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Diagnosis of Papilledema and Pseudopapilledema Using Optical Coherence Tomography

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ABSTRACT

Background: Papilledema is a common clinical problem where the ophthalmologist plays an important role in its diagnosis. Optical coherence tomography (OCT) provides high resolution images of the retina and the retinal nerve fiber layer (RNFL).

Objective: The aim of the work was early and non- invasive diagnosis of papilledema and differentiating it from pseudopapilledema using optical coherence tomography (OCT).

Patients and methods: This observational case control study included a total of 45 eyes stratified into 3 equally groups, 15 each, (Group-1): eyes of healthy normal subjects, (Group-2) eyes with papilledema and (Group-3) eyes with pseudo-papilledema. Patients presented at Ophthalmology Outpatient Clinic, Zagazig University Hospitals. Follow-up visits included an interview with the patient for assessing the presence of ocular symptoms, and for ophthalmologic examination to register all the clinical findings.

Results: There is statistically significant difference between the studied groups regarding result of fundus examination. Normal control group had normal appearance of fundus. Concerning pseudo papilledema, 73.3% had crowded disc and 26.7% had dusen. Concerning papilledema, 40% had mild lesion, 20% had moderate and remaining 40% had severe lesion. There is statistically significant difference between the studied groups regarding morphological changes. Crowded disc and buried optic disc drusen occurred in 73.3% and 26.7% of pseudopapilledema group respectively). There is statistically significant difference between the studied groups regarding superior RNFL. On LSD comparison, the difference is significant between each individual groups. There is statistically significant difference between the studied groups regarding inferior RNFL.

Conclusion: It could be concluded that spectral domain optical coherence tomography can differentiate between papilledema, pseudopapilledema, and a normal disc.

Keywords: Papilledema, Optical Coherence Tomography, Pseudopapilledema

INTRODUCTION

Papilledema is a common clinical problem where the ophthalmologist plays an important role in its diagnosis [(1)]. Pseudopapilledema can be defined as any disc appearance that can be confused with papilledema. The distinction is obviously important because of the profound implications associated with papilledema. The most frequently encountered causes of pseudopapilledema include optic disc drusen, hyperopia, hyaloid remnants, and congenital disc elevations [(2)]. Until a few years ago, diagnosis of papilledema relied solely on fundus examination and retinal angiography. It is important to differentiate pseudoedema from true disc oedema [(3)].

Optical coherence tomography (OCT) has evolved as one of the most important tests in ophthalmic practice. It is a noninvasive imaging technique and provides high resolution, cross-sectional images of the retina, the retinal nerve fiber layer (RNFL) and the optic nerve head. With axial resolution in the 5–7 μm range, it provides close to an in-vivo 'optical biopsy' of the retina [(4)].

Improvement in the quality of OCT can support the diagnosis and management of optic disc edema [(5)]. OCT can be used for quantitative assessment of optic disc edema by analysis of the contour of the optic disc which may be useful in clinical evaluation of optic disc edema [(1)].

Therefore, this study was aimed to evaluate the early and non-invasive diagnosis of papilledema and differentiating it from pseudopapilledema using OCT.

PATIENTS AND METHODS

This observational case control study included a total of 45 eyes stratified into 3 equally groups, 15 each, (Group-1): eyes of healthy normal subjects, (Group-2) eyes with papilledema and (Group-3) eyes with pseudo-papilledema (e.g. optic disc drusen and narrow disc due to hypermetropia). Patients presented at Ophthalmology outpatient clinic, Zagazig University Hospitals.

Inclusion criteria: Eyes of adult patients above 18 years, diagnosed clinically to have swollen disc by funds biomicoscopy.

Exclusion criteria: Patients with other optic disc pathology (glaucoma, congenital anomaly), patients with ocular media opacity and patients with high myopia (> -6 D. due to presence of myopic degeneration).

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Operational Design:

All patients were subjected to the following: full clinical history including age, complaint, ocular trauma or disease, optical correction: glasses, contact lenses and any systemic medical diseases e.g. diabetes mellitus. Ophthalmic examination included the best corrected visual acuity: after refraction, BCVA was estimated using Landolt's broken ring chart which was recorded as its decimal equivalent. Slit-lamp bio-microscopy including the cornea was examined for evidence of corneal scar, corneal edema or keratin precipitates. The anterior chamber examined for depth, regularity, aqueous flare, and cells. Application tonometry to record baseline intraocular pressure. Fundus examination using auxiliary lenses (+78 D lenses) to examine central and mid-peripheral retina to exclude possible pathology e.g., cystoid macular edema, retinal breaks, macular scars. Optic disc photography using Kowa fundus camera.

Optical principles:

The optical design of fundus cameras is based on the principle of monocular indirect ophthalmoscopy [(6)]. A fundus camera provides an upright, magnified view of the fundus. A typical camera views 30 to 50° of retinal area, with a magnification of 2.5x, and allows some modification of this relationship through zoom or auxiliary lenses from 15°.The observation light is focused via a series of lenses through a doughnut-shaped aperture, which then passes through a central aperture to form an annulus, before passing through the camera objective lens and through the cornea onto the retina. The light reflected from the retina passes through the un-illuminated hole in the doughnut formed by the illumination system. As the light paths of the two systems are independent, there are minimal reflections of the light source captured in the formed image. The image forming rays continue towards the low powered telescopic eyepiece. When the button is pressed to take a picture, a mirror interrupts the path of the illumination system allow the light from the flash bulb to pass into the eye. Optic nerve head examination and scanning with Spectral domain OCT (RS-3000, OCT RetinaScan, NIDEK CO. Ltd, Japan) [(7)].

Main Outcome Measures:

Spectral domain optical coherence tomography can differentiate between papilledema, pseudopapilledema, and a normal disc. (a) If the RNFL thickness is normal in all four quadrants, it is more in favor of pseudopapilledema as none (0%) of the patients with TP had a normal RNFL thickness in all four quadrants. Similarly, increased RNFL thickness in all four quadrants is more suggestive of papilledema. (b) The direct visualization of the ONHD is the most important feature on SD-OCT to differentiate between pseudopapilledema and papilledema as the ONHD could be visualized on OCT in all (100%) eyes with buried drusen.

Patient Follow-Up:

Follow-up visits included an interview with the patient for assessing the presence of ocular symptoms, and for ophthalmologic examination to register all the clinical findings.

***Ethical Consideration*:**

An approval of the study was obtained from Zagazig University academic and ethical committee. Every patient signed an informed written consent for acceptance of the operation. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistical analysis:

Data analyzed using Microsoft Excel software. Data were then imported into Statistical Package for the Social Sciences (SPSS version 20.0) software for analysis. According to the type of data qualitative represent as number and percentage, quantitative continues group represent by mean ± SD, correlation by Pearson's correlation or Spearman's. P value was set at <0.05 for significant results & <0.001 for high significant result.

RESULTS

There is statistically non-significant difference between the studied groups regarding age and gender. However, all patients with papilledema had positive systemic history which differs significantly from the other two groups **(Table 1).** Regarding systemic history within patients with papilledema, 46.7% had BIL, 26.7% had brain tumor, cyst and pituitary tumor occur in equal percentage 13.3% each **(Table 2)**.

There is statistically significant difference between the studied groups regarding result of fundus examination. Normal control group had normal appearance of fundus. Concerning pseudo papilledema, 73.3% had crowded disc and 26.7% had dusen. Concerning papilledema, 40% had mild lesion, 20% had moderate and remaining 40% had severe lesion **(Table 3)**.

There is statistically significant difference between the studied groups regarding morphological changes (all cases with papilledema had SRF. Humple shaped occurred in 60% within papilledema group and twenty percent of pseudopapilledema. Crowded disc and buried optic disc drusen occurred in 73.3% and 26.7% of pseudopapilledema group respectively) **(Figure 1)**.

There is statistically significant difference between the studied groups regarding superior RNFL. On LSD comparison, the difference is significant between each individual groups. The highest value occurs in papilledema group followed by pseudo papilledema group then control group. There is statistically significant difference between the studied groups regarding inferior RNFL. The highest value

occurs in papilledema group followed by pseudo papilledema group then control group. There is statistically significant difference between the studied groups regarding nasal RNFL. The highest value occurs in papilledema group followed by pseudo papilledema group then control group. There is statistically significant difference between the studied groups regarding temporal RNFL. The highest value occurs in papilledema group followed by pseudo papilledema group then control group **(Table 4)**.

The best cutoff of horizontal elevation in differentiating papilledema from pseudo papilledema is ≥469 with area under curve 0.867, sensitivity 86.7%, specificity 66.7%, positive predictive value 72.2%, negative predictive value 83.3%, accuracy 76.7% (p<0.001) **(Table 5)**. The best cutoff of vertical elevation in differentiating papilledema from pseudo papilledema is ≥514.5 with area under curve 0.836, sensitivity 86.7%, specificity 73.3%, positive predictive value 76.5%, negative predictive value 84.6%, accuracy 80% (p<0.001) **(Table 6)**.

Table (1) Comparison between the studied groups regarding demographic data:

Parameter	Groups			Test	
	Normal group	**Papilledema group**	**Pseudo papilledema group**	F/χ^2	p
	N=15(%)	**N=15(%)**	**N=15(%)**		
Age: (years) **Mean ±** **Range**	34.53 ±13.5 15 – 52	32.4 ± 8.58 22 – 44	28.4±8.52 16 – 45	1.329	0.276
Gender: **Female** **Male**	7 (46.7) 8 (53.3)	10 (66.7) 5 (33.3)	6 (40) 9 (60)	2.312	0.315
History: **NAD** **Positive**	15 (100) 0 (0)	0 (0) 15 (100)	15 (100) 0 (0)	MC	<0.001**

F One Way ANOVA test χ^2 Chi square test MC Monte Carlo test **p ≤ 0.001 is statistically highly significant

Table (2) Distribution of the studied patients with papilledema according to result of systemic history:

History:	N=15 (%)
NAD	0 (0)
BIH	7 (46.7)
Brain tumor	4 (26.7)
Cyst	2 (13.3)
Pituitary tumor	2 (13.3)

Table (3) Comparison between the studied groups regarding result of fundus examination

Parameter	**Groups**			**Test**	
	Normal group	**Papilledema group**	**Pseudo papilledema group**	χ^2	p
	N=15(%)	**N=15(%)**	**N=15(%)**		
Fundus : Non **Crowded disc** **Dusen** **Mild** **Moderate** **Severe**	 15 (100) 0 (0) 0 (0) 0 (0) 0 (0) 0 (0)	 0 (0) 0 (0) 0 (0) 6 (40) 3 (20) 6 (40)	 0 (0) 11 (73.3) 4 (26.5) 0 (0) 0 (0) 0 (0)	MC	<0.001**
Fundus: **Normal** **Abnormal**	 15 (100) 0 (0)	 0 (0) 15 (100)	 0 (0) 15 (100)	MC	<0.001**

χ^2 Chi square test , MC Monte Carlo test , **p≤0.001 is statistically highly significant

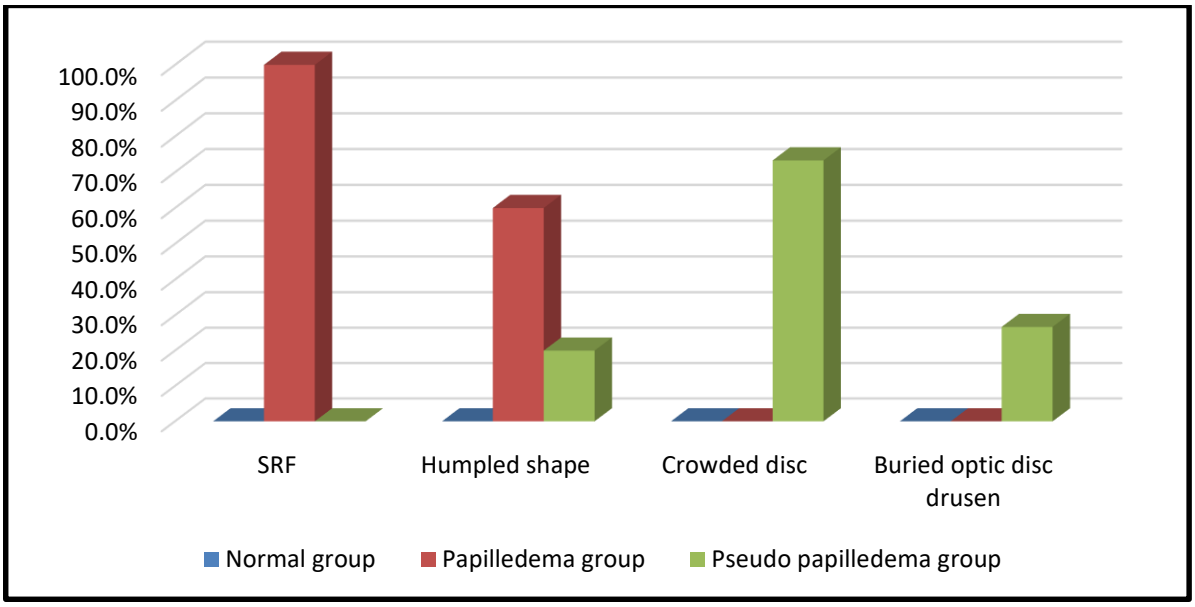

Figure (1): Multiple bar chart showing comparison between the studied groups regarding morphological changes.

Table (4) Comparison between the studied groups regarding RNFL:

RNFL	Groups			Test	
	Normal group	Papilledema group	Pseudo papilledema group	F	p
	N=15(%)	N=15(%)	N=15(%)		
Superior: **Mean ± SD**	125.47±8.03	301.87±105.54	181.0 ± 35.68	29.341	<0.001**
LSD	P_1<0.001**	P_2 0.023*	P_3 0.023*		
Inferior **Mean ± SD**	125.73±7.54	297.6±90.96	196.4 ± 28.53	37.387	<0.001**
LSD	P_1<0.001**	P_2 <0.001**	P_3<0.001**		
Nasal **Mean ± SD**	74.47 ± 4.45	215.13 ± 56.82	114.07 ± 22.57	63.017	<0.001**
LSD	P_1<0.001**	P_2 0.023*	$P_3$0.004*		
Temporal: **Mean ± SD**	65.33 ± 3.68	143.6 ± 31.17	77.2 ± 6.22	78.215	<0.001**
LSD	P_1<0.001**	P_2 0.023*	P_3 0.086		

**p≤0.001 is statistically highly significant, F One way ANOVA test , p1 the difference between normal group and papilledema groups , p2 the difference between papilledema and pseudo papilledema groups , p3 the difference between normal group and pseudo papilledema group

Table (5) Performance of horizontal elevation in differentiating papilledema from pseudo papilledema among the studied patients:

Cutoff	AUC	Sensitivity	Specificity	PPV	NPV	Accuracy	p
≥469	0.822	86.7	66.7	72.2	83.3	76.7	0.003*

**p≤0.001 is statistically highly significant

Table (6) Performance of vertical elevation in differentiating papilledema from pseudo papilledema among the studied patients:

Cutoff	AUC	Sensitivity	Specificity	PPV	NPV	Accuracy	p
≥514.5	0.836	86.7	73.3	76.5	84.6	80	0.002*

**p≤0.001 is statistically highly significant

DISCUSSION

Differentiating papilledema, or optic disc edema secondary to elevated intracranial pressure, from less life/sight-threatening causes of optic nerve head elevation and blurred disc margins (i.e., pseudopapilledema) can be challenging in clinical practice [8].

This distinction is especially difficult when optic disc edema is mild in severity. It is imperative to distinguish between the two conditions, however, as papilledema generally warrants prompt additional testing and may result from life-threatening causes, whereas pseudopapilledema typically does not [9].

This study was done to investigate the role of OCT in detecting disc edema and also to differentiate a Papilledema from pseudo-papilledema to some extent. Our study was done on 15 normal individuals, 15 eyes with papilledema and 15 eyes with pseudopapilledema.

In patients with papilledema, according to the severity: 40 % of patients were mild, 20 % of patients were moderate and 40 % of patients were severe. While in patients with pseudopapilledema, 73.3 % of patients were crowded disc and 26.5 % of patients were optic nerve drusen.

In **Hoye *et al.*** [10] studied the macular and optic disc OCT of 55 patients with papilledema and demonstrated presence of sub-retinal fluid**.** They proposed a direct communication between the sub-retinal space in the macular region and the swollen optic nerve.

In another study done by **Savini *et al.*** [11] revealed that subretinal fluid was found. In our study, 100 % of patients with papilledema were investigated and subretinal fluid was found in all cases.

Previous studies showed RNFL thickness in mild papilledema and pseudopapilledema and the results as to the difference between the thickness in both the groups were variable with **Karam and Hedges** [12] reported no statistically significant difference between the two groups and **Johnson *et al.*** [13] stated the differences in mean RNFL thickness between papilledema and ONHD were significant.

In a study of **Pardon *et al.*** [9] revealed Conventional retinal nerve fiber layer thickness for control, pseudopapilledema, and papilledema groups were statistically significant. The retinal nerve fiber layer thickness of subjects with mild papilledema did not differ significantly from that of subjects with pseudopapilledema (P = 0.03), suggesting that the conventional clinical scan is not able to distinguish mild papilledema from pseudopapilledema.

Other studies have investigated the role of cerebrospinal fluid pressure on optic nerve head biomechanics, demonstrating that elevating cerebrospinal fluid pressure results in increased deformation of the lamina cribrosa and retrolaminar optic nerve, and that this deformation resolves within weeks following an intervention to lower cerebrospinal fluid pressure [14, 15].

Karam and Hedges [12] argued that the study group in all the studies in favor of using OCT as a tool to differentiate between disc edema and pseudopapilledema had subjects with variable causes of disc swelling in the group with disc edema and could not be used to represent papilledema [16]**.** Though previous studies have found total retinal thickness to perform better than retinal nerve fiber layer thickness [17, 18].

Also, **Pardon *et al.*** [9] found that retinal nerve fiber layer thickness was better able to distinguish mild papilledema from pseudopapilledema than total retinal thickness, based on it having a significantly greater area under the receiver operating characteristic curve compared with conventional retinal nerve fiber layer thickness and a higher sensitivity at 95% specificity.

Therefore, the commercial optical coherence tomography analysis techniques could be improved by incorporating additional quantitative parameters to supplement the battery of tests used to detect and monitor optic nerve pathologies.

CONCLUSION

Spectral domain optical coherence tomography can differentiate between papilledema, pseudopapilledema, and a normal disc. Accurate diagnosis of optic nerve head swelling require full history taking and combination of both clinical examination and investigations (fluorescein angiography, ultrasound and OCT).

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REFERENCES

1. **Gaur D, Pai H (2019):** Optical coherence tomography in the evaluation of disc edema. Kerala J Ophthalmol.,31:17-23.
2. **McManaway J, Bonsall D (2006):** Management of common pediatric neuro-ophthalmology problems. In: Wright KW *et al.* editors. Handbook of pediatric neuro-ophthalmology. Springer New York, Springer Science + Business Media, Pp. 413-425**.**
3. **Carta A, Favilla S, Prato M *et al.* (2012):** Accuracy of funduscopy to Identify true edema versus pseudoedema of the optic disc. Invest Ophthalmol Vis Sc., 53:1–6.
4. **Huang D, Swanson E, Lin C *et al.* (1991):** Optical coherence tomography. Science, 254:1178–1181.
5. **Heidary G, Rizzo J (2010):** Use of optical coherence tomography to evaluate papilledema and pseudopapilledema. Semin Ophthalmol., 25: 1 98–205.
6. **Hamann S, Malmqvist L, Costello F (2018):** Optic disc drusen: understanding an old problem from a new perspective. Actaophthalmologica , 96(7): 673-684.
7. **Scott C, Kardon R, Lee A *et al.* (2010):** Diagnosis and grading of papilledema in patients with raised intracranial pressure using optical coherence tomography vs clinical expert assessment using a clinical staging scale. Arch Ophthalmol., 128:7 05–711.

8. **Chiang J, Wong E, Whatham A *et al.* (2015):** The Usefulness of Multimodal Imaging for Differentiating Pseudopapilloedema and True Swelling of the Optic Nerve Head: A Review and Case Series. Clin Exp Optom., 98:12–24.
9. **Pardon L, Cheng H, Tang R *et al.* (2019):** Custom optical coherence tomography parameters for distinguishing papilledema from pseudopapilledema. Optometry and Vision Science, 96(8): 599-604.
10. **Hoye V, Berrocal A, Hedges T, Amaro-Quireza M (2001):** Optical coherence tomography demonstrates subretinal macular edema from papilledema. Arch Ophthalmol., 119:1287–90.
11. **Savini G, Bellusci C, Carbonelli M *et al.* (2006):** Detection and quantification of retinal nerve fiber layer thickness in optic disc edema using stratus OCT. Archives of Ophthalmology, 124: 1111-1117.
12. **Karam E, Hedges T (2005):** Optical coherence tomography of the retinal nerve fibre layer in mild papilloedema and pseudopapilloedema. Br J Ophthalmol., 89:294–8**.**
13. **Johnson L, Diehl M, Hamm C *et al.* (2009):** Differentiating optic disc edema from optic nerve head drusen on optical coherence tomography. Arch Ophthalmol., 127:45–9.
14. **Feola A, Coudrillier B, Mulvihill J *et al.* (2017):** Deformation of the Lamina Cribrosa and Optic Nerve Due to Changes in Cerebrospinal Fluid Pressure. Invest Ophthalmol Vis Sci., 58:2070–8.
15. **Morgan W, Chauhan B, Yu D *et al.* (2002):** Optic Disc Movement with Variations in Intraocular and Cerebrospinal Fluid Pressure. Invest Ophthalmol Vis Sci., 43:3236–42.
16. **Flores-Reyes E, Hoskens K, Mansouri K (2017):** Optic nerve head drusen: imaging using optical coherence tomography angiography. Journal of Glaucoma , 26(9): 845-849.
17. **Vartin C, Nguyen A, Balmitgere T *et al.* (2012):** Detection of Mild Papilloedema Using Spectral Domain Optical Coherence Tomography. Br J Ophthalmol., 96:375–9.
18. **Kupersmith M, Sibony P, Mandel G *et al.* (2011):** Optical Coherence Tomography of the Swollen Optic Nerve Head: Deformation of the Peripapillary Retinal Pigment Epithelium Layer in Papilledema. Invest Ophthalmol Vis Sci., 52:6558–64.