

Assessment of Optic Nerve Head Changes in Patients with Papilledema Using Spectral-Domin Optical Coherence Tomography

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Abstract

Background: Swelling of the optic disc caused by axoplasmic flow stasis in the optic nerve head as a consequence of elevated intracranial pressure is referred to as papilledema (PO) (ICP). Measurements of the ONH and retinal layers using optical coherence tomography (OCT) imaging are reliable and reproducible, including measurements of the average peripapillary retinal nerve fibre layer (RNFL) thickness, average total peripapillary retinal thickness (TRT), and comparisons for all OCT parameters reflecting swelling of the ONH or peripapillary retina. Papilledema (PO) has been shown to affect the optic nerve head (ONH), retinal nerve fibre layer (RNFL), peripapillary total retinal (PTR) thickness, and ganglion cell layer (GCL) by OCTA (OCT). 60 eyes were used in this investigation, which was a prospective case-control study. The patients were picked from Benha University Hospitals' outpatient ophthalmology clinic. Optic nerve group (A) consisted of 30 eyes from 30 healthy controls, 16 of whom had mild papilledema, and 14 of whom had moderate to severe papilledema, which was separated into two groups: Group B (16 patients) and Group C (14 patients). Patients with moderate to severe papilledema (C) had higher levels of ONHV than those with mild papilledema (B). Furthermore, the average ONHV in group (B) was higher than in group (A) (A). However, as compared to healthy people in group A, the CD ratio was lower in patients with papilledema in groups B and C. In group C, the average thickness of the RNFL was considerably larger in all quadrants than in group B.. In addition, group (B) had a thicker average RNFL than group (A). PTR thickness values in group (C) were considerably higher than those in group (A) in all quadrants (B). In addition, the average PTR thickness in group (B) was higher than that in group (A). The difference in GCL thickness between the two groups in our research was not statistically significant. The results of this research demonstrate that all of the OCT measures tested (CD/R, ONHV, PTR, RNFL) are useful in the diagnosis of PO. These metrics may also identify early papilledema, thus they can be used to track PO patients and see whether their condition improves or worsens as a result of therapy. When it comes to diagnosing and monitoring individuals with PO, the only criterion that has demonstrated no sensitivity is GCL.

Key words: Optic Nerve Head Changes, Papilledema, Spectral, Domin Optical Coherence Tomography.

1. Introduction

Papilledema (PO) refers to swelling of the optic disc secondary to axoplasmic flow stasis in the optic nerve head that results from increased intracranial pressure (ICP). It must be distinguished from optic disc swelling from other causes which is simply termed "optic disc edema". Papilledema must also be distinguished from pseudo-papilledema such as optic disc drusen. Since the root cause of papilledema is increased intracranial pressure (ICP) this is an alarming sign which may presage such entities as brain tumor, CNS inflammation, or idiopathic intracranial hypertension (IIH) [1].

Idiopathic intracranial hypertension (IIH), also known as pseudotumor cerebri, may occur at any age but is primarily a disease of obese women between the ages of 15 and 40 [2].

The etiology of IIH is currently unknown. Associated risk factors may include pregnancy, corticosteroid therapy, Cushion's disease aldosteronism, hypervitaminosis A and contraceptive pills [3].

Being a diagnosis of exclusion, other causes of elevated intracranial pressure must be ruled out by history, imaging studies include magnetic resonance venogram (MRV) and examination of cerebrospinal fluid (CSF) [4].

The most common symptom at presentation is headache, typically holocranial, worsen after waking [5].

Papilledema is the most common sign at presentation and is indistinguishable from papilledema

occurring with other causes of raised ICP. Papilledema often produces brief episodes of monocular or binocular visual loss, called transient visual obscurations (TVOs) [6].

Diagnosis of papilledema is made based on modified Dandy criteria, elevated intracranial pressure (ICP) on lumbar puncture, signs and symptom of elevated ICP (7).

Optical coherence tomography imaging reliably and reproducibly demonstrates alterations in the optic nerve head (ONH) and retinal layers in IIH, which includes among others measurement of the average peripapillary retinal nerve fiber layer (RNFL) thickness, average total peripapillary retinal thickness (TRT), comparisons for all OCT parameters reflecting swelling of the ONH or peripapillary retina [8].

The OCT can also be useful in the differentiation between papilledema and other edematous optic neuropathies. showed that the retinal pigment epithelium and the Bruch's membrane in the peripapillary region at the level of the scleral channel drift inwards (towards the vitreous), and that this mechanical deformation results from an increase in the pressure gradient between the perioptic subarachnoid space and the eyeball. This sign is specific for papilledema [9].

Perimetry reveals enlargement of the blind spot, indicative of an enlarged optic nerve head due to papilledema). Other common visual field defects include a generalized reduction in retinal sensitivity, arcuate

defects, nasal step, paracentral scotomata, generalized field constriction, and central scotomata^[10].

The aim of this work was to evaluate the effect of papilledema (PO) on optic nerve head (ONH), retinal nerve fiber layer (RNFL), peripapillary total retinal (PTR) thickness and ganglion cell layer (GCL) by Optical coherence tomography (OCT).

2. Patients and Methods

2.1. Study design

A prospective case control study.

2.2. Settings

The study was carried out on 60 eyes.

The patients were selected from the outpatient ophthalmology clinic of Benha University Hospitals.

The study included 30 eyes from 30 normal healthy control to assess reliability of optic nerve group (A) and 30 eyes of patients recently diagnosed with papilledema which divided into 2 groups, group (B) diagnosed with mild papilledema included 16 patients, group (C) diagnosed with moderate to severe papilledema included 14 patients according to Frisén Scale⁽¹¹⁾.

Inclusion Criteria for normal subjects:

- [1] Age between 18 to 45 years ago as the incidence of increased intracranial hypertension more common in this age.
- [2] Absence of any neurological diseases.
- [3] 3. No previous any intraocular or intracranial surgeries.

Inclusion Criteria for patients:

- [1] Patients with optic disc edema due to papilledema.
- [2] Age >18 years
- [3] Bilateral papilledema with Frisen scale ranging from grade 1 to 5.

Exclusion Criteria for both patients and normal subjects:

- [1] Patients with high refractor errors (> ±5D sphere and ±3D astigmatism).
- [2] Patients with pseudopapilledema as in crowded tilted disc, optic disc drusen.
- [3] Presence of any optic disc changes (glaucoma, optic atrophy).
- [4] Patients with optic disc edema due to optic neuritis.
- [5] Ocular disease as (cataract, chorioretinal scar, post. Uveitis, macular edema, retinal artery or vein occlusion).
- [6] Patients with history of orbital disease and ocular inflammation.
- [7] Any intraocular or intracranial surgeries.

2.3. Methods

- [1] History talking as present history it mean the

complaint, past ocular history of disease or operations or trauma, past medical history of DM or hypertension or headache and previous operations.

- [2] Complete ophthalmological examination was done for every patients.
- [3] Best corrected visual acuity by snellen's chart then convert to LogMAR for statistical analysis.
- [4] Anterior segment examination by Slit lamp examination.
- [5] Fundus examination and color fundus photography with grading papilledema according to frisen scale.
- [6] Optical coherence tomography of optic nerve, we used topcon spectral-domain OCT (SD-OCT)2000 to do optic disc scan by radial or map scan to calculate optic nerve head volume (ONHV), optic disc cube 200 x200 acquisition protocol used for retinal nerve fibre layer (RNFL) thickness measurements of fixed standard 3.4 mm-diameter circular scan, macular cube 512x128 acquisition protocol centred on the optic nerve head in order to measure the peripapillary total retinal (PTR) thickness inside the 3.0 mm-diameter circle area and retinal ganglion cell layer (GCL) thickness.
- [7] All patients underwent neurological assessment and neuroimaging to reveal the etiology of papilledema as idiopathic intracranial hypertension in (26 patients), space occupying lesions brain tumor in (2 patients) and superior sagittal thrombosis in (2 patients).

2.4. Ethical considerations

- No harmful manoeuvres were performed or used.
- An informed consent written in Arabic was taken from the participants.
- Explanation of the study aim in a simple to be understood by participants.
- All data were confidential and not used outside the study without patient's approval.
- Participants had the right to withdraw from the study at any time without giving any reason.

Data management and statistical analysis

Data were collected, coded, revised and entered to the Statistical Package for Social Science (IBM SPSS) version 20. The qualitative data were presented as number and percentages for the qualitative data, mean, and standard deviations. Chi-square test, The one-way (ANOVA) and Kruskal Wallis test were used

P > 0.05: Non significant (NS)

P < 0.05: Significant (S)

P < 0.01: Highly significant (HS).

3. Results:

Table (1) C/D Ratio and Optic Nerve Head Volume (ONHV) among studied groups.

	Group A (n = 30)		Group B (Mild P.O) (n = 16)		Group C (moderate-sever P.O) (n = 14)		Test of Sig.		Sig. bet. grps.		
	Mean	SD	Mean	SD	Mean	SD	Test of Sig.	p value	P ₁	P ₂	P ₃
C/D Ratio	0.48	0.12	0.32	0.11	0.11	0.08	H= 39.142	<0.001*	<0.001*	<0.001*	0.003*
ONH Volume (Rim vol) (mm ³)	0.51	0.14	3.46	1.24	6.15	0.43	F=347.016	<0.001*	<0.001*	<0.001*	<0.001*

F: F for One way ANOVA test, Pairwise comparison bet. each 2 groups was done using Post Hoc Test (Tukey)

H: H for Kruskal Wallis test, Pairwise comparison bet. each 2 groups was done using Post Hoc Test (Dunn's for multiple comparisons test)

p: p value for comparing between the studied groups

p₁: p value for comparing between Group A and Group B

p₂: p value for comparing between Group A and Group C

p₃: p value for comparing between Group B and Group C

*: Statistically significant at p ≤ 0.05

This table shows that mean of C/D ratio and ONH Volume (Rim vol.) among 3 groups.

According to Post Hoc Test there was statistically significant decrease C/D ratio in group C and group B than group A. But there was no significant difference between group B and group C.

And there was statistically significant increase ONH Volume (Rim vol.) in group C than other groups. And there was increased ONH Volume (Rim vol.) in group B than Group A.

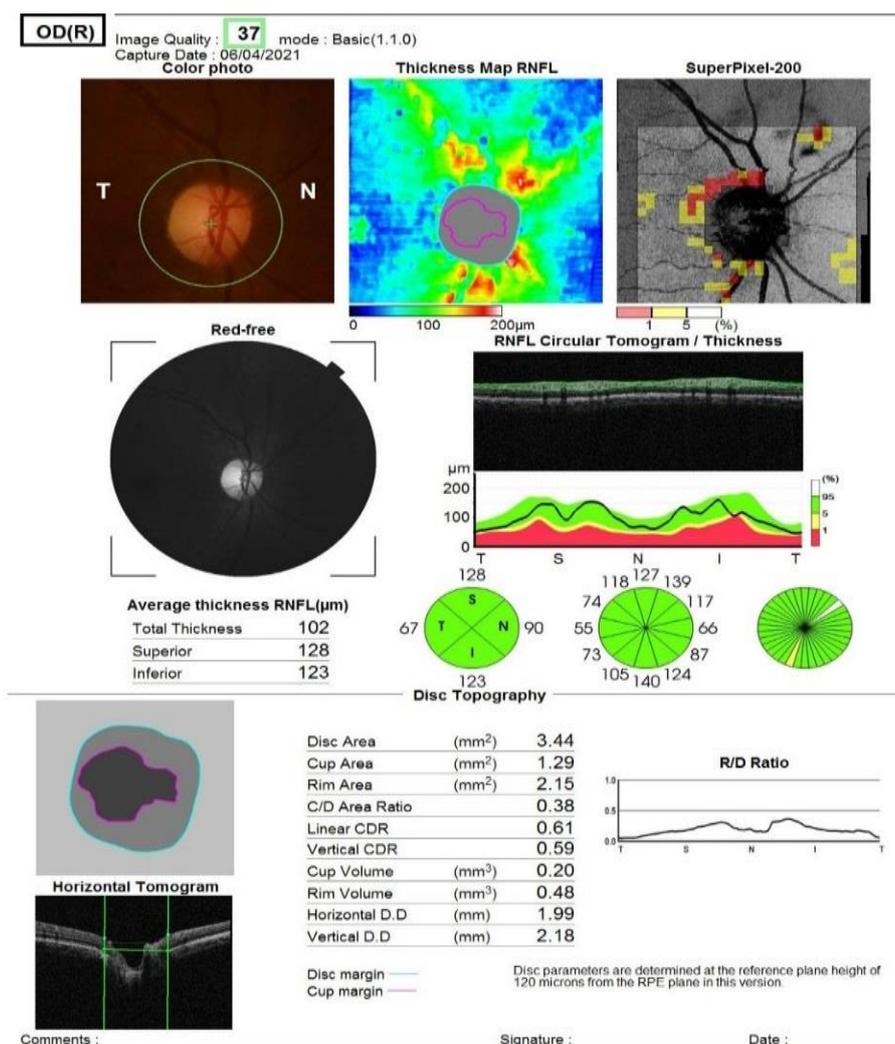


Fig.(1) OCT of ONH in normal

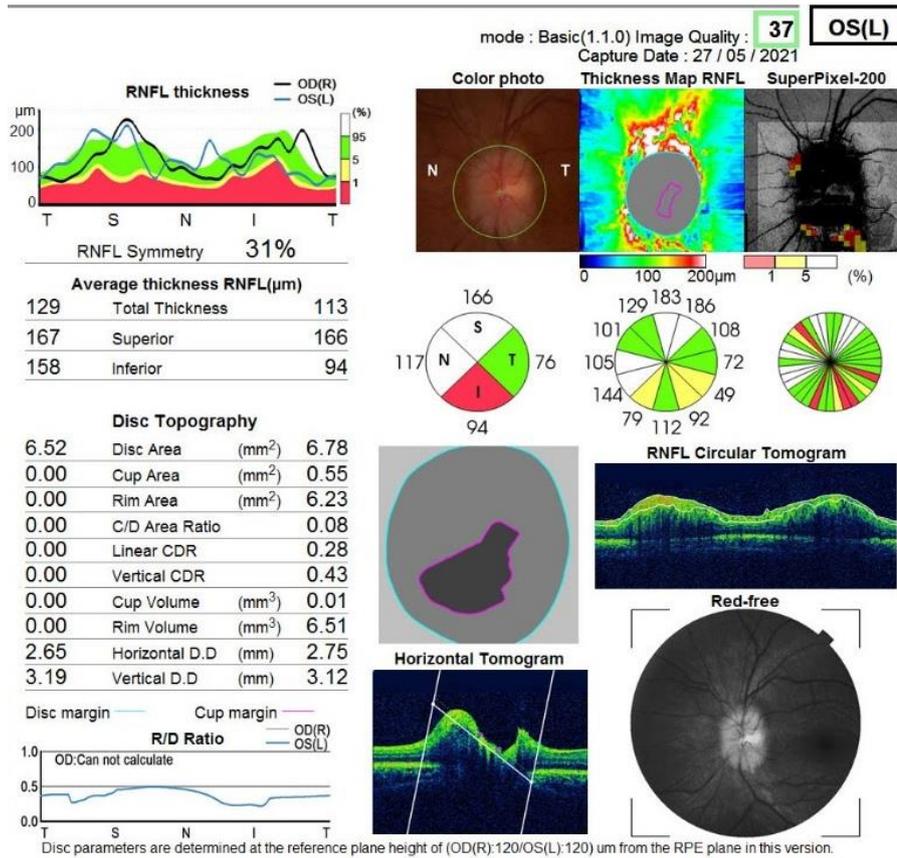


Fig. (2)OCT of ONH in papilledema(G3) group C

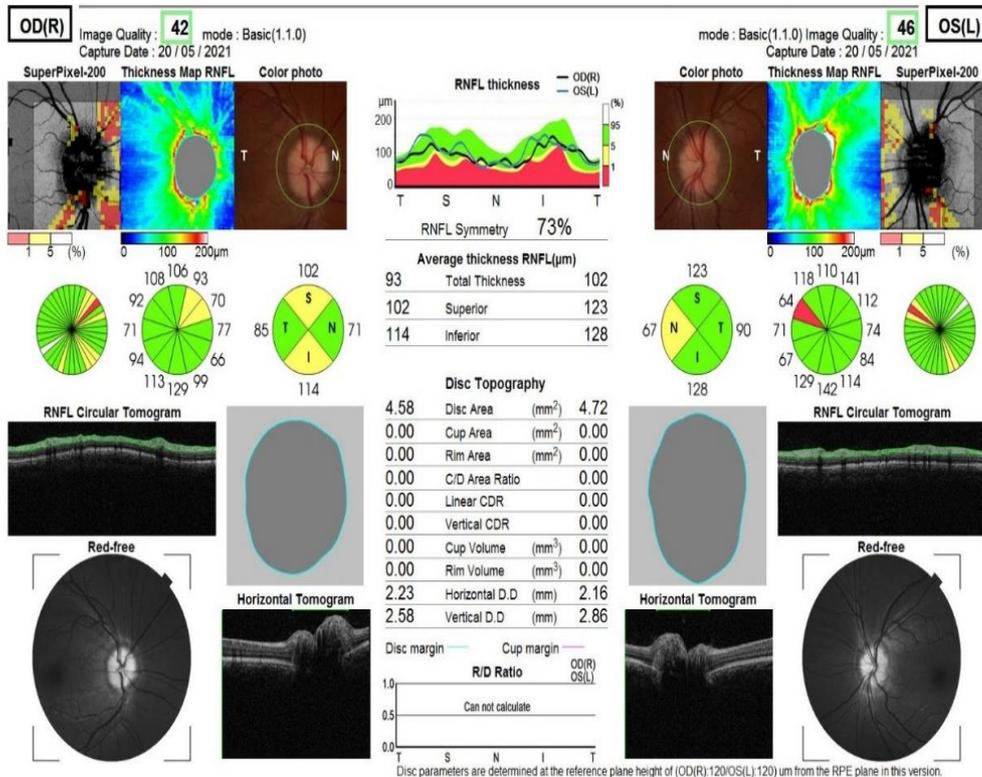


Fig.(3) OCT of ONH in papilledema (G 1) group B

Table (2) Peripapillary total retinal (PTR) thickness among studied groups.

		Group A (n = 30)		Group B (Mild P.O) (n = 16)		Group C (moderate-sever P.O) (n = 14)		One way ANOVA		Sig. bet. grps.		
		Mean	SD	Mean	SD	Mean	SD	F	p value	p ₁	p ₂	p ₃
P.T.R thickness s (um)	S	284.4	16.53	418.3	49.39	540.5	78.04	151.723*	<0.001*	<0.001*	<0.001*	<0.001*
	I	279.7	21.96	420.7	75.45	505.6	71.27	93.579*	<0.001*	<0.001*	<0.001*	<0.001*
	T	271.1	14.72	364.9	46.45	474.9	42.59	186.043*	<0.001*	<0.001*	<0.001*	<0.001*
	N	275.5	17.09	353.3	40.11	448.1	48.70	130.600*	<0.001*	<0.001*	<0.001*	<0.001*

F: F for One way ANOVA test, Pairwise comparison bet. each 2 groups was done using Post Hoc Test (Tukey)

p: p value for comparing between the studied groups

p₁: p value for comparing between Group A and Group B

p₂: p value for comparing between Group A and Group C

p₃: p value for comparing between Group B and Group C

*: Statistically significant at p ≤ 0.05

This table shows that mean of Superior quadrant was 284.4 in group A, 418.3 in group B, 540.5 in group C. Inferior quadrant was 279.70 in group A, 420.7 in group B, 505.6 in group C.

Nasal quadrant was 275.5 in group A, 353.3 in group B, 448.1 in group C.

Temporal quadrant was 271.10 in group A, 364.9 in group B, 474.9 in group C.

According to Post Hoc Test there was statistically significant increase P.T.R thickness in group C than group B and A. and there was significant increase P.T.R thickness in group B than group A.

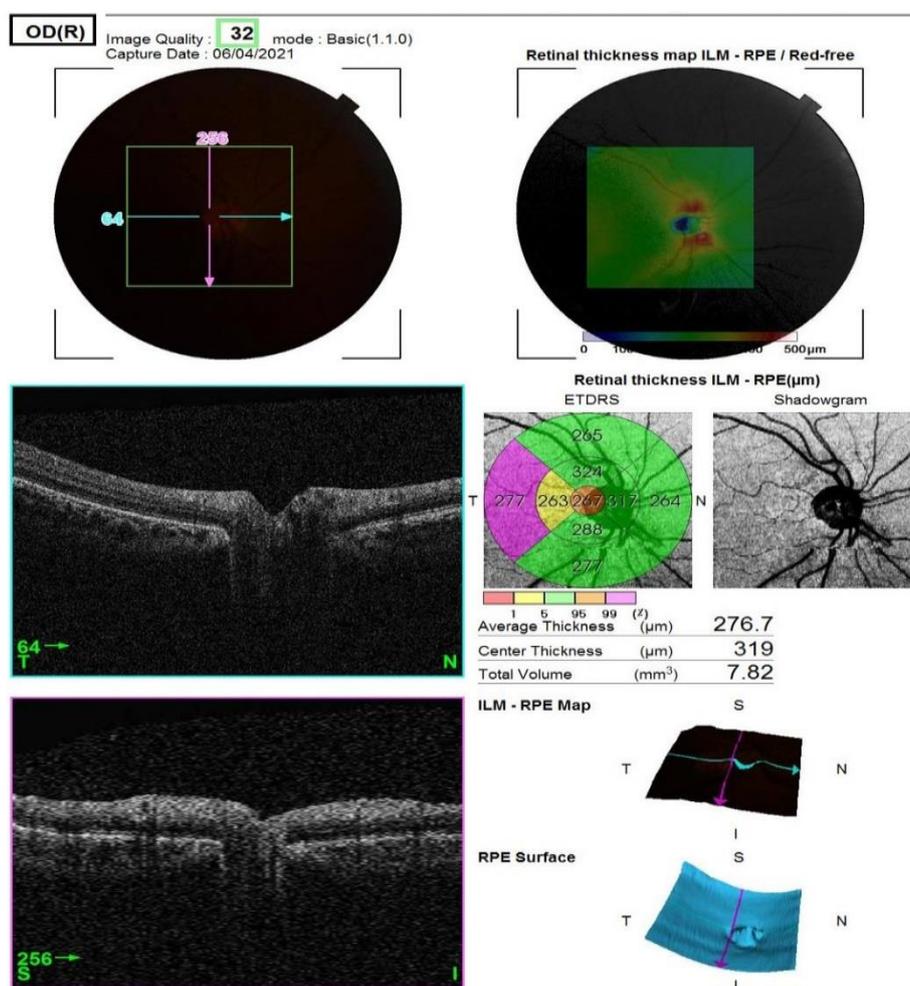


Fig. (4) P.T.R thickness in normal group.

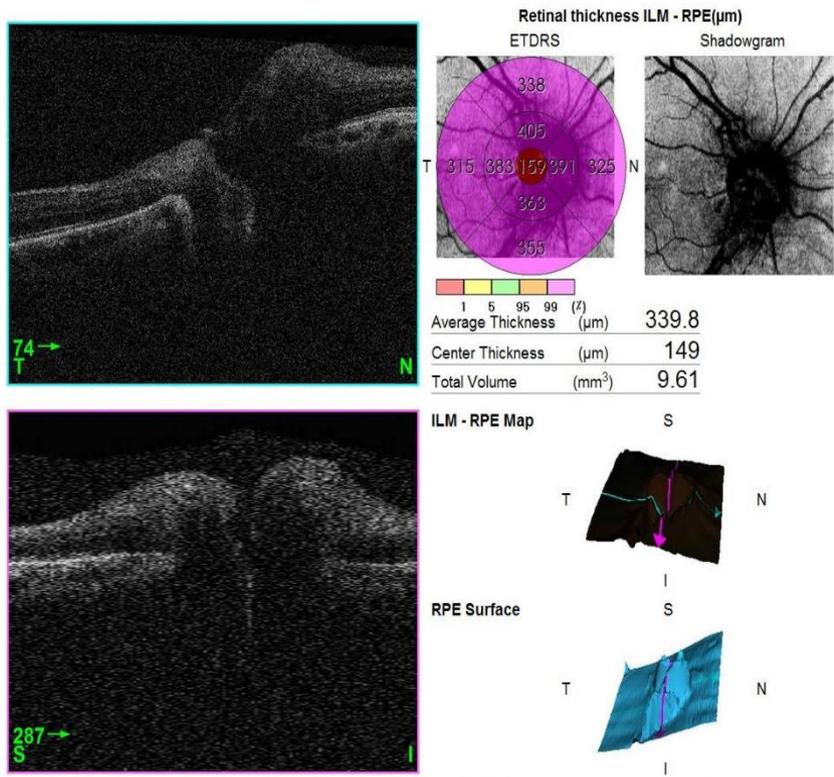


Fig. (5) PTR thickness in papilledema patient group B.

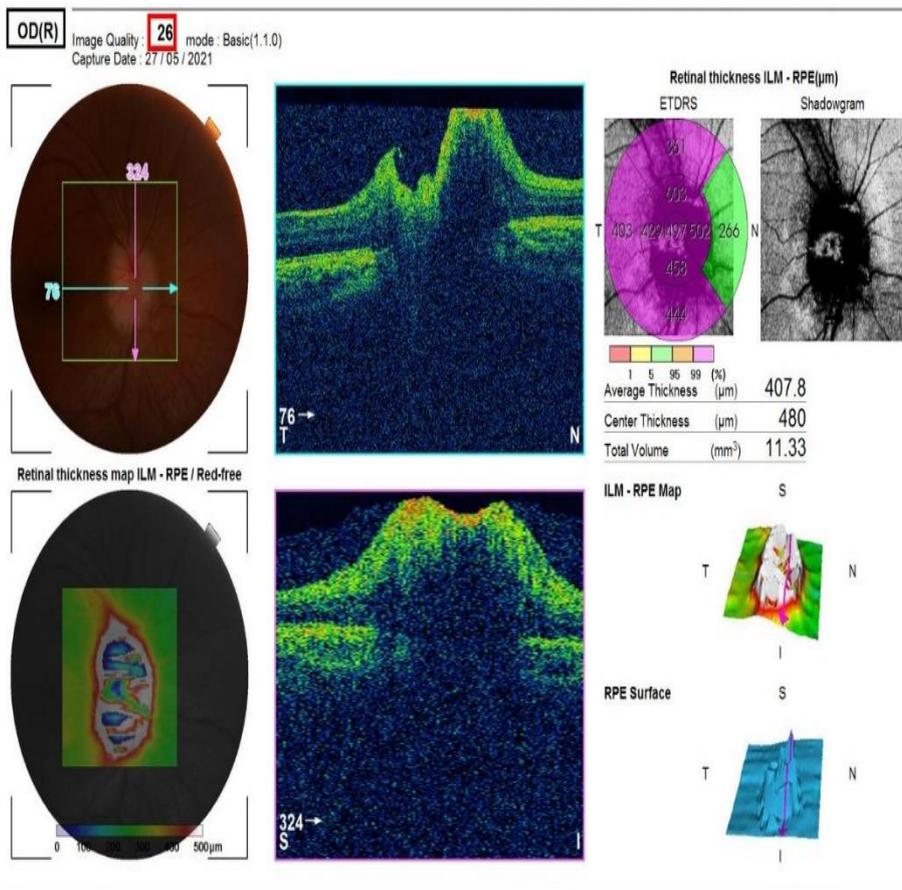


Fig. (6) PTR thickness in papilledema patient group C.

Table (3): Retinal nerve fiber layer (RNFL) thickness among studied groups.

		Group A (n = 30)		Group B (Mild P.O) (n = 16)		Group C (moderate-sever P.O) (n = 14)		One way ANOVA		Sig. bet. grps.		
		Mean	SD	Mean	SD	Mean	SD	F	p value	p ₁	p ₂	p ₃
R.N.F.L	S	121.77	7.48	178.31	20.35	295.93	32.09	388.967	<0.001*	<0.001*	<0.001*	<0.001*
Thickness (um)	I	122.73	6.24	193.38	20.94	288.29	29.33	400.543	<0.001*	<0.001*	<0.001*	<0.001*
	N	80.83	7.12	100.25	6.53	174.21	17.03	409.364	<0.001*	<0.001*	<0.001*	<0.001*
	T	80.23	6.32	117.25	11.13	179.29	19.28	341.427	<0.001*	<0.001*	<0.001*	<0.001*

F: F for One way ANOVA test, Pairwise comparison bet. each 2 groups was done using **Post Hoc Test (Tukey)**

p: p value for comparing between the studied groups

p₁: p value for comparing between **Group A** and **Group B**

p₂: p value for comparing between **Group A** and **Group C**

p₃: p value for comparing between **Group B** and **Group C**

*: Statistically significant at p ≤ 0.05

This table shows that mean of Superior quadrant was 121.77 in group A, 178.31 in group B, 295.93 in group C. Inferior quadrant was 122.73 in group A, 193.38 in group B, 288.29 in group C.

Nasal quadrant was 80.83 in group A, 100.25 in group B, 174.21 in group C.

Temporal quadrant was 80.32 in group A, 117.25 in group B, 179.29 in group C.

According to Post Hoc Test there was statistically significant increase P.T.R thickness in group C than group B and A. and there was significant increase P.T.R thickness in group B than group A.

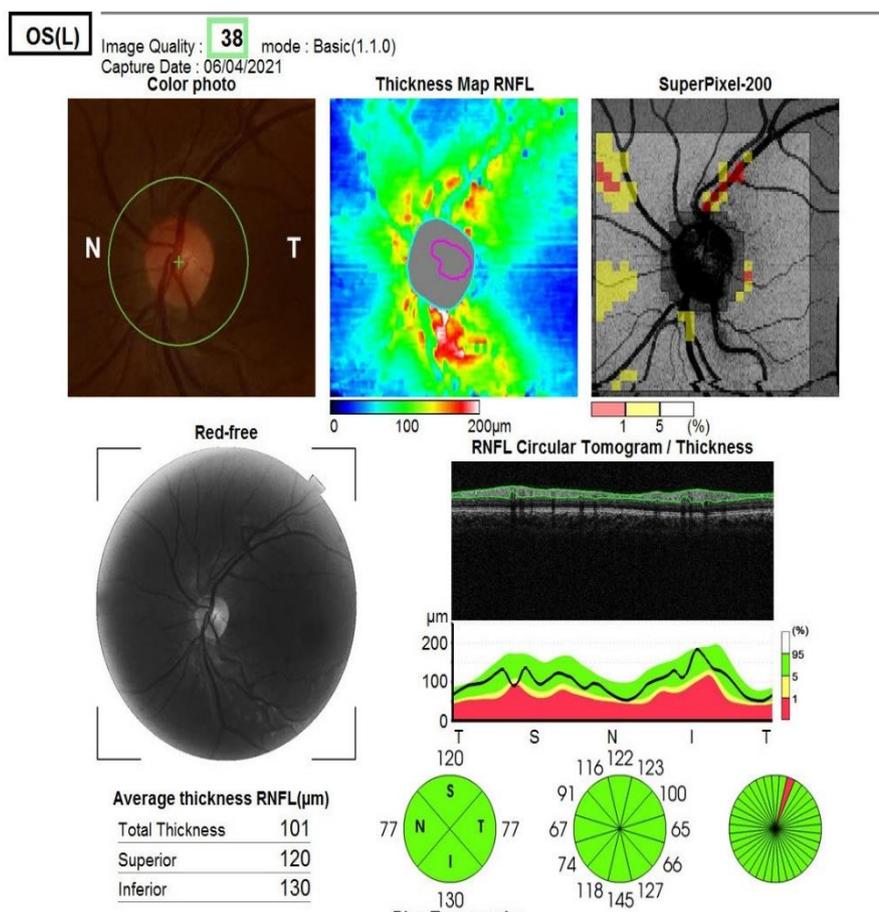


Fig. (7) RNFL thickness in group A.

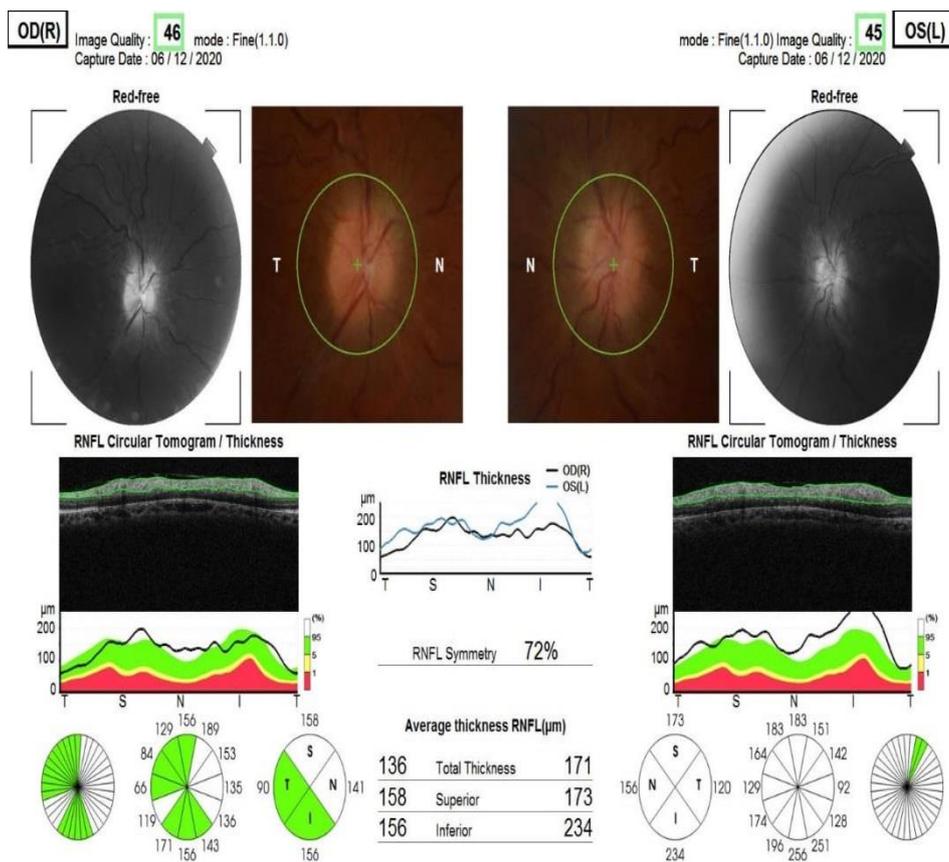


Fig. (8) R.N.F.L thickness in group B.

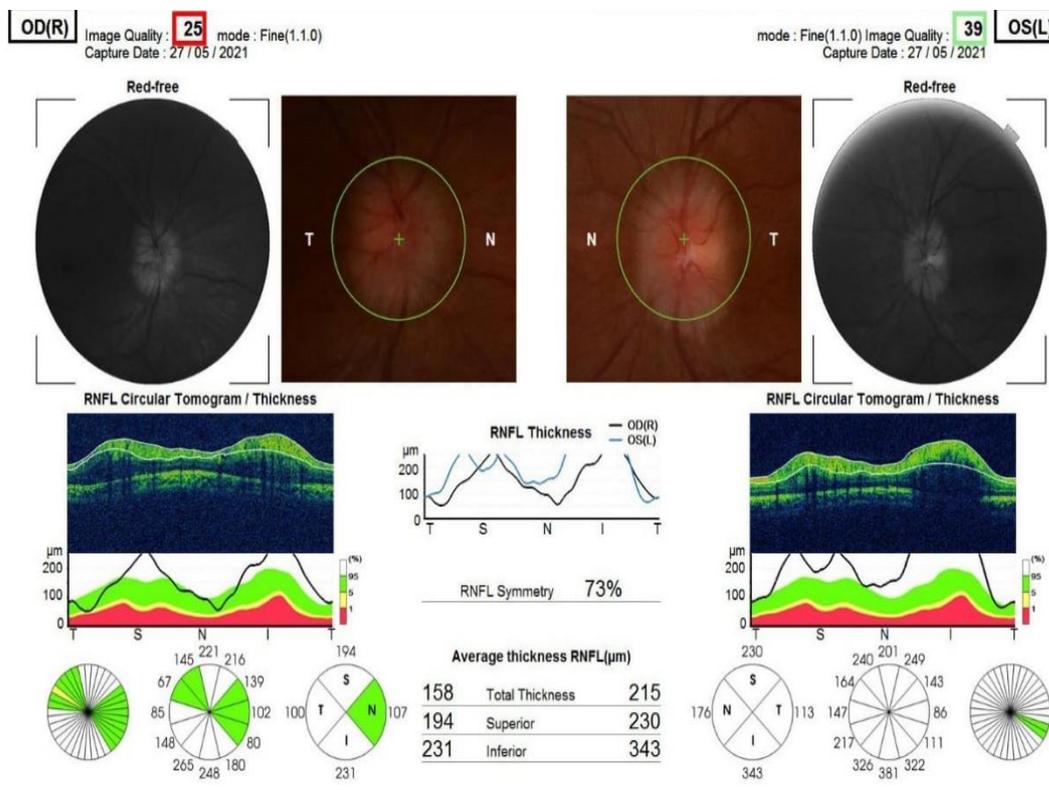


Fig. (9) R.N.F.L thickness in group C.

Table (4) Ganglion cell layer (GCL) thickness among studied groups.

		Group A (n = 30)		Group B (Mild P.O) (n = 16)		Group C (moderate-sever P.O) (n = 14)		One way ANOVA	
		Mean	SD	Mean	SD	Mean	SD	f	p value
GCL Thickness (um)	S	73.23	4.58	72.94	6.59	74.86	5.38	0.574	0.566
	I	73.37	4.24	72.81	5.98	74.86	5.19	0.681	0.510

F: F for One way ANOVA test

p: p value for comparing between the studied groups

This table shows that there was no statistically significant difference between studied groups among GCL thickness

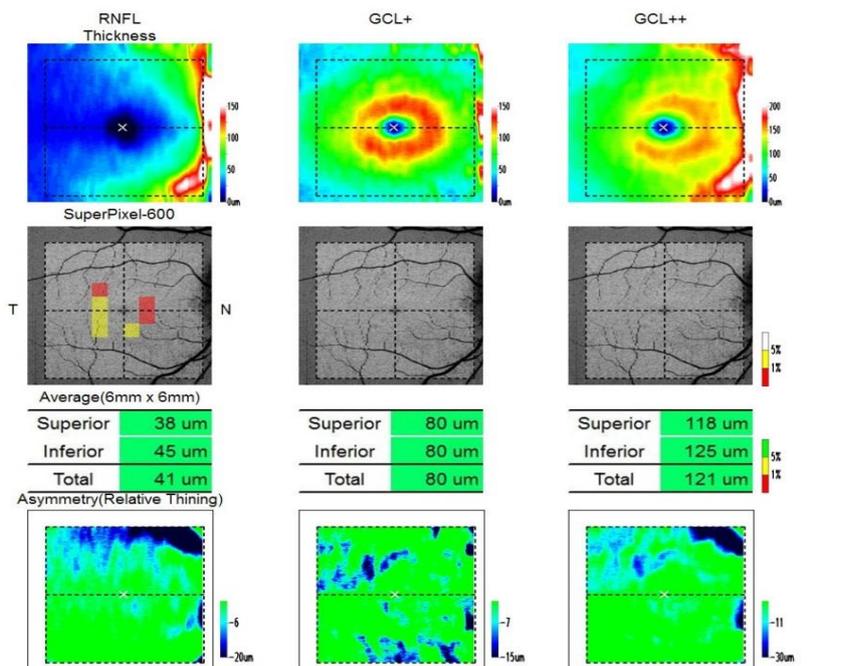


Fig. (10) GCL thickness in normal

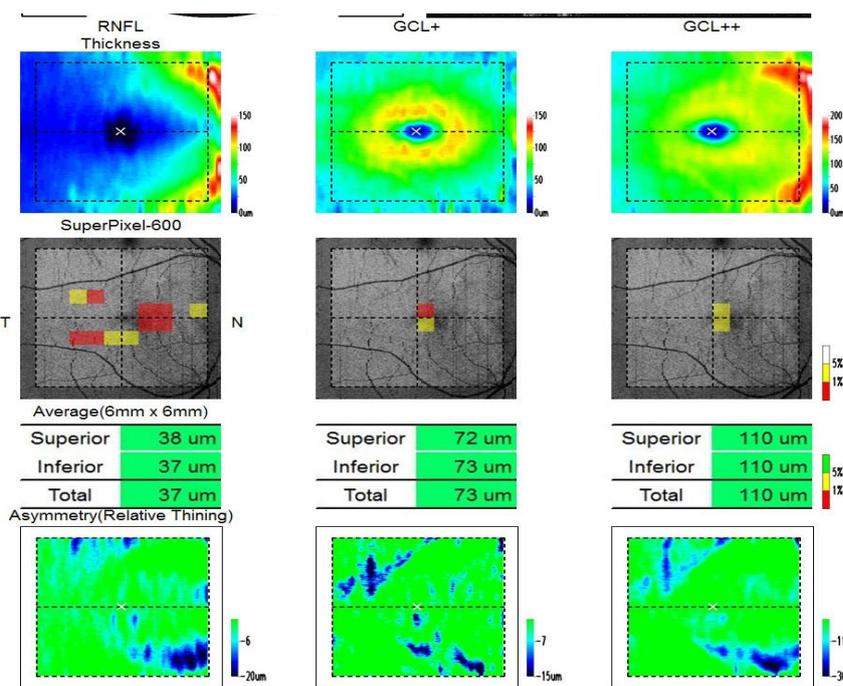


Fig. (11) GCL thickness in papilledema.

4. Discussion

Patients with moderate to severe papilledema (group C) and patients with mild papilledema (group B) had higher ON head volumes than healthy people in our investigation, and the difference between groups B and C was statistically significant.

Compared to healthy people in group A, the CD ratio was lower in patients with papilledema in groups B and C.

In groups (C) and (B), the average thickness of the RNFL was considerably larger in all quadrants compared to group A.

Furthermore, the average thickness of the PTR in group (C) was substantially larger than in group (B) (B).

Groups (C) and (B) had considerably bigger average PTR thickness values than group A in all quadrants.

Furthermore, the average thickness of the PTR in group (C) was substantially larger than in group (B) (B).

Our findings are consistent with earlier research [12].

Twenty-two normal people and twenty-four patients with PO induced by elevated intracranial pressure were investigated by Vardanian et al. [12] in 2011.

The Modified Frise 'n Scale was used by three masked observers to assess OCT high-quality fundus pictures.

A total of 18 eyes were found to have mild PO, while another 18 had moderate-severe PO (6 eyes).

The thickness of the retinal nerve fibre layer (RNFL) was measured using the conventional optic disc cube acquisition technique of 200 x 200 pixels and the thickness of the PTR was measured using the 'macular' cube acquisition methodology of 512 x 128 pixels centred on the optic disc.

Global and quadrant-specific thickness values were determined and compared across the three groups (control, mild PO, moderate-severe PO).

In this study, RNFL and PTR thickness were the primary endpoints.

Researchers found that the average RNFL and PTR thickness in the moderate-to-severe PO, mild PO, and control groups was 299.3 mm, whereas the values in the other groups were 112.4 mm, 96 mm, and 804.5 mm, with the last two values coming in at 463.1 mm and 332.4 mm.

The RNLF and PTR thicknesses of patients with moderate severe PO were compared to those with mild PO and a control group.

The RNLF thickness measurement did not show any differences between mild PO and controls, however the PTR thickness measurement did (p0.001).

Patients with mild and moderate to severe PO had substantially larger average RNFL thickness values than the control group in all quadrants of the body.

Measurement of RNFL thickness was utilised in 2005 (Menke et al) [13] to examine the impact on OCT imaging of disc edema due to inflammatory optic neuropathies or retinal vein occlusions.

According to the findings of this research, the average RNFL thickness in the DE group (122 um) and the control group (91 um) was significantly different.

When comparing the DE and control groups, the average PTR thickness was 329 um, whereas it was 255 um in the former.

Study participants with degenerative disc disease (DE) were shown to have considerably larger RNFL thickening measured by OCT compared to healthy controls.

However, individuals with disc edema due to papilledema, rather than retinal vein blockage, were studied in our research.

One of the first studies to use stratus optical coherence tomography (OCT) to evaluate changes in RNFL thickness in edema of the optic disc was done by Savini and colleagues in 2006.

In this research, nine individuals with optic disc edema were studied, six of them had anterior ischemic optic neuropathy, one had multiple sclerosis-associated papillitis, and the other two had bilateral papilledema.

The RNFL was scanned using stratus OCT to acquire peripheral images.

Seven patients had follow-up measures ranging from 8 to 30 weeks.

Patients with disc edema had a mean RNFL thickness of 217.9 nm, compared to 100.8 nm in controls.

As the illness progressed toward optic atrophy or clinical remission, thinning was noted in individuals who had been well monitored.

In our study, only individuals with papilledema were found to have disc edema.

We employed spectral domain OCT, not stratus OCT, to quantify the thickness of the PTR and RNFL in order to identify disc edema.

5. Conclusion

This study's use of OCT measures (CD/R, ONHV, PTR, and RNFL) demonstrated their efficacy in the early detection of PO.

These metrics may also identify early papilledema, thus they can be used to track PO patients and see whether their condition improves or worsens as a result of therapy.

When it comes to diagnosing and monitoring individuals with PO, the only criterion that has demonstrated no sensitivity is GCL.

When comparing packed optic discs with moderate PO, PTR thickness measurement might be an intriguing method to compare.

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