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## Prognostic Value of Optical Coherence Tomography in Idiopathic Intracranial Hypertension

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### ABSTRACT

Article info Received: Accepted:	rmation 01-11-2022 25-01-2023	<b>Background:</b> Increased intracranial pressure without a tumor or other disorders is a hallmark of the neurological condition known as idiopathic intracranial hypertension [IIH]. The major concern among patients with this condition is the hazardous effects on the optic nerve; so, prediction of optic nerve involvement is a priority for those individuals.			
DOI: 10.21608/IJMA.2023.172274.1541		<b>Aim of the work:</b> To assess the predictive value of the optical coherence tomography [OCT] in the follow up of			
*Corresponding author Email: <u>a.sultan.neuro@hotmail.com</u>		<ul> <li>optic disc edema in patients with idiopathic intracrania hypertension, measuring the thickness of the retinal nerver fiber layer [RNFL] and optic disc, and therefore warran more expedited evaluation and treatment.</li> <li>Patients and methods: A prospective cohort study included 30 patients with IIH. Optical coherence tomography wa completed at baseline and follow-up for six months.</li> </ul>			
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10.21608/IJMA.2023.172274.1541.		<b>Results:</b> The mean RNFL thickness was $107.84 \pm 21.65 \mu\text{m}$ with mean ganglion cell complex [GCC] thickness of $89.94 \pm 9.33 \mu\text{m}$ and mean optic nerve head [ONH] thickness was $615 \pm 189 \mu\text{m}$ . There is a significant decrease in intracranial pressure [ICP] associated with a decrease in RNFL thickness and ONH thickness.			
		<b>Conclusion:</b> OCT imaging can be done as non-invasive quantitative method instead of opening pressure in follow up of patients.			

Keywords: Papilledema; Intracranial Hypertension; Headache; Optical coherence tomography.



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### **INTRODUCTION**

Idiopathic intracranial hypertension is a neurological condition characterized by elevated intracranial pressure in the absence of a tumor or other illnesses <sup>[1]</sup>.

In obese women of childbearing age, the incidence of idiopathic intracranial hypertension was reported to be 2.7-19/100,000/year as opposed to the general incidence of 0.03-2/10,000/year<sup>[2]</sup>. Female gender, obesity/weight gain, endocrine abnormalities in particular [Addisson's disease, hypoparathyroidism], and hypervitaminosis A are high potential risk factors for IIH <sup>[3]</sup>.

The diagnosis of IIH is based on the modified Dandy criteria including [1] Complaints of elevated intracranial pressure [headache, visual disorder, etc.], papilledema, [2] Indication of raised CSF pressure [> 25 cm H<sub>2</sub>O with lumbar puncture in the supine position], [3] Normal CSF structure, [4] Exclusion of other causes, [5] No focal neurological deficit [apart from 6<sup>th</sup> nerve palsy], and [6] Normal brain radiology <sup>[4]</sup>.

Almost all IIH individuals with papilledema have a larger physiologic blind spot on visual field testing. In order to validate a raised pressure entrance and rule out any inflammatory, infectious, or malignant conditions that could mimic IIH, a cerebrospinal fluid [CSF] study is necessary for the diagnosis of IIH. Neuroimaging is required to demonstrate the lack of a brain lesion, normal or tiny ventricles, and normal venous sinuses in order to make the diagnosis <sup>[5]</sup>.

In 93–95 percent of cases, headaches are present, nausea and vomiting are infrequent, and tinnitus affects 50–60 percent of people with IIH. One of the cardinal symptoms is visual symptoms, and 70–75 percent of patients experience transient visual obscurations [TVO]

It is commonly acknowledged that loss of visual acuity is a sign of severe disease. Although fulminant IIH is a well-known, while rare, type of the disease that doctors must be aware of since it requires immediate surgical intervention to prevent noticeable permanent visual losses, it is characterized by severe visual loss within 4 weeks of the onset of symptoms <sup>[7]</sup>.

Optical coherence tomography [OCT] is a promising technique for quantifying changes in papilledema severity and for tracking the success of therapeutic therapies. With the help of time domain variables, OCT, a cross-sectional imaging technology that quantitatively evaluates several layers of the retina, may measure the retinal nerve fibre layer [RNFL] with a resolution of about 10 m <sup>[8]</sup>.

OCT imaging is traditionally used to detect and track increased retinal thickness in patients with retinal edema and reduced peripapillary RNFLT in optic neuropathies <sup>[9]</sup>. Numerous researches imply that OCT can also be utilized to keep track of conditions marked by optic disc edema <sup>[10]</sup>.

### **AIM OF THE WORK**

The aim of the present work is to assess the thickness of the retinal nerve fiber layer and the optic disc to determine the predictive utility of optical coherence tomography [OCT] in the follow-up of optic disc edema in patients with idiopathic intracranial hypertension and to support earlier diagnosis and treatment.

### PATIENTS AND METHODS

A prospective cohort study included thirty patients with idiopathic intracranial hypertension, who were recruited from the Neurology outpatient clinics, Neurology department, Al-Azhar University Hospital, New Damietta.

**Inclusion criteria:** Age  $\geq$  18 years, recently diagnosed IIH patients without medications according to the diagnostic criteria, and all patients without any medications [like diuretics for other reasons] can decrease the papilledema. The diagnosis of IIH was based on the modified Dandy criteria <sup>[4]</sup>.

**Exclusion criteria:** Patients with media opacity interfering with appropriate detailed fundus examination, patients having any other medical problems [diabetic retinopathy, high myopia with retinal detachment] known to be associated with retinal pathology will be excluded from this study, and patients with contraindications to lumber puncture.

A written informed consent was obtained from all participants before inclusion in the study, explaining the value of the study and the procedures that will be conducted. The study is conducted in accordance with Helsinki Standards as revised in 2013. The whole study design was approved by the Local Ethics Committee.

### Methods

For each patient, full history taking including drug history intake especially hormonal contraceptive pills, vitamin A, cortisol and clinical examination, complete general examination [including estimating of Body Mass Index] and neurological examination, full ophthalmological evaluation including grading of papilledema. MRI brain without contrast and MRV brain were performed. Papilledema was graded according to the common Frisen scale [11].

Treatment regimens included Acetazolamide combined with potassium and dietary recommendations for weight-reduction were initiated after examination. Medical dosage was individualized and limited to 500-2000 mg/day. Medical therapy was regularly adjusted to relieve symptoms and papilledema and minimize side-effects.

### OCT of the optic disc

In peripapillary mydriatic OCT, we used Cirrus HD-OCT, Model 400, Germany to measure RNFL thickness, the required signal strength was at least 5 with a range from 1 [lowermost] to 10 [uppermost]. Using Optic Disc Scan Cube scan with 6 mm x 6mm area 200x200 [200 A-scans per B-scan; 200 Bscans]. For perfect registration and repeatability, the disc's center is automatically determined.

RNFL thickness display is of a 3.4 mm radius circle around the disc. A standard dataset of roughly 300 patients is used to compare the TSNIT graph against. A diagram of RNFL thicknesses is shown, and it is contrasted with standardized criteria.

At 3 and 6 months after doing the treatment by the neurology department, the patients will be subjected to follow up fundus examination and grading of papilledema, and optical coherence tomography [OCT] optic disc.

Statistical analysis: Using SPSS 22.0 for Microsoft, all information was gathered, tabulated, and statistically examined [SPSS Inc., Chicago, IL, USA]. Using the Shapiro Walk test, the distribution of the data was examined for normality. Frequencies and relative percentages were used to depict qualitative data. The difference between the nominal variables was calculated using the chi square test [2] and Fisher exact, as shown. For parametric and nonparametric data, respectively, the mean and SD [standard deviation] were used to express quantitative data. To determine the difference between quantitative variables in two groups for non-parametric variables, parametric and independent t test and Mann Whitney test were utilized. P-values 0.05 were used in all twotailed statistical comparisons to denote significance.

### RESULTS

The mean visual acuity was  $0.033 \pm 0.118$ with mean opening pressure  $26.15 \pm 6.74$  cm H2O and the mean intraocular pressure being  $14.85 \pm 3.32$  mm Hg [table 1].

The majority observed grade was grade I [46.8%] and grade II [44.7%]. While grade III was found in 6.4% of the eyes and grade IV in 2.1% [table 2].

At baseline, the mean retinal nerve fiber layer [RNFL] thickness was  $107.84 \pm 21.65 \,\mu\text{m}$  with mean ganglion cell complex [GCC] thickness was  $89.94 \pm 9.33 \,\mu\text{m}$  and mean optic nerve head [ONH] thickness was  $615 \pm 189 \,\mu\text{m}$  [table 3].

Regarding fundus examination at follow up among the papilledema patients, there is a significant decrease in papilledema severity after treatment. OCT follow up showed significant decrease in intracranial pressure [ICP] associated with a decrease in retinal nerve fiber layer [RNFL] thickness and ONH thickness [table 4].

Retinal nerve fiber layer [RNFL] thickness was positively correlated with mean opening pressure, ganglion cell complex [GCC] thickness, optic nerve head [ONH] thickness, and papilledema grades [table 5].

		All patients [n=30]	
Age [years]	Mean $\pm$ SD	$38.77 \pm 10.68$	
	Range	24 - 60	
Sex	Female	25 [83.3%]	
	Male	5 [16.7%]	
<b>BMI</b> $[kg/m^2]$	Mean $\pm$ SD	$26.55\pm2.64$	
Residence	Rural	17 [56.7%]	
	Urban	13 [43.3%]	
Duration since headache attack [days]	Mean $\pm$ SD	$14.37\pm2.81$	
Symptoms distribution among the	Pulsating tinnitus	26 [86.7%]	
studied patients	Visual disturbances	19 [63.3%]	
	Headache	29 [96.7%]	
	Nausea and vomiting	27 [90%]	
Fundus examination at baseline	Normal optic disc head	13 [21.7%]	
[n=60]	Optic disc swelling [papilledema]	47 [78.3%]	

### Table [1]: Demographic and clinical distribution of the studied patients

 Table [2]: Papilledema severity and clinical grades at baseline among the papilledema patients

		Papilledema patients [n=47 eyes]			
		No.	%		
Grade I [mild]		22	46.8%		
Grade II [moderate]		21	44.7%		
Severe	Grade III	3	6.4%		
	Grade IV	1	2.1%		

Table [3]: OCT findings at baseline of the studied patients

		All patients [n=60 eyes]	
RNFL thickness [µm]	Mean $\pm$ SD	$107.84 \pm 21.65$	
GCC thickness [µm] Mean ± SD	Mean $\pm$ SD	$89.94 \pm 9.33$	
ONH thickness [µm] Mean ± SD	Mean $\pm$ SD	$615 \pm 189$	
<b>OCT baseline RNFL parameters</b>	Superior [mean $\pm$ SD]	$94.15 \pm 12.55$	
	Inferior [mean $\pm$ SD]	$86.23 \pm 11.46$	
	Nasal [mean $\pm$ SD]	$62.28 \pm 5.54$	
	Temporal [mean $\pm$ SD]	$43.95 \pm 12.59$	

Table [4]: Fundus examination at follow up among the papilledema patients

Studied patients [n=60 eyes]					Р			
		Baseline		3 months		6 months		
		No.	%	No.	%	No.	%	
Normal		13	21.7%	16	26.7%	21	35%	
Grade I [mild]		22	36.7%	27	45%	33	55%	
Grade II [moderate]		21	35%	15	25%	6	10%	0.009
Severe	Grade III	3	5%	2	3.3%	0		
	Grade IV	1	1.7%	0		0		
ICP [cmH2O] Mean ± SD		30.54	$\pm 4.63$	21.83	$\pm 5.14$	18.6	$5 \pm 4.57$	<0.001
RNFL thickness [µm] Mean ± SD		107.84	± 21.65	72.41	± 10.45	59.9	$4 \pm 7.33$	<0.001
ONH thickness [µm] Mean ± SD		615 -	± 189	561	±158	492	$2 \pm 117$	0.001

 Table [5]: Correlation between Mean opening pressure, Papilledema grades and RNFL thickness

	RNFL thickness			
	r	Р		
Mean opening pressure	0.283	.017*		
Mean deviation	-0.456	<0.001*		
Pattern standard deviation	-0.388	.006*		
GCC thickness	0.540	<0.001*		
ONH thickness	0.511	<0.001*		
Papilledema grades	0.463	<0.001*		

### DISCUSSION

Presently, the peripapillary retinal nerve fiber layer edema is measured by optical coherence tomography [OCT] [RNFL]. A more recent noninvasive imaging technique called OCT angiography [OCT-A] enables us to see and measure the ONH vasculature. OCT-A has the capacity to identify anomalies in ONH perfusion, according to studies <sup>[12]</sup>.

The current study showed that normal optic disc head was found in [22.4%] of the eyes and optic disc swelling was found in 77.6%. Optic disc swelling or papilledema is caused by poor axoplasmic outflow as a result of elevated intracranial pressure and high perineural tension <sup>[13]</sup>. However, according to Nogueira *et al.* <sup>[14]</sup>, the optic disc head was normal in 30 eyes [69.77%], while 25 eyes [58.14%] had optic disc edema, 6 eyes [13.95%] had pallor on fundoscopy, and 7 patients [31.82%] had central system venous thrombosis. nervous Additionally, significant а statistically association between edema and visual acuity was found [p = 0.037].

Regarding baseline RNFL parameters distribution, the current study showed that the mean nasal RNFL was 62.28 ± 5.54, mean temporal was  $43.95 \pm 12.59$ , mean superior was 94.15  $\pm$  12.55 and mean inferior was 86.23  $\pm$ 11.46. The study by Labib and Raouf <sup>[15]</sup> reported that compared to controls, patients' overall mean RNFL density was considerably higher [P = 0.000], they also reported that grades of papilledema and peripapillary RNFL correlated significantly positively with total retinal thickness. Also, according to Eren et al. <sup>[16]</sup>, the patient group's mean RNFL thickness increased statistically significantly in comparison to the control group [p 0.01]. Eight quadrants of both groups' eyes were examined, and it was discovered that the patient group's RNFL thickness was statistically higher than the control groups in every segment [p 0.01 for every segment]. However, no significant difference [p= 0.453] in RNFL thickness was seen among individuals in the IIH group and those in the control group, according to Nogueira et al.<sup>[14]</sup>.

The present study also revealed that the mean RNFL thickness was  $107.84 \pm 21.65 \mu m$  with mean GCC thickness was  $89.94 \pm 9.33 \mu m$  and mean ONH thickness was  $615 \pm 189 \mu m$ . In agreement with our findings **Nogueira** *et al.* <sup>[14]</sup>

reported that the mean RNFL thickness was  $111.637\pm24.941 \ \mu\text{m}$  with mean GCC thickness was  $90.535\pm9.766 \ \mu\text{m}$ . Also, **Eren** *et al.* <sup>[16]</sup> reported that the mean RNFL thickness was  $127.19\pm 24.26 \ [94.00-204.00] \ \mu\text{m}$  with mean GCC thickness was  $101.72\pm7.46 \ [80.38-130.72] \ \mu\text{m}$ . the study reported that RNFL but not GCC was significantly differed between IIH cases and controls. Furthermore, **Albrecht** *et al.* <sup>[17]</sup> reported that in IIH patients, the ONH volume was elevated and associated with CSF tension.

A substantial positive relationship between the degrees of papilledema, peripapillary RNFL, and total retinal thickness was also found, according to **Auinger** *et al.* <sup>[18]</sup>. Additionally, overall retinal thickness corresponds more favorably with a minor papilledema degree than peripapillary RNFL thickness, according to **Vartin** *et al.* <sup>[19]</sup>.

In the Idiopathic Intracranial Hypertension Treatment Trial [IIH TT] by **Auinger** *et al.*<sup>[18]</sup>, both Frisén grades and ICP levels [as determined by LP] were strongly linked with the OCT variables of RNFL, total retinal content, and ONH volume; however, the association was better with Frisén grades [r > 0.76] than with LP opening pressures [r > 0.24].

The diagnosis and monitoring of papilledema are two clinical applications of RNFL thickening related to papilledema. According to **Huang-Link** *et al.*<sup>[20]</sup>, in individuals with acute IIH, RNFL thickness normalizes both temporarily and permanently after therapy.

Additionally, the results of IIH treatment are associated with RNFL OCT imaging. According to research by **Skau** *et al.* <sup>[21]</sup> and **Rebolleda** *et al.* <sup>[22]</sup>, RNFL thickness reductions following therapy are linked to improvements in visual field mean deviation. Care must be used when referring RNFL decline over time to clearing papilledema because increasing optic atrophy from RGC injury can provide a similar OCT pattern. The concordant decrease in RNFL thickness and macular GCL IPL thickness, according to **Chen** *et al.* <sup>[23]</sup>, shows optic nerve injury and might be a sign that a treatment has failed. Additionally, RNFL thickness OCT imaging is more sensitive than clinical findings.

Kaufhold *et al.* <sup>[24]</sup> used SD-OCT similarly to the present investigation, but they concentrated on optic nerve head [ONH] volume as a potential measure of therapy efficacy and illness progression in IIH. The volume of the ONH computed using SD-OCT served as a criterion for the diagnosis of and progression in IIH in that cross-sectional pilot investigation, in which 19 patients with IIH were compared with 19 controls. In fact, the measurement of ONH volume finally proved to be more accurate than intracranial pressure. Additionally, Rebolleda et al. [22]'s correlation analysis of the optic disc's morphology and changes in the perimetric threshold using OCT showed that the severity of papilledema quantitatively correlates with the visual field sensitivity. Defects in the visual field improved clearance concurrently with the edema's following treatment. This raises the possibility that OCT could be employed in IIH to track the degree of papilledema and the success of treatment.

The current study showed that RNFL was positively correlated with papilledema grade and mean opening pressure. However, in general, the optic nerve changes [either the papilledema, the field changes and the oct parameters] are not necessarily correlate to the CSF opening pressure <sup>[25]</sup>, because simply there diagnostic criteria for IIH is without papilledema [13 eyes in the current study don't have papilledema], and this is attributed to the bony optic canal size which is the junction that influences the rate of the CSF permeation to the subarachnoid space around the optic nerve <sup>[26]</sup>. This is evidenced in our results through a very weekly positive correlation to the CSF opening pressure [r=0.2]; however, it is more correlated to the papilledema and the other related parameters. OCT is very helpful in the followup of IIH patients with papilledema, however, it is not of the same value as a diagnostic tool and can't replace the LP to first diagnose IIH patients <sup>[27]</sup>. This validates our conclusion that OCT imaging can be used as a non-invasive quantitative approach in place of opening pressure in patient follow-up.

**Limitations of the study:** lack of control group and the small number of patients are the main limitations of the study.

**Conclusion:** As it may aid in the identification of modest disc swelling, OCT imaging is more sensitive than clinical findings and can be used as a non-invasive quantitative approach in place of opening pressure in patient follow-up.

**Future recommendations:** Further comparative studies with larger sample size and longer follow-up are needed to confirm that with GCCT measurements, OCT gives a more reliable estimate of early retrograde optic nerve atrophy, even in cases without papilledema or visual loss.

### **Conflict of Interest and Financial Disclosure:** None

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