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Correlation between Retinal Nerve Fiber Layer and Clinical Grading of Papilledema in Patients with Idiopathic Intracranial Hypertension

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ABSTRACT

Background: Idiopathic intracranial hypertension (IIH), also defined as primary pseudotumour cerebri condition, is a neurological disorder marked by elevated intracranial pressure (ICP) and papilledema with no recognized etiology.
Aim of The Work: To evaluate papilledema in individuals associated with idiopathic intracranial hypertension according to Frisen grading based on descriptive features and its correlation with retinal nerve fibre layer (RNFL) thickness using spectral domain optical coherence tomography(OCT).
Patients and Methods: Our study is a cross sectional observational study that was demonstrated on 48 eyes with papilledema due to IIH. Patients were undergone full ophthalmolgical examination with emphasis on optic disc features and OCT imaging of peripapillary RNFL of optic nerve head (ONH).
Results: with statistically analysis of RNFL thickness in 4 quadrants showing that follow ISNT rule . The mean of average RNFL in mild papilledema is (98.30 ± 24.97), in moderate (162.69 ± 36.96) and in severe (247.40 ± 37.69). That indicates progression of papilledema highly significant correlated with increasing RNFL thickness. Average RNFL thickness values were analysed under ROC curve to give cut off points help as an indicator for diagnosis clinical severity of papilledema.
Conclusion: OCT has the potential to be a useful imaging tool in the identifying and monitoring of IIH, especially when combined with other clinical data. It is now being used in concert with other imaging techniques and clinical factors to detect early variations in the ONH and retinal layers before and after intracranial hypertension therapy.

Keywords: *Retinal Nerve Fiber Layer; Papilledema; Idiopathic Intracranial Hypertension.*

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INTRODUCTION

Idiopathic intracranial hypertension (IIH) is a neurological condition marked by elevated intracranial pressure (ICP) and papilledema with no recognized etiology. The incidence of overweight is largest recognized risk factor for the condition and more frequent among working-age females [1, 2]

The Frise' n Scale has been used to grade papilledema, or optic disc enlargement caused by increased intracranial pressure. To stage optic disc edema, this scale incorporates visual characteristics of the optic disc and peripapillary retina.[3]

Although neuroimaging is crucial in the diagnosis and treatment of IIH, it is insufficient for monitoring the morphologic and functional properties of the optical disc. Optical coherence tomography (OCT) is a more accessible imaging technique than magnetic resonance imaging (MRI) for examining the RNFL in the ocular area of the optic nerve head.[4]

OCT is a simple, rapid, and non-invasive procedure for obtaining in vivo cross-sectional pictures of the macula and optic nerve head, and it may be employed for both freshly identified and chronic IIH patients.[5]

The thickness of the peripapillary Retinal nerve fiber layer (RNFL) is a relevant metric, and recent advancements in diagnostic technology have made it possible to assess RNFL thickness noninvasively.[6]

Spectral-domain optical coherence tomography (SDOCT) measures the thickness of the peripapillary RNFL at a micrometre scale and has been effectively employed for both identification and disease advancement.[7]

SDOCT is the greatest widely utilized diagnosing tool for detecting structural alterations in glaucoma and other non-glaucomatous optic neuropathies.[8]

In individuals with IIH, OCT imaging accurately and consistently shows changes in the optic nerve head (ONH) and retinal layers. The median peripapillary retinal nerve fiber layer thickness (RNFL), median total peripapillary retinal thickness (TRT), ONH volume, and ganglion cell plus inner plexiform layer thickness

(GCL+IPL) in the macula area were all assessed at baseline.[9]

the study aimed to evaluate papilledema in individuals associated with idiopathic intracranial hypertension according to Frisen grading based on descriptive features and its correlation with retinal nerve fibre layer (RNFL) thickness using spectral domain optical coherence tomography(OCT)

PATIENTS AND METHODS

The current work is cross sectional observational study conducted at the Ophthalmology departments in Nasser Institute for research and treatment, Alazhar university hospitals (Al-Hussien Hospital &Sayed Galal Hospital) from September 2020 to January 2022 on 48 eyes of 24 cases above 20 years old with optic disc edema and diagnosed as idiopathic intracranial hypertension.

Exclusion criteria: Patients who refused to take part in our study, patients with optic atrophy either Primary due to compression, secondary due to chronic papilloedema ,presence of any optic disc changes other than papilledema (glaucoma, congenital anomalies, disc tumors, and optic disc drusen) , cases of media opacity that impair vision such as corneal anomalies (dystrophies and opacities) or patients with cataracts of grade III-IV or mature cataracts that prevented fundus visibility.

Ethical considerations : A clear printed approval was taken from each patient before included in the study .

Methodology:

Full history and clinical examination :with special emphasis on best-corrected visual acuity (BCVA) which was transformed to a logMar for statistical evaluation, color vision and pupillary reflexes (direct and indirect).

Grade 0 (Normal Optic Disc)
-Prominence of the retinal nerve fiber layer at the nasal, superior, and
inferior poles in inverse proportion to disc diameter.
-Radial nerve fiber layer striations, without tortuosity.
Grade 1 (Minimal Degree of Edema)
-C-shaped halo that is subtle and grayish with a temporal gap; obscures underlying retinal details.
-Disruption of normal radial nerve fiber layer arrangement striations.
-Temporal disc margin normal.
Grade 2 (Low Degree of Edema)
-Circumferential halo.
-Elevation (nasal border).
-No major vessel obscuration.
Grade 3 (Moderate Degree of Edema)
-Obscuration of 1 segment of major blood vessels leaving disc.
-Circumferential halo.
-Elevation (all borders).
-Halo (irregular outer fringe with fingerlike extensions).
Grade 4 (Marked Degree of Edema)
-Total obscuration on the disc of a segment of a major blood vessel on the disc.
-Elevation (whole nerve head, including the cup).
-Border obscuration (complete).
-Halo (complete).
Grade 5 (Severe Degree of Edema)
-Obscuration of all vessels on the disc and leaving the disc.

Table 1: modified Frisén scale

Examination of the posterior segment: using slit lamp biomicroscopy and indirect ophthalmoscopy, with a focus on the condition of the optic disc and classified according to Modified Frise' n scale [3] as shown in table (1)

OCT : measurement of retinal nerve fiber layer thickness and OCT total retinal thickness.

For OCT analysis:

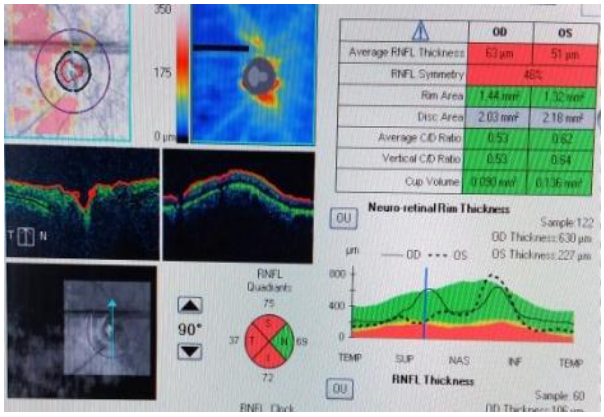

Fig 1: The OCT image (Peripapillary retinalnerve fiber layer (RNFL) thickness in four Quadrants

The circular image had to be centred on the nerve, the signal strength had to be at least 5 (range,1[lowest]-10 [highest]), Peripapillary RNFL thickness measurement was performed in four quadrants using the standard optic disc cube 200×200 acquisition protocol. Values for RNFL thickness obtained from each A-scan were averaged to find the overall average thickness as well as the average thickness for each of the quadrants (temporal, inferior, nasal, and superior) as shown fig (1).

Statistical analysis

For linear relationships between normally distributed data, the Kruskal-Wallis test was employed, and for non-normal variables/non-linear monotonic relationships, the Spearman rank correlation equation was used. Statistical significance was referred to as two-sided p values less than 0.05.

RESULTS

Demographic data:

This study was conducted on 48 eyes of 24 patients with 2 males and 22 females. As regard the mean of their age (35.42 ± 7.60), the mean of their BCVA (0.79 ± 0.16) ,color vision was normal and pupillary responses were affected RAPD in 2 eyes (4.2%).

For statistical purpose and according to fundoscopy examination papilledema grades of MFS were summariezed as mild papilledema includes grades (0,1) represents 20 (41.7%) , moderate papilledema includes grade (2) represents 13 (27.1%) and severe papilledema includes grades (3,4) represents 15 (31.2%).

Correlations between papilledema severity and RNFL thickness were done using Spearman correlation coefficient by Kruskal-Wallis test table (2). As noted P values in 4 quadrants (nasal, temporal, superior, inferior) are < 0.001 which means highly significant correlation between papilledema severity and RNFL thickness in 4 quadrants . Positive correlation coefficient means that clinical severity of papilledema are progressing with increasing average RNFL thickness fig (2,3).

When analyzing the values of average RNFL thickness and its relation with papilledema severity under ROC curve give cut off point which help in diagnosis. Mild papilledema is diagnosed with (≤ 118) µm, moderate severity with range (>118 – 188) µm and severe papilledema with (>188) µm table (3).

RNFL		Clinical severity of papilledema			Test value	P-value	Sig.
		Mild	Moderate	Severe			
		No. = 20	No. = 13	No. = 15			
Average RNFL thickness	Mean ± SD	98.30 ± 24.97	162.69 ± 36.96	247.40 ± 37.69	37.368≠	0.000	HS
	Range	47 – 139	94 – 220	195 – 326			
Inferior	Mean ± SD	131.05 ± 47.65	206.38 ± 54.26	330.40 ± 54.83	34.670≠	0.000	HS
	Range	0 – 209	136 – 297	258 – 432			
Superior	Mean ± SD	119.60 ± 35.55	221.23 ± 62.10	322.67 ± 96.60	34.176≠	0.000	HS
	Range	60 – 192	114 – 319	219 – 629			
Nasal	Mean ± SD	74.55 ± 29.41	134.62 ± 62.94	206.27 ± 38.59	33.743≠	0.000	HS
	Range	0 – 126	58 – 320	152 – 288			
Temporal	Mean ± SD	67.55 ± 14.97	88.00 ± 17.83	129.67 ± 28.31	31.484≠	0.000	HS
	Range	32 – 97	54 – 121	83 – 176			

Table 2: Correlation between severity of papilledema with average RNFL thickness and RNFL quadrants (RNFL : retinal nerve fiber layer)

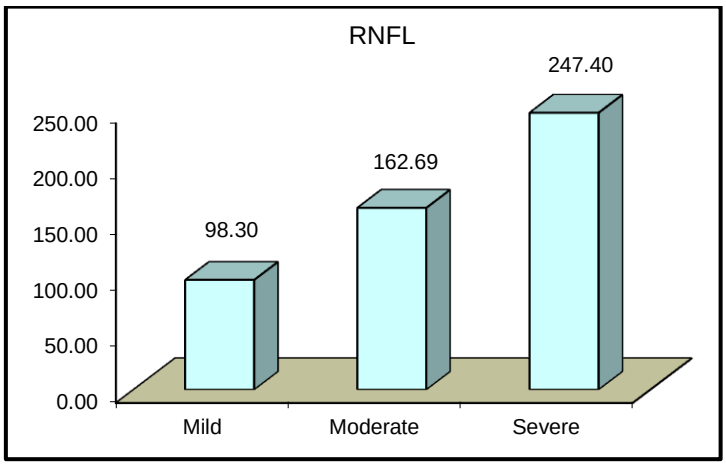

Fig 2: Relation between clinical severity of papilledema with average RNFL thickness.

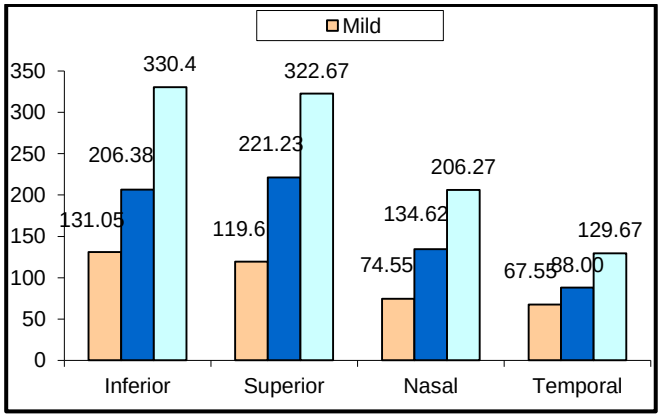

Fig 3: Relation between clinical severity of papilledema with RNFL quadrants.

	Clinical severity of papilledema		
	Mild	Moderate	Severe
Average RNFL thickness	≤ 118	(>118 – 188)	>188
Inferior	≤ 175	(>175 – 266)	>266
Superior	≤ 135	(>135 – 262)	>262
Nasal	≤ 92	(>92 – 145)	>145
Temporal	≤ 80	(>80 – 97)	>97

Table 3: ROC curve of Clinical severity of papilledema regarding median RNFL thickness, RNFL thickness in four quadrants.

DISCUSSION

Papilledema is edema of the optical disc caused by elevated intracranial pressure, and it is one of the main common causes of optic disc edema. Classically, edema is bilateral, with early indications and symptoms like headache, tinnitus, transitory vision obscuration, and diplopia, as well as the maintenance of visual acuity. When treating a patient with papilledema, it's critical to use neuroimaging to rule out the existence of intracranial expanding lesions or ventriculomegaly. If a neuroimaging examination finds no blockage of the cerebral venous flow system or exhibits evidence of obstruction, the identification of idiopathic intracranial hypertension (IIH), frequently referred to as pseudotumor cerebri disorder, should be considered.[10]

The evaluation of visual function, generally by measuring visual acuity and automated perimetry and fundoscopic variations, is critical for the diagnosis and management of these individuals. Many people think that an eye fundus exam, particularly when combined with retinography, is sufficient for assessing these individuals. However, in addition to being subjective, examiner-dependent, and non-quantitative, the intensity of edema determined only by fundoscopy may be vulnerable to inaccuracies.[11]

Even among expert examiners, studies have revealed that there is little agreement on the categorization of papilledema. Furthermore, less skilled physicians may have difficulty identifying more subtle edemas, as well as effectively tracking whether the edema is diminishing or not.[12, 13]

In this situation, noninvasive imaging methods such as optical coherence tomography may be a suitable alternative for improving diagnosis and patient follow-up.[14]

In fact, earlier research has revealed that OCT may be used to measure the thickness of the peripapillary retinal nerve fiber layer (RNFL) to determine optical disc edema.[15]

However, in cases of extreme edema (grade 3 or greater on the Frisén scale), the quantification of papilledema using OCT measurements of the thickness of the peripapillary RNFL may be subject to errors due to flaws in the demarcation of the rising and falling boundaries of the peripapillary RNFL, preventing a more reliable estimation of the edema severity.[12]

Recent advancements in SD-OCT enabled the segmentation and evaluation of the retina's inner layers. As lately indicated by Afonso et al., lowering the overall macular thickness and its inner layers identified by SD-OCT, particularly by evaluating the retinal ganglion cell (RGC) layer and the inner plexiform layer (IPL), is an essential observation in patients with chronic papilledema, and this decrease would relates to the loss of vision activity and responses from the RGC obtained by pattern reversal electro retino gram (PERG) .[16]

Other researchers believe that in individuals with papilledema, the diminution of the inner layers of the retina (RGC + IPL) acquired by SD-OCT might disclose early symptoms of neuronal and axonal death, even in the existence of optic disc edema. This would enable more aggressive therapy measures to be used in order to prevent or reduce additional vision loss.[17]

This study includes 48 eyes ,the mean of their BCVA (0.79 ± 0.16) showing insignificant relation between visual acuity and RNFL thickness with (p=.883)

According to results the mean of inferior RNFL quadrant is (213.75 ± 99.16), superior (210.58 ± 108.80), nasal (131.98 ± 70.51) and temporal (92.29 ± 33.67). The mean of RNFL thickness in 4 quadrants show increased RNFL thickness inferiorly > superiorly > nasally and > temporal quadrant (following the ISNT rule). So, in mild papilledema , RNFL thickness of nasal and temporal quadrant is important to confirm the diagnosis.

In this study, clinical grades of papilledema is classified as mild (41.7%), moderate (27.1%) and severe (31.2%) when analyzing values of median RNFL thickness and RNFL in all quadrants showing highly significant Correlation between severity of papilledema and RNFL thickness (P value< 0.01).

According to statistical data, in mild papilledema the mean of inferior quadrant is (131.05 ± 47.65), superior (119.60 ± 35.55), nasal (74.55 ± 29.41), temporal (67.55 ± 14.97) and average RNFL thickness is (98.30 ± 24.97). In moderate papilledema the mean of inferior quadrant is (206.38 ± 54.26), superior (221.23 ± 62.10), nasal (134.62 ± 62.94), temporal (88.00 ± 17.83) and average RNFL thickness is (162.69 ± 36.96). In severe papilledema the mean of inferior quadrant is (330.40 ± 54.83), superior (322.67 ± 96.60), nasal (206.27 ± 38.59), temporal (129.67 ± 28.31) and average RNFL thickness is (247.40 ± 37.69).

When analyzing the values of average RNFL thickness and its relation with papilledema severity under ROC curve give cut off point which help in diagnosis. Mild papilledema is diagnosed with (≤ 118) µm, moderate severity with range (>118 – 188) µm and severe papilledema with (>188) µm. This study shows that OCT and MFS are complementing approaches for following up patients with papilledema. However, as disc edema worsens, OCT failure rates rise, indicating that OCT can be more beneficial at low levels of papilledema using existing methods. The greater relationship between MFS grade and RNFL thickness

implies that RNFL thickness measures should be prioritized.

As a result, the OCT may be a highly differential diagnosis in instances of papilledema in a variety of ways, including quantifying optic disc edema, assessing response to established therapies, aiding in the differential diagnosis with other edematous optic neuropathies, and detecting axonal loss and knowing the processes regarding loss of vision, particularly through ultrastructural evaluation of the macula

Our study has significant limitations, including a limited sample size, particularly at the higher levels of papilledema. With high degrees of papilledema, measuring error may develop, and OCT algorithm failure rates can become considerable. Disc hemorrhages may also damage accuracy by affecting reflectivity in an unpredictable way.

CONCLUSION

OCT has the ability to be a useful imaging tool for the identification and monitoring of IIH, especially when combined with other clinical data. It is now being used in concert with other imaging techniques and clinical factors to detect early variations in the ONH and retinal layers before and after intracranial hypertension therapy. It's also a valuable investigative tool for studying the pathogenesis of papilledema and evaluating papilledema by verifying or supplementing a clinical examination, particularly in low grades. The importance of OCT in the treatment of IIH will rise as more research is done to enhance picture quality and categorization, as well as big human investigations are completed.

Conflict of interest : none

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