Correlation Between Optical Coherence Tomography, Pattern Electroretinogram and Visual Evoked Potential in Primary Open Angle Glaucoma patients.

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Short title: OCT, Pattern Electroretinogram and Visual Evoked Potential in POAG patients

ABSTRACT

Purpose: Primary open angle glaucoma (POAG), which affects 33 million people globally, is the most prevalent kind of glaucoma. It is characterised by the loss of retinal ganglion cells and their axons.

Aim and objectives; to study the correlation between structural changes by optical coherence topography (OCT), and functional changes by VEP and PERG in primary open angle glaucoma in order to use these modalities in early diagnosis of primary open angle glaucoma**.**

Patients and methods; Prospective observational cross-sectional study. The study was held in Mansoura University Ophthalmic Center on sample size of 35 adult patients with open angle glaucoma aiming to study the correlation between three modalities involved in the study, assuming significance level of 0.1%, in a period of one year.

Results; IOP ($r= 0.551$; $p=0.001$), C/D ratio (OCT) ($r= 0.348$; $p=0.041$), and P50 (ERG) ($r= 0.555$; $p=0.001$) are statistically significantly positively correlated with P50 (ERG), VA ($r= -0.425$; $p=0.011$) and RNFL thickness ($r= -0.501$; $p=0.002$) are statistically significantly negatively correlated with P100 (VEP), while IOP ($r= 0.378$; $p=0.025$) is statistically significantly positively correlated with it**.**

Conclusion: Functional electrophysiological testing, or VEP for short, is a non-invasive, objective method for identifying optic nerve damage early in glaucoma to stop or slow the disease's progression to an irreversible stage and eventual blindness.

Keywords; POAG, IOP, VEP, PERG, RNFL.

INTRODUCTION

Over 67 million individuals worldwide suffer from glaucoma, which is the second most prevalent cause of bilateral blindness[1]**.** Primary open angle glaucoma (POAG), which affects about 33 million people globally, is the most prevalent kind of glaucoma of all known forms. It is characterised by the loss of retinal ganglion cells and their axons[2,3,4]**.** According to several studies, glaucomatous individuals may even experience alterations in the optic disc and loss of the retinal nerve fibre layer (RNFL) before any visual abnormalities manifest[5]**.**

Primary open-angle glaucoma, which is thought to be the most prevalent kind of glaucoma, is described as a progressive optic neuropathy. Early identification of glaucoma is crucial since the condition is treatable and the visual damage it causes is permanent. Evaluation of the optic disc alterations, thickness assessment of the retinal nerve fibre layer, and identification of any visual field abnormalities are necessary for an early diagnosis[6]**.**

The most significant risk factor for POAG that is now recognised is increased intraocular pressure (IOP), and all forms of therapy, whether medical, laser or surgical are used to lower it[7,8]**.**

It is well recognised that new imaging technologies and electrophysiological testing enhance glaucoma progression identification and tracking[6]**.** When used in conjunction, OCT and visual evoked potential (VEP) can assess the degree of optic nerve damage and have a high diagnostic capacity for the early alterations of POAG. This allows for the evaluation of both the effectiveness and early diagnosis of POAG[9].

The initial purpose of OCT was to measure tissue thickness in vivo. It offers several benefits, including the ability to assess and measure the cross-sectional peri-papillary RNFL thickness, give high-resolution cross-sectional imaging, and identify glaucoma early on[10,11].

OCT technology has advanced significantly recently, and now includes spectral-domain imaging, which provides a number of benefits over the more conventional time-domain OCT methods[12].

The minimally invasive technology known as electroretinography (ERG) provides a direct and objective means of assessing retinal function[13]. When the eye's surface records a complex field potential in response to a pattern of light that evenly covers the field of vision, the result is known as an electroretinogram[14].

The strength and duration of the flash stimulus, along with the condition of light/dark adaptation, which in turn depends on the length of time and intensity of exposure to any background light, determine the pattern of an ERG response[14].

An important diagnostic method that can pinpoint the precise cell type from the retinal neurones that is responsible for the loss of vision and its physiological process is the electroretinogram (ERG)[15]. With a long history of effectiveness, the pattern electroretinogram (PERG) is the most often utilised ERG method for glaucoma diagnosis[16]. The potential shown by the occipital visual cortex in response to visual inputs with an implicit time or long latency response is known as VEP[17].

The VEP is very useful in detecting any visual conduction disturbance of the anterior part of the visual pathway; however, it is not specific regarding the exact aetiology. It is very useful in the assessment of visual function. It is a non-invasive technique having a marvellous temporal resolution. Additionally, it may be applied to assess the total visual pathway integrity in newborns and young toddlers who are not yet vocal[18].

For recording any VEP response, a stimulus is presented to the person for a specific number of times, and the cortical responses are augmented and averaged using a computer and projected to an oscilloscope screen or it can be printed out on paper. It is usually obtained by stimulation of each eye separately, while covering the other eye[18].

VEP as an electrophysiological test has been used in glaucoma diagnosis. Also, it is used for the evaluation of any optic nerve disorder[19]. VEP parameter (P100) both latency and amplitude can be used to assess early glaucomatous damage even before retinal ganglion cell atrophy occurs[20].

As far as we are aware, no research has been done to correlate peri-papillary RNFL thickness measured by OCT with both rod and cone response in PERG and P100 measured by VEP in Egypt. In this study, data will be collected and analyzed to detect if there is a correlation between OCT, VEP and PERG in POAG.

PATIENTS AND METHODS

This is a prospective observational cross-sectional study aiming to show the correlation between structural changes by OCT, and functional changes by VEP and PERG in patients with POAG in order to use these modalities in early diagnosis of POAG.

Over the course of a year, 35 adult patients with open angle glaucoma were included in the study at the Mansoura University Ophthalmic Centre, with a significance level of 0.1%.

Inclusion criteria: Patients with POAG aged between forty and seventy years were included in this study.

Exclusion criteria: This study excluded participants with lens disease, glaucoma patients receiving medical therapy, posterior segment pathology impairing visual acuity, and dense leucomatous corneal opacification in the direct visual axis.

Every patient underwent a comprehensive ophthalmic evaluation, which included collecting personal information, reviewing medical history, measuring IOP using a Goldmann applanation tonometer, examining the fundus with a Volk lens that was 90 diopters, refraction, uncorrected and best-corrected visual acuities, and refraction.

- **Optical coherence tomography (OCT)**:

OCT-based measurement of the optic nerve head (ONH) characteristics and RNFL thickness. A scanning beam of 840 nm wavelength and 50 nm bandwidth is focused on the fundus using infrared scanning camera.

The true Map TM software is an informative analysis tool of 3D OCT-1000. A three dimensional optic disc cube with scan length 6.0x6.0 mm, scan resolution 512x128 pixels, and fixation disc protocol is performed to obtain an image for optic nerve head and peripapillary retinal nerve fiber layer.

The cube consists of 50 000 A- Scans per second with optic disc in the center. The option of disc modify (7 points) was opened from the modification menu to ensure adequate centration on optic disc. The 7 green points are separately dragged to the actual disc boundaries if there is any deviation, then modification is completed by pressing on “Exit modify”. Saving of changes is done before pressing on report button.

RNFL measurements are calculated from a peripapillary circle, 3.4 mm in diameter, presented in the final printed report as the following: 12 clock-hour sectors, four quadrants, superior and inferior halves, and total peripapillary mean thickness.

- **Visual evoked potential (VEP):**

VEP is recorded monocularly for each eye in every patient. Benoxinate 0.4% eye drops is instilled prior to application of the corneal electrode.

The recording electrodes used are four electrodes; electrode A is cup-shaped, a reference electrode is often put on the earlobe or on the midline on top of the head, and a ground electrode is placed across the forehead using a rubber band. A silver electrode is connected to the back of the head 3–4 cm above the inion, and Electrode B is positioned 3–4 cm off the midline.

All electrodes are soaked in water and soap before starting application in addition to cleaning of forehead and scalp by cleaning gel (Nuprep) and then by soap and water to get the best conductivity. The pupil of the examined eye should not be dilated. The fellow eye is occluded with light pressure to prevent blinking artefacts.

- **Pattern Electroretinogram (PERG):**

The patients are informed about the nature of the test to ensure their cooperation. The patients’ pupil are dilated with tropicamide 1% eye drops, 2.5% phenylephrine hydrochloride eye drops. Then their eyes properly patched to ensure good dark adaption for 30 minutes.

Then we applied 3 types of electrodes to the patient:

a) The forehead is thoroughly cleaned by a piece of cotton soaked in alcohol to remove any dirt. An ECG adhesive electrode was applied to the forehead, which referred to the reference electrode (negative electrode). The pinch connector was connected to the nipple of the ECG electrode, and the pin ends of the pinch connector are then plugged into the receptacle of the 1 to 2 splitter. The two leads from the splitter are then plugged in R-ve and L-ve positions on the patients cable (R=right eye, L=left eye).
b) The ear lobule is scrubbed by a piece of cotton soaked in alcohol and then an ear clip is filled with gel and applied to it. This is referred to the ground electrode.
c) Then, the eye patch is removed to apply the corneal electrodes, the room is lit using red tinted lamp only to enable corneal electrodes placement (positive electrodes). Benoxinate Hcl 0.4% eye drops was instilled in eyes prior to application of the corneal electrodes.
d) The corneal electrode has a convex surface with 4 knobs projecting from it to ensure proper lid opening. On its concave side, it had a peripheral ring of gold foil which when scratched, the electrode was discarded. This intact gold foil ensured good electric conductivity. The lens is of no dioptric power and made of plastic material.

Ethical Considerations:

The Institutional Review Board (IRB), Mansoura Faculty of Medicine, Mansoura University (IRB Code Number: MS.19.10.869) approved the protocol before the study could be carried out. Every patient provided written, informed consent. A clear explanation of the study's purpose, methodology, and length was provided. Patients retained the ability to decline participation, with no impact on the anticipated level of medical treatment. Patients were free to leave the research at any moment, with no consequences and no explanation needed.

Statistical Data Analysis:

SPSS 26.0 for Windows was used to gather, tabulate, and statistically analyse all of the data (SPSS Inc., Chicago, IL, USA). Numbers and percentages were used to describe the qualitative data. The terms range (minimum and maximum), mean, standard deviation, and median were used to characterise quantitative data. Every statistical comparison had two tails and was considered significant. A P-value of less than 0.05 suggests a significant difference, p <0.001 a highly significant difference, and P> 0.05 a non-significant difference. A Chi-square (X2) test of significance was employed to compare the proportions of various qualitative factors. When comparing parametric quantitative data between two independent groups, the independent T-test was employed.

RESULTS

The mean age of patients is (55.89 ± 8.764 years), Slightly more than half 20 (57.1%) of patients are males while 15 (42.9%) are females as shown in Table (1).

According to OCT findings of our studied sample, the mean C/D ratio was (0.69 ± 0.157), ranging from 0.3 to 0.9, and the mean RNFL thickness was (68.46 ± 18.228), ranging from 35 to 102 µm (Table 2)

Table 1: Demographic characteristics of the studied sample:

		All patients (n= 35)
Age (40- 70 years)		55.89 ± 8.764
Gender	**Male**	20 (57.1%)
	Female	15 (42.9%)

Table 2: OCT findings of the studied sample:

OCT	Mean & SD	Median	Range	IQR
C/D ratio	0.69 ± 0.157	0.72	0.3, 0.9	0.58, 0.82
RNFL thickness	68.46 ± 18.228	65.00	35, 102	56.00, 85.00

As shown in table (3), regarding VEP findings of our studied sample, the mean P100 was (139.57 ± 24.154) ranging from 102 to 207.

Table 3: VEP findings of the studied sample:

VEP	Mean & SD	Median	Range	IQR
P100	139.57 ± 24.154	136.00	102.0, 207.0	120.00, 151.00

ERG findings in our study showed that the mean P50-N95 was (1.37 ± 0.343), ranging from 0.9 to 2.3, and the meanP50 was (61.17 ± 11.126), ranging from 46 to 98 (Table 4).

Table 4: ERG findings of the studied sample:

ERG	Mean & SD	Median	Range	IQR
P50-N95	1.37 ± 0.343	1.30	0.9, 2.3	1.20, 1.40
P50	61.17 ± 11.126	58.00	46.0, 98.0	54.00, 65.00

Table 5 illustrates the measurements of our studied sample, VA and IOP, it was found that the mean VA was (0.29 ± 0.173), and the mean IOP was (19.34 ± 2.9) mmHg.

Table 5: Visual acuity and IOP of the studied sample:

All patients (n= 35)		VA	IOP
Mean & SD		0.29 ± 0.173	19.34 ± 2.9
Measurements	1	0.10	16
	2	0.10	18
	3	0.20	21
	4	0.40	16
	5	0.50	18
	6	0.20	21
	7	0.50	17
	8	0.30	24
	9	0.10	21
	10	0.20	24
	11	0.20	21
	12	0.10	24
	13	0.50	18
	14	0.60	17
	15	0.30	18
	16	0.10	17
	17	0.10	19
	18	0.20	22
	19	0.40	17
	20	0.50	18
	21	0.20	22
	22	0.50	18
	23	0.30	24
	24	0.10	20
	25	0.20	24
	26	0.20	21
	27	0.10	25
	28	0.50	18
	29	0.60	16
	30	0.30	19
	31	0.10	14
	32	0.10	17
	33	0.20	18
	34	0.40	16
	35	0.60	18
Data is expressed as mean and standard deviation.			

Table (6) shows that C/D ratio was negatively correlated with both gender (r= -0.401; p=0.017) and RNFL thickness (r= -0.365; p=0.031), while it was positively correlated with P50 (ERG) (r= -0.348; p=0.041).

Table 6: Correlation between C/D ratio and other studied parameters:

C/D ratio	Correlation coefficient	P
Age	0.174	0.319
Gender	-0.401	**0.017**
VA	-0.162	0.354
IOP	0.161	0.356
RNFL thickness	-0.365	**0.031**
P100 (VEP)	0.236	0.172
P50-N95 (ERG)	-0.116	0.505
P50 (ERG)	0.348	**0.041**
P is significant when < 0.05.		

Table (7) demonstrates that RNFL thickness was statistically significantly negatively correlated with IOP (r= -0.479; p=0.004), C/D ratio (OCT) (r= -0.365; p=0.031), and P100 (VEP) (r= -0.501; p=0.002).

Table 7: Correlation between RNFL thickness and other studied parameters:

RNFL thickness	Correlation coefficient	P
Age	-0.099	0.573
Gender	0.097	0.580
VA	0.280	0.103
IOP	-0.479	**0.004**
C/D ratio (OCT)	-0.365	**0.031**
P100 (VEP)	-0.501	**0.002**
P50-N95 (ERG)	0.017	0.924
P50 (ERG)	-0.227	0.190
P is significant when < 0.05.		

Table (8) shows that P100 (VEP) was statistically significantly negatively correlated with VA (r= -0.425; p=0.011) and RNFL thickness (r= -0.501; p=0.002), while it was statistically significantly positively correlated with IOP (r= 0.378; p=0.025).

Table 8: Correlation between P100 (VEP) and other studied parameters:

P100 (VEP)	Correlation coefficient	P
Age	-0.206	0.236
Gender	0.205	0.238
VA	-0.425	**0.011**
IOP	0.378	**0.025**
C/D ratio (OCT)	0.236	0.172
RNFL thickness	-0.501	**0.002**
P50-N95 (ERG)	0.175	0.314
P50 (ERG)	0.241	0.162
P is significant when < 0.05.		

Table (9) demonstrates that P50-N95 (ERG) was statistically significantly positively correlated with gender (r= 0.484; p=0.003) and P50 (ERG) (r= 0.555; p=0.001).

Table 9: Correlation between P50-N95 (ERG) and other studied parameters:

P50-N95 (ERG)	Correlation coefficient	P
Age	0.228	0.189
Gender	0.484	**0.003**
VA	0.221	0.203
IOP	0.277	0.108
C/D ratio (OCT)	-0.116	0.505
RNFL thickness	0.017	0.924
P100 (VEP)	0.175	0.314
P50 (ERG)	0.555	**0.001**
P is significant when < 0.05.		

Table (10) illustrates that P50 (ERG) was statistically significantly positively correlated with IOP (r= 0.551; p=0.001), C/D ratio (OCT) (r= 0.348; p=0.041), and P50 (ERG) (r= 0.555; p=0.001).

Table 10: Correlation between P50 (ERG) and other studied parameters:

P50 (ERG)	Correlation coefficient	P
Age (years)	0.169	0.332
Gender	0.213	0.220
VA	-0.169	0.331
IOP	0.551	**0.001**
C/D ratio (OCT)	0.348	**0.041**
RNFL thickness	-0.227	0.190
P100 (VEP)	0.241	0.162
P50-N95 (ERG)	0.555	**0.001**
P is significant when < 0.05.		

DISCUSSION

Glaucomatous optic neuropathy is thought to be a particular experimental human model of selective and progressive injury to both retinal ganglion cells and their axons, according to a number of histologic research investigations (RNFL). Consequently, this damage can result in dysfunction at the level of the retina, demonstrated by either flash or PERG waveforms, in addition to delayed responses from the occipital cortex, discovered by VEP waveforms[21].

It's interesting to note that glaucoma patients show aberrant PERG parameter records, including lower amplitude and delayed latency. The abnormal PERG recordings observed in cases of ocular hypertension or glaucoma have been attributed to inner retinal layers dysfunction (i.e. ganglion cell layer and RNFL) based on numerous experimental studies in which section of the optic nerve and the ensuing retrograde retinal ganglion cell degeneration produce a progressive loss of the PERG recordings[22].

Remarkably, this interpretation—which links structural and functional defects at the retinal level—hasn't been verified in vivo in human eyes yet. It has recently been thought that OCT, a novel non-invasive technique that permits cross-sectional imaging of the eye, has the capacity to quantify the RNFL thickness with a high degree of repeatability. It's interesting to note that there was a strong link between OCT-calculated measurements of retinal ganglion cell thickness and the stage of illnesses primarily affecting the retinal ganglion cells in humans, including glaucoma[23].

Furthermore, there has been a substantial correlation found between measures of RNFL thickness acquired by OCT in vivo and PERG recordings in real human eyes with ocular hypertension[24].

The purpose of the study was to examine the relationship between structural alterations detected by OCT and functional alterations detected by VEP and PERG in primary open angle glaucoma in order to utilise these modalities in the early detection of the condition.

The demographic features of the analysed sample were displayed by our results, which revealed that the mean age of the patients was 55.89 ± 8.764 years. Out of the total patients, 15 (42.9%) were female and 20 (57.1%) were male.

According to a research by Pakravan et al.[25] on glaucoma patients in Iran, the incidence of POAG differed by gender at a ratio of 37:50. This finding is consistent with another study conducted in the United States by Vajaranant et al.[26] that found that women have more visual impairment from glaucoma than males do (OR = 1.20; 95% CI 0.99–1.45). Additionally, data on the incidence of glaucoma worldwide was provided by Ryskulova et al.[27].

In a follow-up investigation, Dohvoma et al.[28] examined the medical records of individuals who received a glaucoma diagnosis between January 2016 and January 2018. The ratio of men to women was 1.5. The research's final conclusion showed that around 30.2% of the sample population were under 40 years old, with a mean age of 49.1 ± 19.95 years.

Males with glaucoma were more prevalent than females in our research. Some writers, like Olushola et al.[29], have documented this male preponderance, while other authors, like Ntim et al.[30], observed no discernible difference between the sexes.

In the study conducted by Dohvoma et al.[28], the average age of the patients was 49.1 years. Several African writers have demonstrated that the average age at which POAG is diagnosed is between 45 and 55 years old, which is consistent with the findings of numerous other studies conducted by Ntim et al.[30].

According to OCT findings of our studied sample, the mean C/D ratio was (0.69 ± 0.157), ranging from 0.3 to 0.9, and the mean RNFL thickness was (68.46 ± 18.228), ranging from 35 to 102µm.

Parisi et al.[31] used OCT to evaluate the thickness of the RNFL. By simultaneously recording pattern electroretinograms (PERGs) and visual evoked potentials (VEPs) using high-contrast chequerboard stimuli reversed at a rate of two reversals per second, the function of the retina and visual pathway was assessed.

In a different investigation, Parisi et al.[31] displayed the RNFL values in one glaucomatous eye and one normal control eye. In the RNFL temporal evaluation, the RNFL thickness in normal control eyes varied from 68.9 to 102.3 µm (mean, 84.9 6 9.67 µm), whereas in the RNFL overall assessment, it ranged from 92.5 to 126.6 µm (mean, 119.57 6 11.02 µm). They discovered that the RNFL total thickness in glaucomatous eyes ranged from 12.9 to 109.3 µm (mean, 51.5 & 25.7 µm). This was a substantial decrease from the control eyes' levels. The RNFL temporal thickness was lower than that of the control eyes, ranging from 10.0 to 84.0 µm (mean, 40.0 & 19.7 µm). Neither age nor IOP were connected with RNFL thickness values.

Chauhan and Marshall[32] made conjectures on the precision of the OCT method while measuring the thickness of the RNFL. Nonetheless, they observed a strong link between the signal generated by OCT and the ablation of the inner retina caused by an excimer laser.

Increased C/D ratio is a well-known risk factor for the evolution of glaucoma (0.3 healthy, 0.7 glaucomatous), as demonstrated by Torabi et al.[33]

Different research by Beck et al.[34] revealed that patients with African descent (AD) had an average Cup/Disc ratio of 0.35, whereas patients from Caucasian descent had an average of 0.24. This indicates that AD patients had greater vertical Cup/Disc ratios.

Also, the result of another study performed by Dohvoma et al.[28] found that the mean C/D ratio was 0.6 ± 0.2 with an asymmetry of cup/disc ratio in 35.42% of patients.

As shown in our results regarding VEP findings of our studied sample, the mean P100 was (139.57 ± 24.154) ranging from 102 to 207.

According to Parisi et al.[31], when VEP was applied to eyes with primary open angle glaucoma, the P100 implicit duration was found to be substantially longer and the N75-P100 amplitude to be much smaller than in normal eyes.

ERG findings in our study showed that the mean P50-N95 was (1.37 ± 0.343), ranging from 0.9 to 2.3, and the mean P50 was (61.17 ± 11.126), ranging from 46 to 98.

Regarding Pattern Electroretinogram, Parisi et al.[31] discovered that, in comparison to normal eyes, eyes suffering from POAG had considerably longer P50 implicit times and much smaller P50-N95 amplitudes.

Another study done by Parisi et al.[35] confirmed that, When RNFL thickness was determined by OCT and PERG was conducted utilising high-contrast checks, extending 60 minutes of visual arc, there was no correlation found between RNFL thickness and either PERG P50 implicit duration or P50-N95 amplitude. These findings imply that not all P50 components originate from the innermost layers of the retina (i.e., retinal ganglion cells or RNFL).

The measurements of our examined sample VA and IOP were presented in this work. The mean VA was determined to be 0.29 ± 0.173 and the mean IOP to be 19.34 ± 2.9 mmHg.

However, Torabi et al.[33] showed that even in cases when IOP is physiologically or medically decreased with anti-glaucoma medications, the condition progresses in many glaucomatous patients experiencing visual impairment.

According to research by Cho et al.[36], despite similar rates of primary open angle glaucoma (POAG), 52–92% of patients also have normal tension glaucoma (NTG), whose rate varies greatly among various patient population groups, with African Americans (AD) having a higher rate of NTG than European Americans (ED). Additionally, the mean IOP differs amongst Asian nations; Japan's mean IOP readings were lower than Korea's.

Dohvoma et al.[28] showed in another research that 26.8% of patients had an IOP of more over 21 mmHg. In 35.42% of patients, the central corneal thickness (CCT), as determined by pachymetry, was thin.

This study demonstrated that gender and RNFL thickness are statistically significantly negatively correlated with C/D ratio, while P50 (ERG) is statistically significantly positively correlated with it.

According to Wangsupadilok et al.[37], there was a statistically significant link found in the correlation coefficient between the cup-to-disc (C/D) ratio and CCT.

Previous research has shown an association between CCT and cup-to-disc ratio, as reported by Herndon et al. [(38),] Hewitt et al.[39], and Prata et al.[40]. These studies' findings indicated a negative association between cup-to-disc ratio and CCT, meaning that patients with higher cup-to-disc ratios and thinner CCTs were more likely to have more severe glaucomatous optic neuropathy.

Additionally, a research by Nwokocha et al.[41] shows a favourable correlation between the optic disc size as determined by evaluating its vertical diameter and the RNFL thickness as evaluated by the Stratus OCT equipment. The inferior ($p = 0.04$) and superior ($p = 0.03$) quadrants, the average measurement ($p = 0.02$), and the temporal quadrant (to a lesser extent) all showed evidence of this link.

These findings support earlier histological research showing that an increase in the size of the optic nerve head (ONH) is associated with an increase in the number of optic nerve fibres[42]. While the retrobulbar section of the optic nerve was evaluated in these investigations, one may anticipate that a comparable association would also be present in the peripapillary RNFL as determined by OCT .

In a different Italian research, Savini et al.[43] discovered a positive connection between RNFL thickness and optic disc size. Although they could not discover any connection between the nasal retinal fibres.

This study showed that IOP ($r= -0.479$; $p=0.004$), C/D ratio (OCT) and P100 (VEP)were statistically significantly negatively correlated with RNFL thickness.

Cup-to-disc ratio (CDR) has an adverse correlation with both BCVA and IOP, although the relationship is not statistically significant, according to Elmaghrabi et al.[44] It has a strong statistically significant direct correlation with CDR as evaluated clinically. Without statistical significance, there was a direct correlation between cup-to-disc ratio and cup area. All sector thickness and average peripapillary RNFL showed an inverse relationship with cup-to-disc ratio; the relationship was statistically significant only for the average thickness.

Kamal et al.[45] demonstrated a statistically significant correlation (p 0.74) between the cup-to-disc ratio and glaucoma, with 78.3% of those with higher ratios also having glaucoma.

Our study showed that VA and RNFL thickness measured by OCT are statistically significantly negatively correlated with P100 latency measured by (VEP), while IOP ($r= 0.378$; $p=0.025$) is statistically significantly positively correlated with it.

Parisi et al.[31] found that patients with POAG had longer VEP P100 implicit times and smaller VEP N75-P100 amplitudes. These findings are consistent with those of earlier research conducted by Bobak et al.[46], Marx et al.[47], Parisi et al.[48], Parisi et al.[35], and Atkin et al.[49]. However, the NFL thickness VEP and association did not achieve statistical significance.

Recalling that VEP recordings originate from both retinal activity and neural conduction throughout the entire visual pathway and are dependent on the timing and strength of afferent stimuli to the calcarine cortex may help to explain the lack of correlation between RNFL thickness measurements and VEP responses[48.]

Numerous psychophysical studies, including those conducted by Marx et al.[47] and Parisi et al.[48], have confirmed that abnormal VEP recordings observed in glaucoma patients may be caused by disrupted conduction of the optic nerve and visual pathways as a result of ganglion cell layer and retinal nerve fibre layer dysfunction. Furthermore, the observed extended time and diminished amplitude of the input to the occipital brain may be attributed to additional variables impacting the entire visual pathway. These results are linked to injury to the human dorsal lateral geniculate nucleus, both anatomically and physiologically.

A research by Parisi et al.[31] on individuals with glaucoma observed a reduction in VEP responses, which might be attributed to damage at the dorsal lateral geniculate nucleus level.

According to Nassar et al.[50], average visual acuity (VA) and visual field mean deviation (MD) correlated positively.

However, there was an inverse relationship between age and MD. Additionally, there was a significant connection between N75 delay and pattern standard deviation (PSD). Additionally, the average total RNFL thickness values, PSD, and VA showed a negative connection.

A research by Nassar et al.[50] found a favourable association between average overall RNFL thickness and MD in terms of visual field (MD and PSD). Conversely, the average total RNFL thickness and PSD had a negative connection.

Vincenzo et al.[51] assessed the correlation between OCT, PERG, and VEPs in individuals with POAG. They discovered a strong association between the PERG P50 implicit time and P50-N95 amplitude and the VEP and PERG parameters. Conversely, no associations were discovered between the VEP parameters and the RNFL thickness values. Furthermore, RNFL thickness and pattern reversal visual evoked potential (PRVEP) responses did not correlate.

Grippo et al.[52] found no evidence of a substantial alteration in P100 latency in patients with ocular hypertension or glaucoma. Moreover, there was no correlation seen between the extended delay and the decrease of visual field. Thus, rather than representing damage, they infer that VEP is a sign of retinal ganglion cell death. Therefore, it is not very helpful in identifying early nerve dysfunction.

VEP with blue on yellow pattern stimulation is a highly helpful method in identifying early glaucomatous damage, as demonstrated by Horn et al.[53]. This is predicated on the idea that the blue wave-sensitive or short wavelength-sensitive neural pathway is the first to be impacted by glaucoma. As a result, our S-cone VEP may identify extremely early changes that traditional VEP would miss[50].

This study showed that gender and P50 (ERG) are statistically significantly positively correlated with P50-N95 (ERG). IOP, C/D ratio (OCT), and P50 (ERG) are statistically significantly positively correlated with P50 (ERG).

An investigation by Goyal et al.[54] discovered that elevated IOP causes a brief drop in VEP amplitude. They showed that, in comparison to controls, individuals with ocular hypertension and glaucoma had a prolonged positive wave (P-100) latency. Additionally, it was shown that glaucomatous patients' eyes had a longer delay than individuals with ocular hypertension.

Parisi et al.[31] observed in another investigation that in glaucomatous eyes, there was a substantial correlation between the RNFL overall and RNFL temporal values and the PERG parameters (P50 implicit time and P50-N95 amplitude). Conversely, no associations were seen between RNFL values and VEP parameters (P100 implicit time and N75-P100 amplitudes). The visual field mean deviation (MD) values and RNFL thickness (both overall and temporally) showed a modest connection in eyes with primary open-angle glaucoma. However, there was a strong correlation found between the visual field corrected pattern standard deviation (CPSD) measurements and both the overall and temporal RNFL values. In contrast, there was no discernible relationship between RNFL thickness values and electrophysiologic (PERG and VEP) characteristics in control eyes.

Nassar et al.[50] discovered a positive association between N75 delay and the standard deviation of the visual field pattern (PSD) in another investigation. Conversely, there was a negative relationship between PSD and N75-P100 amplitude.

CONCLUSION

Finally, our data show that, although no link has been observed between NFL thickness and VEP changes in individuals with POAG, there is a strong correlation between NFL thickness as determined by OCT and PERG changes.

As a well-respected electrophysiological test, VEP can be used as a non-invasive objective test to identify early optic nerve damage in glaucoma patients, preventing or delaying the condition's advancement to an irreversible stage that would ultimately result in total blindness.

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