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Optical Coherence Tomography Angiography (OCTA) of optic disc in primary angle closure glaucoma

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Abstract
Background: A significant factor in blindness is primary angle closure glaucoma (PACG). With the new development of optical coherence tomography angiography (OCTA), we may be able to better understand how the integrity of the microvasculature affects the etiology of glaucoma. This work's aim is to assess disc perfusion, neuronal structure, and visual field abnormalities, as well as the papillary and peripapillary the retinal vascular density (VD) in eyes with primary acute angle closure crisis (PAACC).
Methods: The case control study had been carried out on 40 eyes of 20 patients with unilateral PAACC and served as the case group with the contralateral eye has no symptoms or signs suggesting a previous attack and served as the control group.
Results: In relation to the best corrected visual acuity (BCVA), intraocular pressure (IOP), visual field (VF) mean deviation (decibels), the retinal nerve fiber layer (RNFL) thickness (m), ganglion cells complex (GCC) thickness (m), vertical cup-to-disc ratio (VCDR), inside disc vessel density (IVD), and all quadrants—with the exception of the nasal quadrant—a statistically substantial variance was existed between both groups. When contrasted with the control group, the PACG's all vessel density and structural measurements were considerably lower. Glaucomatous eyes have much lower papillary and Peripapillary VD than normal ones. The peripapillary plexus was significantly associated with RNFL, MD, VCDR, and GCC.
Conclusions: In glaucomatous eyes with RNFL and GCC thinning, OCTA is an effective tool for diagnosing vascular modifications. When compared to the opposite normal eyes, papillary and peripapillary retinal VD dramatically reduced in acute PACG eyes. There was a substantial association between various glaucomatous modifications and peripapillary retinal VD.

Keywords: Optical coherence tomography angiography, primary angle closure glaucoma and optic disc

Introduction
A significant factor in blindness is primary angle closure glaucoma (PACG). In 2010, 3.9 million people around the world were affected by PACG, and it is predicted that this number would increase to around 5.3 million by 2020 [1, 2].
The optic nerve head (ONH) is the base of clinical glaucoma diagnosis for a very long time. The ability to obtain detailed visualization and quantification of ONH structures through the use of ophthalmic imaging further strengthens its role in glaucoma diagnosis and progression detection [3] unknown processes underlie PACG-induced optical neuropathy. Glaucomatous optical neuropathy and loss of vision are mainly come on by inadequacy of vascularity and mechanical compression [4].
Mechanical compression is widely considered as the primary mechanism of PACG, particularly acute PACG [5].
Extremely high intraocular pressure (IOP) causes apoptosis of ganglion cells and associated axons. In the process of injury in primary open-angle glaucoma (POAG), these modifications are significant particularly in cases of NTG (normal tension glaucoma). Factors of vascularity is may play a role in PACG pathogenesis. [6, 7].
The optic nerve head microcirculation may be examined & measured using a variety of techniques ONH. A novel method called optical coherence tomography angiography (OCTA) can rapidly and precisely monitor the microcirculation of the retina and the disc [8].
Since 2002, OCT has been a non-invasive imaging method that has been utilized extensively in ophthalmology.

The use of OCTA, a functional extension of OCT, to identify micro-vascular alterations in numerous retinal disorders is increasing. Despite the fact that many different technologies have been used to demonstrate how glaucoma affects the retinal microvasculature and ocular blood flow, their ability to clarify the function of the vascular system has been our knowledge of the importance of microvasculature integrity in the progression of glaucoma may be improved by the new development of OCTA [9].

This study aimed to assess disc perfusion, neurological structure, and field of vision abnormalities, as well as the papillary and peripapillary retinal vascular density (VD) in eyes with primary acute angle closure crisis (PAACC).

Patients and Methods

This case control work was performed on 20 patients (40 eyes) with unilateral primary acute angle-closure crisis (PAACC) and served as the case group with the contralateral eye has no symptoms or signs suggesting a previous attack and served as the control group.

The work was carried out following agreement from Tanta University Hospitals' Ethical Committee, Egypt. From January 2020 to December 2020. The patients provided signed permission after being fully briefed.

Exclusion criteria were previous acute angle closure crisis in the contralateral eye, secondary angle-closure, proof of any retina disease, significant optical media opacity that may involve quality of image, patient's refusal.

All patients were subjected to: history taking, visual acuity (VA), best corrected visual acuity (BCVA).

Examination of anterior segments utilize slit lamp bio microscopy and included: Corneal examination for presence or absence of corneal edema, Anterior chamber depth assessment using van Herick technique, Pupil examination for its shape and regularity, Intra ocular pressure measurement was done using Goldmann applanation tonometer.

Posterior segment examination and evaluation of optic disc when possible. Anterior chamber angle examination (Gonioscopy): slit lamp Gonioscopy was carried out utilizing a low light source (Static gonioscopy) Goldman three mirror lens (magnification: 25), dynamic gonioscopy (indentational) was done after static gonioscopy to differentiate between appositional and synechial angle closure using Zeiss 4 mirror lens.

The following were performed on all participants 3 weeks after resolution of the attack: 24-2c Visual field test using Zeiss HFA 3 Model 850, OCT (vertical cup-to-disc ratio (VCDR), ganglion cells complex (GCC), thickness of retinal nerve fibre layer (RNFL)) and OCTA to assess vascular density in papillary and peripapillary atrophy (PPA) both were obtained by The Zeiss Cirrus 5000 HD-OCT, it has an A-scan velocity of (27,000 scans/sec) having a 2 mm scanning depth and a five micro axial resolution. The 840 nm wavelength of light is used by the equipment. FastTrack, an eye tracking system, was used to track eye movements and reduce motion artifacts. Only scans with signal strength equal to 6 or higher were used.

In order avoid accidental movement of the subjects being examined due to discomfort position, all patients were examined without using of mydriatic eye drops. It was also made sure that the headrest and the chair were adequate in height. If an eye with good central vision was being examined, an internal fixation target use was preferred. For the other eye with normal vision, we utilized an external fixation light in a situation of a significant vision decline.

The OCTA images were captured using a 3×3-mm scan focused on the head of the optic nerve. To assess The head of the optic nerve microcirculation, vessel density was analyzed to get differences between the eye of previous AACC and the normal eye. Vessel density was included in temporal, nasal, inferior, superior sectors and intrapapillary VD. Comparisons between the normal eyes used as the control groups in the procedure that results in the superficial peripapillary VD and the eyes treated with prior AACC. The vascular area density (percent) surrounding the ONH was assessed utilizing the device's density assessment function from ILM to NFL.

This scan creates a 6 by 6 mm macular cube of data for the macula, focused on the fovea. The 512 128 arrangements, that comprises 128 horizontal B-scans made up of 512 A-scans apiece, was used. Cirrus HD-OCT assessment both the IPL and GCL. In a 6 mm cube that is focused on an oval annulus that is in the middle of the fovea, the thickness map shows the thickness measurements of IPL+GCL.

The average and minimal thickness data of IPL+GCL are displayed in the thickness table. In predetermined areas, the macular GCL's thickness was automatically determined. The GCA algorithm's splitting of the inner layers of retina automatically summarizes the inner plexiform layer (IPL) and the ganglion cell (GCL) depending on the 3-D (3 dimensions) data from procedure of the macular cube. The macular RNFL and IPL's outer borders have been compared to create the segmentation of GCL-IPL.

The fovea isn't included in assessments of the average, minimum, or the 6 thickness map-defined sectors: inferior, superonasal, superotemporal, superior, inferonasal, and inferotemporal. The scanning method of (200 × 200) Optic Disc Cube was used to scan the head of the optic nerve and the RNFL at the peripapillary. It comprises 200 horizontal linear B-scans, each of which is composed of up of 200 A-scans, and it covers a 6 x 6 mm area. An estimation of a circle with a diameter of 3.46 mm that is centered on the BMO (Bruch's membrane opening) is where Cirrus HD-OCT assesses the RNFL thickness.

Statistical analysis

SPSS v20 (Armonk, NY: IBM Corp.) was utilized for the statistical analysis. In order to compare quantitative data, Wilcoxon signed test values for abnormally distributed values and paired Student's t-test for regularly distributed variables were used. The values of quantitative variables were reported as range (minimum and maximum), mean, standard deviation, median, and interquartile range (IQR). The normality of the distribution was examined by the Shapiro-Wilk test. Numbers and percentages (%) were utilized to represent the variables of quality. The coefficient of pearson is used for quantitative variables with odd distributions, whereas the Pearson coefficient is used to correlate properly distributed data. Significant results were defined as two tailed P values <0.05.

Results

Table 1 displays the demographic data and affected eye of the participants under study.

Table 1: Shows the distribution of the examined cases by the affected eye's demographic data (n = 20).

Parameters			N (%)
Age (years)			52.45±11.22
Sex		Male	7(35%)
		Female	13(65%)
Affected eye	OD	Disease	11 (55%)
		Controlled	9(45%)
	OS	Disease	9(45%)
		Controlled	11(55%)

Data are presented as mean±SD or frquancy (%) OD: right eye, OS: left eye. There is a statistically significance variations between that two groups related to VF (MD) dB (decibel), BCVA, IOP. Table 2

Table 2: Comparison between disease and controlled according to IOP mmHg, BCVA (decimal), VF (MD) dB (decibel) (n= 20)

	Disease	Controlled	Z	p
IOP mmHg	45.30±8.85	16.25±3.67	3.889*	<0.001*
BCVA(decimal)	0.13±0.25	0.74±0.25	3.345*	0.001*
VF(MD)dB	-8.26±8.67	-0.98±1.18	14.402*	<0.01*

Data are presented as mean±SD IOP: Intraocular pressure, BCVA: best correct visual acuity, VF: visual field

There is a statistically significance variation among both groups related to RNFL thickness (µm), GCC(µm) and VCDR, also there is a statistically important variation among the 2 groups related to IVD and all quadrants except in nasal quadrant as in the case group, iVD the vessel density in all quadrants was lower Table 3.

Table 3: Comparison between disease and controlled according to RNFL thickness (µm), GCC (µm), VCDR, Peripapillary vessel density (VD %), iVD (%) (n= 20)

	Disease	Controlled	t	p
RNFL thickness(µm)	85.55±24.83	99.15±10.16	2.145*	0.045*
GCC(µm)	80.10±10.51	89.25±11.05	2.441*	0.025*
VCDR	0.54±0.26	0.36±0.14	2.621*	0.017*
Superior	34.0±7.88	40.40±1.82	3.470*	0.003*
Inferior	34.41±7.49	40.02±1.88	3.083*	0.006*
Nasal	37.17±7.57	40.61±3.14	1.855	0.079
Temporal	31.41±6.26	38.25±4.42	3.729*	0.001*
Average Peripapillary Vessel density (VD %)	34.24±6.78	39.82±1.67	3.469*	0.003*
iVD (%)	11.61±4.41	27.01±6.25	8.432*	<0.001*

Data are presented as mean±SD. GCC: ganglion cells complex, RNFL: retinal nerve fiber layer, IVD: inside disc vessel density, VCDR: vertical cup-to-disc ratio.

When contrasted to the control group, the PACG's entire vessel density and structural parameters were considerably lower. There was an important relation of the peripapillary plexus to the RNFL, MD, VCDR and GCC Table 4, figure 1.

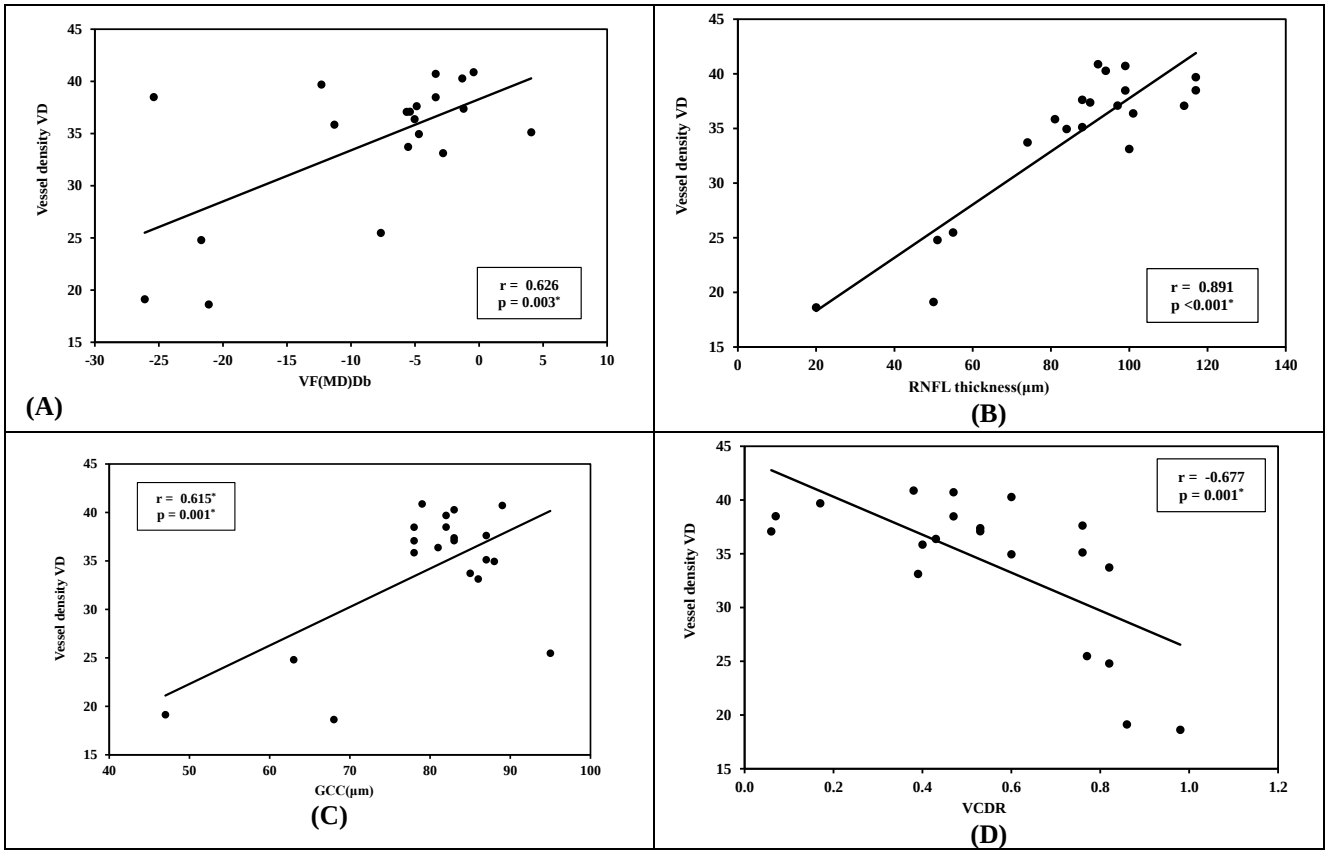

Fig 1: Correlation between Peripapillary Vessel density (VD %) and (A)VF (MD) dB, (B) RNFL thickness (µm), (C) GCC, (D) VCDR (n= 20)

Table 4: Correlation between Peripapillary vessel density VD and different parameters (disease) (n= 20)

	Peripapillary Vessel density VD	
	r	p
VF(MD)dB	0.626	0.003*
RNFL thickness(µm)	0.891	<0.001*
GCC(µm)	0.615	0.004*
VCDR	-0.677	0.001*
IVD		
VF(MD)dB	0.254	0.280
RNFL thickness (µm	-0.274	0.242
GCC(µm)	-0.075	0.752

VF: visual field, GCC: ganglion cells complex, RNFL: retinal nerve fiber layer, VCDR: vertical cup-to-disc ratio.

Case

Female patient aged 38 years old presented with AACG in her right eye. By Goldman a planation tonometer IOP was 48 mmHg. By examining the angle, it was closed angle (Schafer grade 0). BCVA was 6/60 in OD and 6/6 OS. No abnormalities in the other eye. 3 weeks after resolution of the attack the investigations had done were: 24-2c VF, OCT (RNFL, GCC), OCTA of ONH. Figure 2, 3.

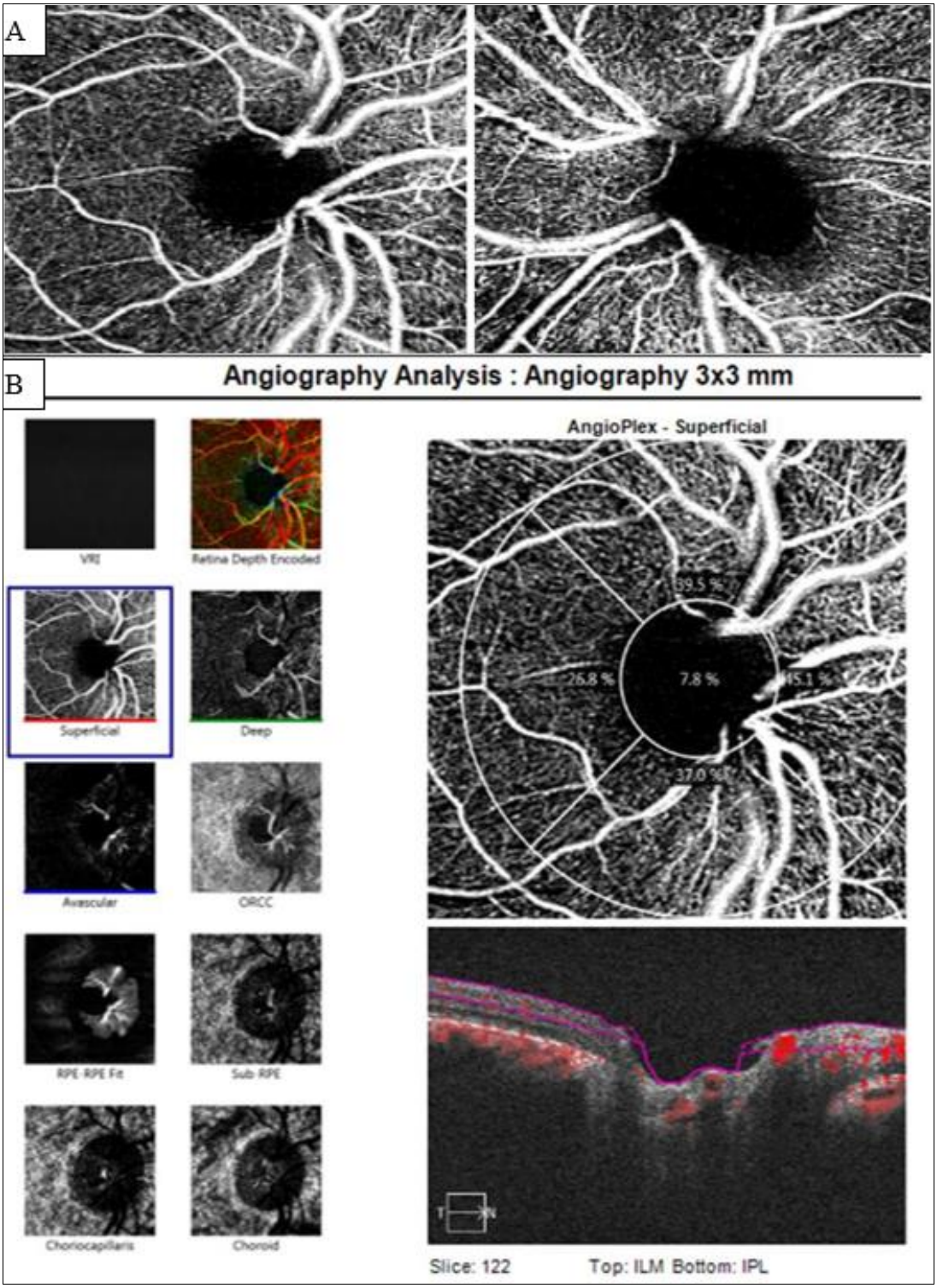

Fig 2: OCTA of ONH of (A) the right and the left eyes show decrease VD in right eye, (B) the right eye shows VD %. Superficial Peripapillary VD % at inferior, superior, nasal and temporal sectors. Inrapapillary VD % (iVD).

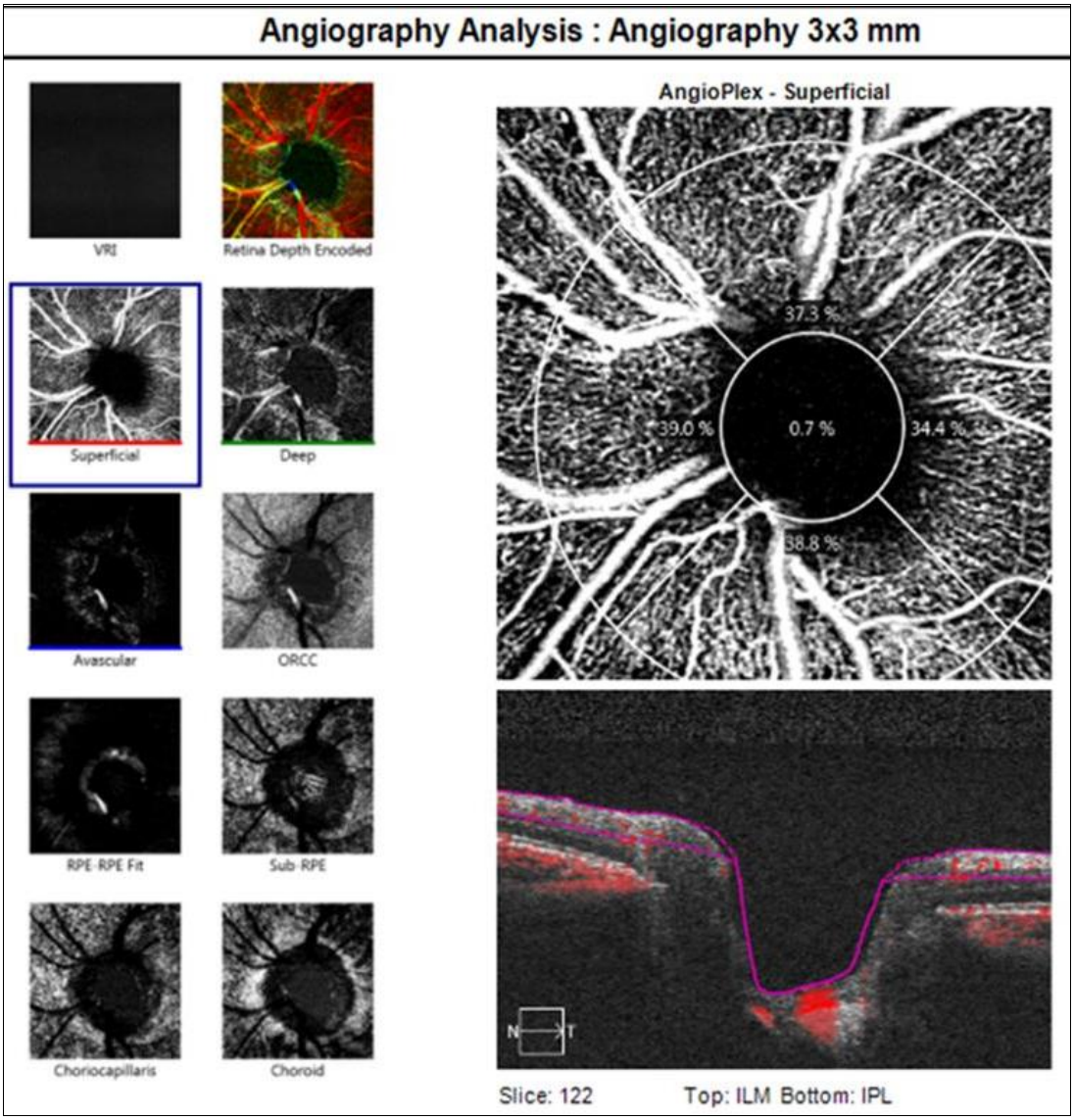

Fig 3: OCTA of the ONH at the left eye shows VD %. Superficial Peripapillary VD % at inferior, superior, nasal and temporal sectors. Inrapapillary VD % (iVD).

Discussion

Globally, around 64.3 million individuals have glaucoma as of the year 2013, and that find is predicted to increase to 76.0 million by 2020 [2]. In the study in case group, the OD is 55% of cases. Our patients were 13 females and 7 males their age ranged from 25.0 – 71.0 years.

In addition, Yip *et al.*'s research [10] consisted of 29 (58 eyes) age-matched controls and 24 (32 eyes) glaucoma patients, and Jia [11]observed that the mean age in the normal group was 52±10 years, which was sixteen years less than the group with glaucoma.

In this present study it was found that IOP in the diseased eyes was 12.0 – 52.0 mmHg and in the control eyes was 12.0 – 22.0 mmHg, the control group was lower than the control group.

Gazzard *et al.*, [12] revealed in their study the mean pre-treatment IOP in the group of PACG was 37.0 mm Hg, higher than the POAG.

Jia, [11] Zhang *et al.*, [13] who found that IOP is not in approval, however there were no important variations among the glaucoma and control groups.

Regarding BCVA in all cases, it was found that BCVA mean in the diseased eyes was 0.13±0.25 while in control eyes, it was 0.74±0.25.

According to research by Zhang *et al.*, [13] the median BCVA in acute PACG eyes was 20/40 and 20/20 in normal eyes.

In the current research, it was indicated that acute PACG eyes had worse mean deviations (MD) than normal eyes, with mean SD values of -8.26 8.67 in the affected eyes and -0.98 1.18 in the control eyes.

The research by Zhang *et al.* [13] concurs with this study in that it found that acute PACG eyes' MD of visual field tests was poorer than that for normal eyes.

While Wang *et al.*, [14] in their study reported that visual field mean deviation (-7.7±6.7 against -3.3±1.8 dB, P = 0.002), compared to the fellow eyes, the acute post angle closure eyes had a significantly worse visual function MD.

Based on the findings of the current work, the glaucoma group's average values for RNFL and GCC were lower than those of the control group, VCDR was 0.54±0.26 in the diseased eyes but0.36±0.14 in the controlled eyes. There was a statistically significance difference in RNFL, GCC and VCDR between glaucomatous and healthy eyes.

Jia *et al.*'s [11] observation that the glaucoma group had considerably lower VF, C/D area ratio, rim area, and thickness of NFL is agreement with the findings of this work. Additionally, Zhang *et al.* [13] found that when relative to the normal eyes, the affected eyes indicated a thinner RNFL, GCC, and VCDR.

In contrary, Wang's study *et al*., [14] observed that the GCC and retinal nerve fiber layer thicknesses were the same in both.

According to Zhu *et al*.'s research [15], the uncontrolled IOP group had identical GCC, MD, and PSD but had higher IOP and thinner RNFL than the well-controlled group.

In the present study, OCT-A was used to assess the VD in PACG eyes. The superficial peripapillary retinal VD was determined to be 34.24% in acute PACG eyes, which was substantially less than the level of 39.89% in the unaffected eyes.

For all VD values, a statistically substantial variation was existed among healthy and glaucomatous eyes. The VD in glaucomatous eyes was considerably reduced contrasted with the control group in each of the evaluated regions. Papillary vascular density and the IVD revealed a statistically important variations between the two groups.

Our results showing that peripapillary flow index and peripapillary vascular density in glaucomatous eyes were considerably reduced contrasted with individuals having healthy eyes and were strongly connected with visual field pattern standard deviation in glaucomatous eyes are comparable to the findings of Liu *et al*.'s study [8].

Additionally, the control group indicated greater VD than the glaucoma group in the end face segmentation layers of the optic disc, according to Yip *et al*. [10] Wang *et al*. [14] reports. The vessel density and structural measures in the PACG were substantially reduced than those in the control group, according to Rao *et al*.'s cross-sectional research [16]

According to the current research, the peripapillary plexus significantly correlated with the RNFL, MD, CDR, and GCC.

The results of this study were in line with Wang *et al*.'s study **[14]** which found that in the APAC eyes, the VF MD and PSD had a significant association with the peripapillary retinal vascular density. The sensitivity of the peripapillary vascular density was shown to be equivalent to RNFL thickness by Rao *et al*. **[16]**

According to Zhang *et al*.'s study **[13]** acute PACG eyes had much less peripapillary VD than normal eyes. In acute PACG eyes, peripapillary retinal VD was negatively connected with VF mean deviation and cup-to-disc ratio and positively associated with RNFL and GCC thicknesses. Peripapillary retinal VD and glaucoma-related variables did not correlate in unaffected eyes. According to Liu *et al*. **[8]** VD and the standard deviation of the visual field pattern in glaucomatous eyes were substantially associated.

It was advised that OCT angiography is a trustworthy technique for identifying vascular abnormalities in glaucomatous eyes that demonstrate RNFL and GCC thinning.

Conclusions

OCT angiography is an effective technique for identifying vascular modifications in glaucomatous eyes that demonstrate RNFL and GCC thinning. Papillary and peripapillary retinal VD considerably reduced in acute PACG eyes contrasted with the contralateral normal eye. Significant correlations were found among peripapillary retinal VD and other glaucomatous modifications.

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Conflict of Interest: Nil

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