whether the baseline structural parameters can predict the final visual functional outcome.

## Analysis

The data were collected in a predesigned proforma and spread on Microsoft Excel Worksheet, and statistical analysis of the study was done using SPSS IBM Statistical Package software version 21.0. Descriptive statistics; mean, median, range were used to summarize the various variables at baseline and 6 months. Mann–Whitney test and student *t* test were used for comparing nonparametric and parametric data, respectively. Multiple linear regression was done to analyze the changes in various parameters for 6 months. Correlation between two variables was analyzed with Spearman correlation and

Pearson correlation for nonparametric and parametric data, respectively. $P <= 0.05$ was considered to be significant.

## Results

A total of 27 patients were included in our study, of which 21 were females and 6 were males. The mean age of patients was 31 ± 7.53 years. The mean duration of symptoms was 4.5 months. Headache constituted the most common symptom and was present in 90.7% of cases (n = 27), followed by transient visual obscuration in 40.7%. Other symptoms were diminution of vision in 29% and diplopia in 20.3% of cases. Twenty-six patients presented with bilateral papilledema while one patient had unilateral papilledema.

A total of 40 controls were included with a mean age of 29.03 ± 7.1 years comprising 28 females and 12 males.

There was a significant difference in OCT parameters between cases (27 patients; 54 eyes) and control (40 controls; 80 eyes) at baseline [Table 1]. The OCT features showed changes over the period; there was a reduction in RNFL thickness and disc height. While GCL-IPL complex showed statistical improvement from the baseline (63.35 ± 23.5) to 6 weeks visit (71.5 ± 17.12) [$P = 0.0006$], after which there was marginal improvement till 6 months [Fig. 2]. At 6 months, all OCT parameters showed a significant difference from the control group [Table 1]. None of our patients showed RNFL atrophy at 6 months follow-up. Even at 6 months, all OCT parameters showed a significant difference from the control group [Table 1]. None of the patients showed RNFL atrophy at 6 months follow-up. GCL-IPL thickness at 6 months was normal in 59.25% (n = 54) of patients and was reduced in 40.74% of patients (n = 54). Around 25% of patients with normal GCL-IPL thickness and 18% of patients with lower GCL-IPL thickness had increased RNFL thickness at 6 months. The ODH showed a strong and significant positive correlation with RNFL (r = 0.622; $P =< 0.001$) and a strong negative correlation with GCL IPL layer (r = −0.604; $P =< 0.001$) at presentation.

There was a gradual improvement in visual functions over the 6 months. A significant difference was present between the baseline values and values at 6 months in the functional parameters [Table 2].

To observe the relationship between the structural and functional parameters, correlation analysis was done at baseline and final visit. To understand whether the baseline structural parameters can predict the final visual functional outcome, we correlated the structural parameters at the baseline with the final visual outcome at 6 months; for this analysis GCL-IPL value at 6 weeks was considered.

### Correlation at baseline

At baseline, the increased RNFL values correlated with poorer mean deviation on visual field analysis and increased VER P100 latency (r = 0.35; $P = 0.008$). On the contrary, a thin GCL-IPL complex was associated with lower visual acuity, mean deviation, and contrast sensitivity. Similarly, increased ODH at baseline had correlated with poorer mean deviation and delayed VER P100 latency. Table 3 shows the correlation between various OCT parameters and functional parameters.

### Correlation at 6 months

A statistically significant correlation was documented between ODH and GCL-IPL thickness values at 6 months, with the functional parameters performed at 6 months. However, RNFL values at 6 months did not show any significant correlation with any of the functional parameters at 6 months [Table 4].

### Baseline structural parameters versus final outcome correlation

Baseline values of GCL-IPL thickness and ODH had a moderate and significant correlation with visual acuity, contrast sensitivity, and mean deviation at 6 months. However, baseline RNFL values did not show any significant correlation with final functional parameters in our study [Table 5]. The GCL-IPL values at 6 weeks follow-up had a stronger correlation with final functional parameters as depicted in Table 5.

Fig. 3 denotes the graphical representation of the correlation between baseline ODH and GCL values with mean deviation, contrast sensitivity, and visual acuity at 6 months.

**Table 1: Values of structural and functional parameters of cases and controls at baseline and 6 months**

| STRUCTURAL PARAMETERS | AT BASELINE | | | AT SIX MONTHS | | |
|---|---|---|---|---|---|---|
| | CASES (*n*=54) | CONTROLS (*n*=80) | *P* | CASES (*n*=54) | CONTROLS (*n*=80) | *P* |
| RNFL (µm) | 269.97±91.09 | 88.11±2.17 | <0.001 | 93.35±27.58 | 88.11±2.17 | 0.16 |
| RGCL-IPL complex (µm) | 63.35±23.58 | 79.85±3.31 | <0.001 | 73.96±11.11 | 79.85±3.3 | 0.0003 |
| Optic disc height (µm) | 1053.18±207.03 | 0 | <0.001 | 444.44±218.66 (median :448) | 0±0 | <0.0001 |
| FUNCTIONAL PARAMETERS | | | | | | |
| BCVA (logMAR) | 0.13±0.16 | 0±0 | <0.001 | 0.02±0.06 (median: 0) | 0±0 | 0.01 |
| Contrast sensitivity | 1.466±0.028 | 1.66±0.005 | <0.001 | 1.59±0.10 | 1.66±0.03 | <0.0001 |
| Colour Vision | Normal-75.93% Abnormal-24.07% | Normal-100% | - | Normal:92% Abnormal:8% | Normal: 100% | - |
| Mean deviation | -9.92±6.82 | -1.90±0.441 | <0.001 | 4.60±5.5 (median: 2.9) | 1.90±0.44 | 0.0045 |
| VER amp P100 (µV) | 7.13±3.14 | 14.70±1.03 | <0.001 | 11.33±3.75 | 14.70±1.03 | <0.0001 |
| VER latency P100 (ms) | 121.10±10.82 | 100.53±2.12 | <0.001 | 107.59±8.95 | 100.53±2.12 | <0.0001 |
| mfERG P1 amp (NV) | 895.16±53 | 1669.85±284.19 | <0.001 | 1303.88±565.72 | 1669.85±284.19 | <0.0001 |
| MfERG P1 IT (ms) | 48.035±3.959 | 42.466±0.917 | <0.001 | 44.17±1.84 | 42.46±0.917 | <0.0001 |

**Table 2: Baseline and final values (at 24 weeks) of functional parameters (*n*=54)**

| Parameters | Visual acuity | Contrast sensitivity | mf ERG A IT | VER A L | Mean Deviation |
|---|---|---|---|---|---|
| Baseline | 0.13 | 1.46 | 895.17 48.03 | 7.13 120.87 | −9.92 |
| 24 weeks | 0.024 | 1.60 | 1391.39 44.17 | 11.34 107.14 | −4.60 |

A: Amplitude, IT: Implicit time, L: Latency

**Table 3: Correlation between structural and functional parameters at baseline**

| Structural parameters | Visual acuity | Contrast sensitivity | Mean deviation | VER P100 amplitude | VER P100 latency | mfERG P1 amplitude | mfERG P1 implicit time |
|---|---|---|---|---|---|---|---|
| RNFL | *r*=0.18; *P*=0.17 | *r*=−0.12; *P*=0.36 | *r*=−0.49; *P*=0.0007 | *r*=0.06; *P*=0.6 | *r*=0.35; *P*=0.008 | *r*=−0.13; *P*=0.34 | *r*=0.16; *P*=0.24 |
| GCL-IPL | *r*=−0.4; *P*=0.02 | *r*=0.34; *P*=0.01 | *r*=0.4; *P*=0.002 | *r*=0.12; *P*=0.4 | *r*=−0.25; *P*=0.07 | *r*=0.02; *P*=0.85 | *r* = −0.4; *P*=0.001 |
| ODH | *r*=0.16; *P*=0.23 | *r*=−0.22; *P*=0.1 | *r*=−0.5; *P*=0.0005 | *r*=−0.21; *P*=0.1 | *r*=0.55; *P*=<0.0001 | *r*=−0.28; *P*=0.03 | *r*=0.27; *P*=0.04 |

**Table 4: Correlation between structural and functional parameters at 6 months**

| Structural parameters | Visual acuity | Contrast sensitivity | Mean deviation | VER P100 amplitude | VER P100 latency | mfERG P1 amplitude | mfERG P1 implicit time |
|---|---|---|---|---|---|---|---|
| RNFL | *r*=0.03; *P*=0.78 | *r*=0.2; *P*=0.1 | *r*=0.17; *P*=0.2 | *r*=−0.17; *P*=0.2 | *r*=−0.33; *P*=0.01 | *r*=−0.35; *P*=007 | *r*=−0.2; *P*=0.14 |
| GCL-IPL | *r*=−0.28; *P*=0.03 | *r*=0.54; *P*<0.0001 | *r*=0.52; *P*<0.0001 | *r*=−0.17; *P*=0.2 | *r*=−0.27; *P*=0.04 | *r*=0.02; *P*=0.88 | *r*=0.01; *P*=0.9 |
| ODH | *r*=0.4; *P*=0.001 | *r*=−0.01; *P*=0.9 | *r*=−0.12; *P*=0.34 | *r*=−0.19; *P*=0.16 | *r*=−0.18; *P*=0.18 | *r*=−0.13; *P*=0.32 | *r*=0.1; *P*=0.4 |

**Table 5: Correlation between baseline structural parameters and final functional parameters at 6 months**

| Structural parameters | Visual acuity | Contrast sensitivity | Mean deviation | VER P100 amplitude | VER P100 latency | mfERG P1 amplitude | mfERG P1 implicit time |
|---|---|---|---|---|---|---|---|
| RNFL (at baseline) | *r*=0.14; *P*=0.27 | *r*=−0.08; *P*=0.56 | *r*=−0.26; *P*=0.06 | *r*=−0.12; *P*=0.40 | *r*=0.02; *P*=0.88 | *r*=−0.17 ; *P*=0.22 | *r*=−0.05; *P*=0.72 |
| GCL-IPL (at baseline) | *r*=−0.37; *P*=0.005 | *r*=0.33; *P*=0.14 | *r*=0.36; *P*=0.006 | *r*=−0.04; *P*=0.8 | *r*=−0.12; *P*=0.38 | *r*=−0.07; *P*=0.60 | *r*=−0.33; *P*=0.01 |
| GCL-IPL (at 6 weeks) | *r*=−0.34; *P*=0.01 | *r*=0.44; *P*<0.001 | *r*=0.45; *P*<0.001 | *r*=−0.07; *P*=0.5 | *r*=−0.12; *P*=0.35 | *r*=0.09; *P*=0.5 | *r*=−0.07; *P*=0.5 |
| ODH (at baseline) | *r*=0.4; *P*=0.002 | *r*=−0.34; *P*=0.01 | *r*=−0.45; *P*=0.0007 | *r*=−0.05; *P*=0.72 | *r*=0.06; *P*=0.67 | *r*=−0.01; *P*=0.92 | *r*=0.1; *P*=0.47 |

## Discussion

The emerging popularity of the use of OCT in neuro-ophthalmic disorders is due to its ability for excellent imaging of each layer of the retina and optic disc. The present study was conducted to observe the changes in OCT parameters and their relationship with the functional parameters.

RNFL thickness is a commonly used parameter for the detection and monitoring of papilledema. RNFL thickness is increased in patients with IIH due to the axoplasmic flow stasis[8] and has been noted to reduce with time.[9]

In the present study, the RNFL thickness was significantly higher at the baseline and progressively decreased over 6 months suggestive of resolution of papilledema. However, the OCT-derived RNFL thickness alone does not differentiate treatment response from the development of optic atrophy.[10]

Ganglion cell layer–inner plexiform layer (GCL-IPL) thickness specifically helps to evaluate the integrity of the optic nerve in the setting of disc edema.[5] Thinning of the GCL-IPL complex in the presence of normal RNFL may be suggestive of optic atrophy.[1] In our study, we found that the mean GCL-IPL thickness was significantly lower at baseline as well as at 6 months follow-up, while the RNFL thickness at 6 months was almost within the normal range. A similar observation has been made by Marzoli *et al*.[11] and Labib *et al*.[12] where they reported that 10% and 13% of their patients, respectively, in various stages of papilledema had thinner GCL-IPL even when the RNFL was still elevated. Athappilly also reported a similar observation in their 18 patients where they found GCL-IPL was significantly thinner than the control group at every follow-up, while RNFL was significantly thicker at initial stages.[13] Interestingly, in the linear analysis, we found that GCL-IPL

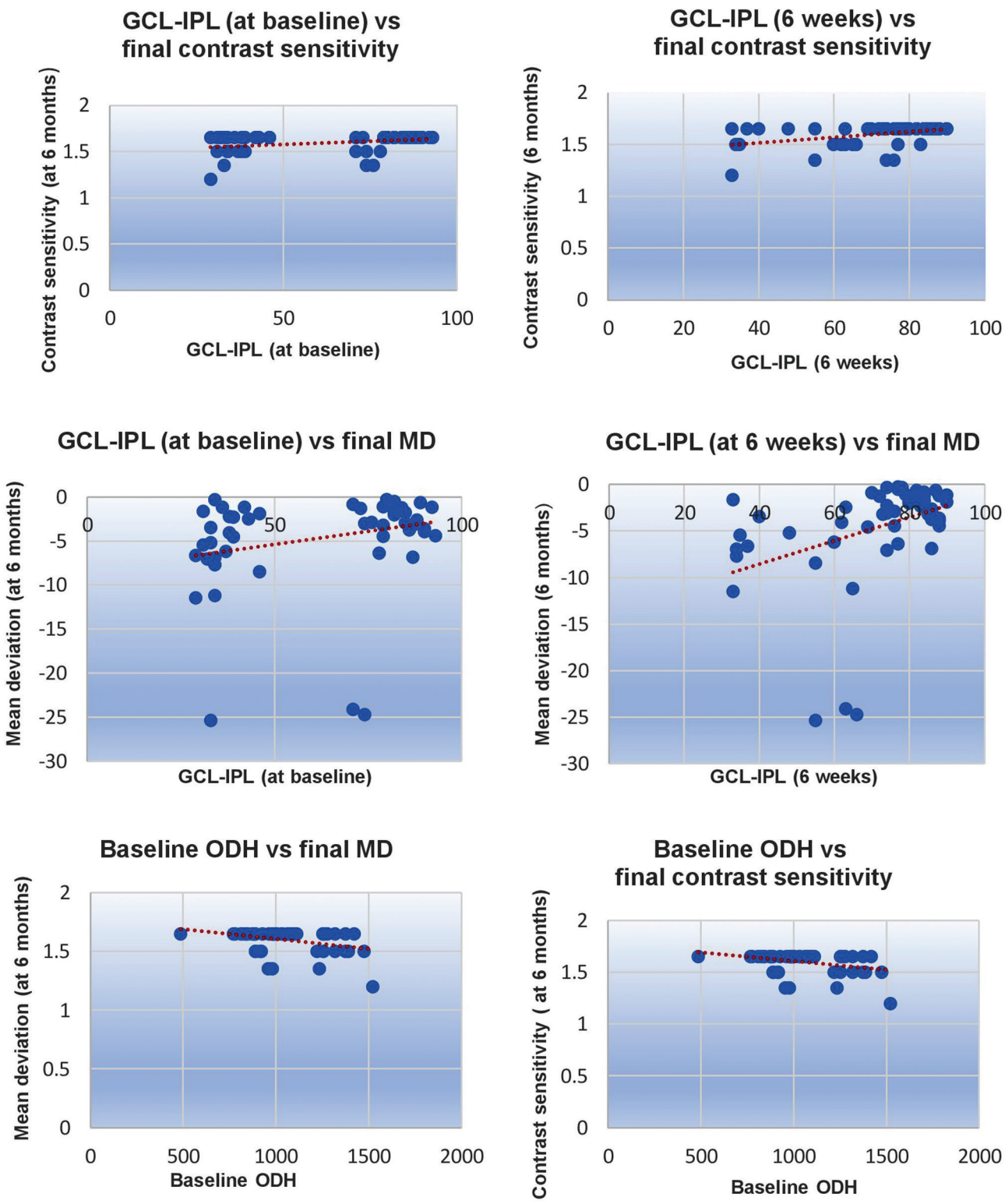


**Figure 3:** Correlation graph between baseline GCL and final contrast sensitivity (upper left) and GCL at 6 weeks and final contrast sensitivity (upper right). Correlation between baseline GCL and final mean deviation (middle left) and GCL at 6 weeks and final mean deviation (middle right), Correlation between baseline optic disc height and final mean deviation (lower left) and between baseline optic disc height and final contrast sensitivity (lower right)

thickness showed statistically significant improvement from baseline value to that of 6 weeks follow-up, followed by an improving trend over the 6 months, which was not statistically significant.

Commercial OCT algorithms can sometimes fail to identify the RNFL as well as GCL-IPL boundaries in the setting of significant papilledema due to the disorganization of retinal layers in presence of retinal swelling.[7] This

may be the reason for false lower values of the GCL-IPL layer in our study at the baseline; in addition, with the resolution of edema, the delineation became sharper and hence the improvement in its thickness. Research-derived algorithms (Iowa Reference Algorithm) that take advantage of three-dimensional information are more robust and can accurately segment GCL-IPL thickness in almost all cases of papilledema.[7] Idiopathic Intracranial Hypertension Treatment Trial (IIHTT) reported only 3% of their patients with GCL-IPL thinning compared to controls at presentation by using this algorithm. However, they reported thinning of the GCL-IPL layer in 50% of the patients at 6 months. The thinning of GCL in the presence of thickened or normal RNL could suggest early retrograde optic nerve damage.

Both RNFL and GCL-IPL layers showed a significant correlation with mean deviation at baseline. GCL-IPL also showed a moderate correlation with visual acuity and contrast sensitivity at baseline. At 6 months, RNFL did not show a significant correlation with any of the visual functional parameters; however, the thicker GCL-IPL complex was associated with better mean deviation and contrast sensitivity. Thus, the GCL IPL thickness may provide an indirect assessment of functional outcomes.

Rebolleda *et al*.[14] in their study found a significant correlation between baseline RNFL and final mean deviation at 1 year. They reported that the mean RNFL at 1 year had normalized in 90% of eyes, with a statistically significant inverse correlation with baseline mean deviation. Skau *et al*.[15] also reported a similar correlation between change in RNFL over 3 months with a change in mean deviation. Both these studies were done on the stratus model of OCT in which GCL-IPL evaluation was not available. To understand the predictive value of baseline OCT parameters, a correlation between the baseline structural parameters and the final visual functions was sought. Baseline thicker GCL-IPL values correlated significantly with the improved visual acuity, mean deviation, and contrast sensitivity at 6 months. However, baseline RNFL thickness did not show a statistically significant correlation with any of the final visual functional parameters. As there was a significant improvement in the GCL-IPL layer between baseline and 6 weeks follow-up, we correlated the final functional parameters with GCL-IPL at 6 weeks. Interestingly, the relationship was stronger at this time point (visual acuity: r = −0.34, $P$ = 0.01; mean deviation: r = 0.44, $P$ < 0.001; and contrast sensitivity: r = 0.45, $P$ < 0.001). Athappilly *et al*.[13] in their retrospective study also found that baseline RNFL did not correlate with the final mean deviation (r = 0.012; $P$ = 0.95). Nonetheless, they also observed that the GCL-IPL layer thickness at the second visit significantly correlated with final mean deviation albeit at 1 year (r = 0.47; $P$ = 0.007) Chen *et al*.[5] in their retrospective study of 31 patients with visual acuity of less than 20/25 also observed a similar relationship between the mean deviation and GCL-IPL measured by Iowa protocol. Interestingly, they also found that GCL-IPL at 2–3 weeks correlated better with the final visual outcome.

Although all these studies, including the present study, have heterogeneity in their methodology, the results indicate that GCL-IPL can be used as a marker to predict the final visual outcome in patients of IIH. Contrary to these results, IIHTT reported no significant correlation between OCT parameters and visual function. The study included patients with only mild visual field defects (mean deviation of −2.00 dB to −7.00 dB), which might explain the dissimilar results.

The Iowa 3D segmentation protocol to measure RNFL and GCL-IPL requires superior technical skills and is time-consuming to be replicated in a busy outpatient department. However, optic disc height (ODH) evaluated by IIHTT by using a 5-line raster scan seemed to be a faster and simpler method of assessment of optic disc edema. The optic disc height was measured manually for each line, and an average of 5 lines was considered for final evaluation. The study reported a strong correlation of ODH with peripapillary RNFL thickness and total retinal thickness.[7] In our study, we followed the same method and found a strong and significant correlation of ODH with RNFL and GCL-IPL layer [0.622 (<0.001) and −0.604 (<0.001), respectively]. ODH gradually decreased over 6 months and showed a good correlation with visual functional parameters both at baseline and at 6 months. The baseline ODH showed moderate and significant correlation with final mean deviation,contrast sensitivity and visual acuity. Increased ODH values at baseline were associated with poorer functional outcome at 6 months. These results suggest that till a more robust segmentation algorithm for measurement of RNFL and GCL layer becomes available, ODH can be used as a tool to monitor and prognosticate patients of IIH.

Limitations of our study include relatively small sample size and use of the commercial algorithm for measurement of RNFL and GCL layer.

## Conclusion

It is a matter of time before the commercially available algorithms become more reliable because of the increased resolution of OCT and improved segmentation algorithms. For the time being, it is important to identify artifacts in the GCL-IPL measurements, particularly in the presence of disc edema. In the setting of severe papilledema, RNFL can misguide the prognosis. Despite the limitation, the GCL-IPL thickness can be a valuable tool for an objective evaluation of the integrity of the optic nerve in patients with IIH, and ODH can be used as an alternative or in combination with GCL-IPL in these cases.

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### Conflicts of interest

There are no conflicts of interest.

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