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RESEARCH ARTICLE
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MORPHOLOGICAL CHANGES OF THE MACULA ON OPTICAL COHERENCE TOMOGRAPHY ANGIOGRAPHY IN THE DIABETIC POPULATION

Dr. Faiza Mushtaque[1], Dr. Fizzah Farooq[2*], Dr. Fahad Khan[3], Dr. Qurat ul Ain Sheikh[4], Dr. Tahira Sadaf[5], Dr. Kajal[6]

[1]Senior Women Medical Officer, Department of Ophthalmology and Visual Sciences, Dr Ruth K. M. Pfau Civil Hospital, Karachi, Pakistan, MBBS: Dow Medical College, Dow University of Health Sciences (DUHS), FCPS (Ophthalmology): College of Physicians and Surgeons Pakistan (CPSP)
[2*]Women Medical Officer, Department of Ophthalmology and Visual Sciences, Dr Ruth K. M. Pfau Civil Hospital, Karachi, Pakistan, MBBS: Dow Medical College, Dow University of Health Sciences (DUHS), FCPS (Ophthalmology): College of Physicians and Surgeons Pakistan (CPSP) MRCS (Glasgow): Royal College of Physicians and Surgeons of Glasgow
[3]Ophthalmologist, Al Baseer Eye Hospital, Karachi, Pakistan, MBBS: FCPS (Ophthalmology): College of Physicians and Surgeons Pakistan (CPSP)
[4]Senior Registrar, Dow Medical College, Dow University of Health Sciences (DUHS), Karachi, Pakistan, MBBS: Sindh Medical College, DUHS, FCPS (Ophthalmology): College of Physicians and Surgeons Pakistan (CPSP)
[5]Senior Registrar, Liaquat National Hospital and Medical College, Karachi, MBBS: Karachi Medical and Dental College, FCPS (Ophthalmology): College of Physicians and Surgeons Pakistan (CPSP)
[6]MBBS: Peoples University of Medical and Health Sciences for Women, Nawabshah, Pakistan

***Corresponding Author: Dr. Fizzah Farooq**
[*]Women Medical Officer, Department of Ophthalmology and Visual Sciences, Dr Ruth K. M. Pfau Civil Hospital, Karachi, Pakistan, MBBS: Dow Medical College, Dow University of Health Sciences (DUHS), FCPS (Ophthalmology): College of Physicians and Surgeons Pakistan (CPSP) MRCS (Glasgow): Royal College of Physicians and Surgeons of Glasgow

Abstract

Objective: This study aims to investigate morphological alterations in the macula using Optical Coherence Tomography Angiography (OCTA) among diabetic patients, focusing on quantitative changes in the foveal avascular zone (FAZ) and qualitative retinal microvascular features, with the ultimate goal of understanding early diagnostic markers for diabetic retinopathy (DR).

Methods: A descriptive, observational, cross-sectional study was conducted at the Ophthalmology Department of Dr. Ruth K. M. Pfau Civil Hospital, Karachi. A total of 315 diabetic patients, aged 18 years and above, were evaluated using OCTA. The scan parameters were standardized, and the FAZ area, intraretinal microvascular abnormalities (IRMA), microaneurysms, capillary non-perfusion, and neovascularization were documented and analyzed against the duration of diabetes and stage of diabetic retinopathy (NPDR, PDR, ADED).

Results: NPDR was the most prevalent stage of DR (72.7%). The mean FAZ area was significantly larger in patients with PDR and ADED stages, with mean values reaching up to 2.79 mm² in the

most advanced disease. Significant differences were found in FAZ size between different DR stages. Over 80% of patients with DR showed microaneurysms, while non-perfusion areas and IRMA were more prevalent in advanced stages. The duration of diabetes was strongly associated with the extent of FAZ enlargement and severity of retinal changes.

Conclusion: OCTA provides a high-resolution, non-invasive, and reproducible method for detecting microvascular changes in diabetic patients before clinical symptoms manifest. FAZ area and retinal microvascular abnormalities can be used as sensitive biomarkers for DR staging and prognosis. Integrating OCTA into routine diabetic screening can significantly reduce vision loss through early detection and timely intervention.

Keywords: Diabetic Retinopathy, Optical Coherence Tomography Angiography, Foveal Avascular Zone, NPDR, PDR, Microvascular Abnormalities, OCTA

1. Introduction

Diabetes mellitus (DM) is one of the most pressing global health challenges of the 21st century, affecting over 537 million people worldwide as of 2021 [1]. Diabetic retinopathy (DR), a frequent and serious microvascular complication of diabetes, is a major cause of preventable blindness in adults of working age [2]. In Pakistan, recent estimates place the national diabetes prevalence at 26%, with DR affecting approximately 28.78% of these individuals. Alarmingly, 8.6% of these cases are vision-threatening [3].

DR is classified into two primary stages: non-proliferative diabetic retinopathy (NPDR) and proliferative diabetic retinopathy (PDR) [4]. NPDR is characterized by microaneurysms, intraretinal hemorrhages, venous beading, and capillary non-perfusion. As the disease progresses to PDR, neovascularization, vitreous hemorrhage, and tractional retinal detachment become prominent features [5].

Among all diabetic complications affecting the eye, diabetic macular edema (DME) is the leading cause of central vision loss. It can occur at any stage of DR and is associated with the breakdown of the blood-retinal barrier (BRB), leading to extracellular fluid accumulation within the macula [6].

While traditional fluorescein angiography (FA) has long been the standard for assessing retinal vasculature, it comes with significant limitations including invasiveness, cost, and risks of adverse reactions [7]. The evolution of optical imaging has led to the development of Optical Coherence Tomography (OCT), which provides cross-sectional, high-resolution images of retinal layers. More recently, Optical Coherence Tomography Angiography (OCTA) has emerged as a revolutionary non-invasive modality that provides detailed images of the retinal and choroidal vasculature without the need for dye injection [8,9].

OCTA utilizes motion contrast to differentiate moving blood cells from static tissue, enabling the visualization of microvascular abnormalities such as FAZ enlargement, capillary dropout, IRMA, and neovascularization. Several studies have suggested that these vascular changes may precede clinical signs of DR, making OCTA an essential tool for early diagnosis and follow-up [10–12].

This study was conducted to analyze the macular morphology using OCTA in a diabetic population and to determine correlations between vascular changes and clinical severity of diabetic retinopathy.

2. Materials and Methods

2.1 Study Design and Setting

This descriptive, cross-sectional, observational study was conducted at the Department of Ophthalmology and Visual Sciences 2 at Dr. Ruth K. M. Pfau Civil Hospital, Karachi, affiliated with the Dow University of Health Sciences. The study spanned from January to December 2022.

2.2 Ethical Considerations

Ethical approval was obtained from the Institutional Review Board (IRB) under reference number IRB-2531/DUHD/Approval/2022/1082. All participants provided written informed consent.

2.3 Sample Size and Sampling

Using OpenEpi (Version 3), the required sample size was calculated to be 315 based on a prevalence of diabetic retinopathy at 28.78%, a 95% confidence level, and a 5% margin of error.
A **non-probability consecutive sampling** method was used, enrolling all eligible patients presenting during the study period who fulfilled the inclusion criteria.

2.4 Inclusion and Exclusion Criteria

Inclusion Criteria:

- Confirmed diagnosis of diabetes mellitus
- Age ≥ 18 years
- Clear OCTA images (quality index ≥ 40%)

Exclusion Criteria:

- History of ocular surgeries or laser treatments (diode, focal, or PRP)
- Intravitreal anti-VEGF therapy
- Retinal diseases unrelated to diabetes (e.g., age-related macular degeneration)
- Media opacities causing poor scan quality

2.5 Imaging Protocol

OCTA imaging was conducted using a high-resolution spectral-domain OCTA system with a central wavelength of 1050 nm. Each scan covered a 6×6 mm² area centered on the fovea and included 500 A-scans and 500 B-scans per volume. Eye tracking was enabled during acquisition to reduce motion artifacts.

2.6 Data Collection

Clinical and demographic data were recorded, including:

- Age, sex, duration of diabetes
- Stage of diabetic retinopathy (based on ETDRS)
- FAZ area in μm² (right and left eyes)
- Presence of microaneurysms, IRMA, capillary dropout, neovascularization

Data were entered and analyzed using **SPSS v25**. Means, standard deviations, frequencies, and percentages were calculated. One-way ANOVA and chi-square tests were used for statistical comparisons (significance set at $p < 0.05$).

3. Results

3.1 Patient Demographics

Out of 315 patients, 56.2% were male and 43.8% female. The **mean age** was **58.9 ± 8.2 years**, with a range of 40 to 80 years. The **average duration of diabetes** was **8.1 ± 3.9 years**, ranging from 1 to 20 years.

3.2 DR Stage Distribution

Right Eye (n=22 scanned):

- NPDR: 72.7%
- PDR: 15.6%
- ADED: 11.7%

Left Eye (n=22 scanned):

- NPDR: 71.4%
- PDR: 14.3%
- ADED: 14.3%

Rare diagnoses included macular edema and NPDR with vitreomacular traction.

3.3 FAZ Area Summary

Eye	Mean FAZ Area (µm²)	SD (µm²)	Min	Max
Right	784,186.9	981,767	74,000	4,636,055
Left	596,108.8	409,832	151,000	1,795,000

Patients with **ADED** showed the largest FAZ areas, indicating extensive capillary loss.

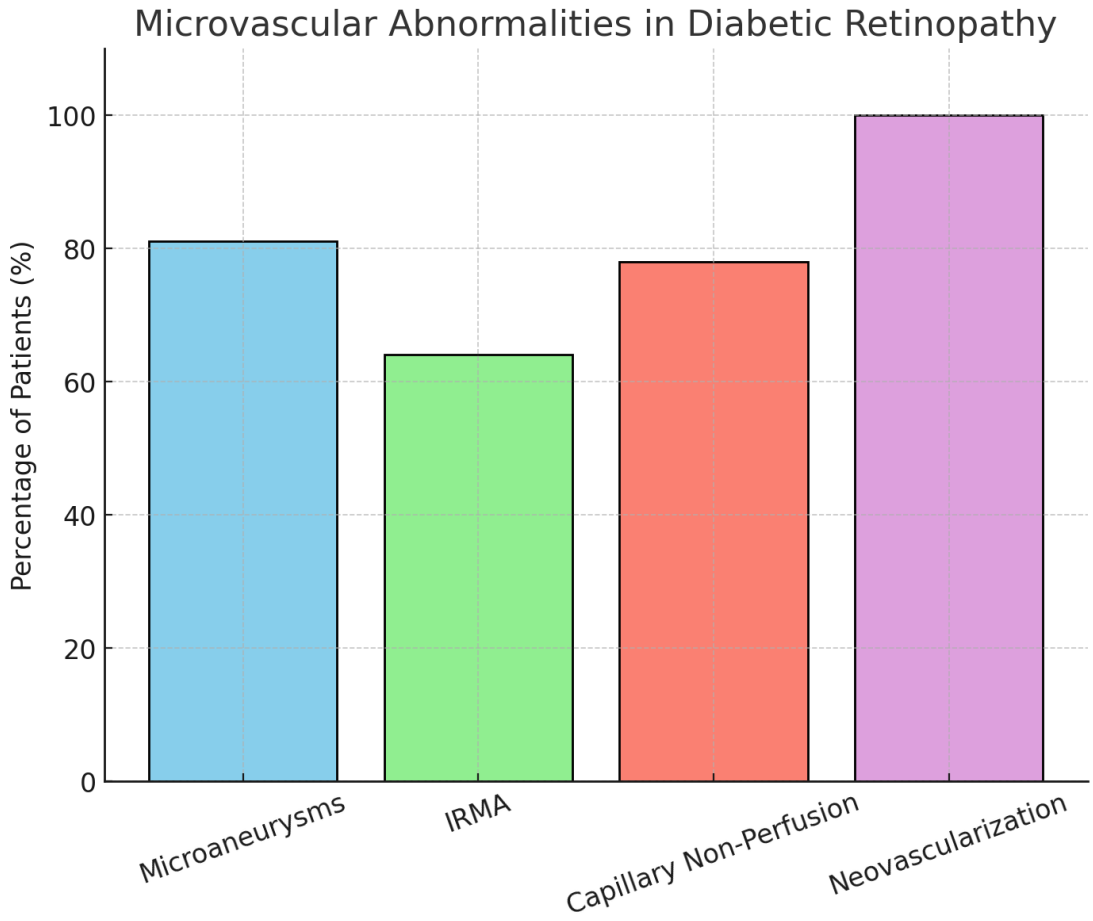
3.4 FAZ by DR Stage

DR Stage	Mean FAZ Right Eye (µm²)	Mean FAZ Left Eye (µm²)
NPDR	426,849	357,451
PDR	602,356	601,424
ADED	2,792,933	1,373,410
Normal	220,430	356,836
Macular Edema	–	617,578–1,048,359

A statistically significant FAZ enlargement ($p < 0.01$) was observed between NPDR and ADED.

3.5 Microvascular Abnormalities

Microaneurysms: Present in 81% of patients with NPDR or higher stages.
IRMA: Detected in 64% of PDR and ADED patients.
Capillary Non-Perfusion: Seen in 78% of patients with moderate to severe NPDR
.**Neovascularization:** Exclusively noted in patients with PDR or ADED.



4. Discussion

This study highlights the potential of OCTA to redefine how diabetic retinopathy is diagnosed and staged. The strong correlation between FAZ area and DR severity is consistent with previous research by Hwang et al. (2015) and de Carlo et al. (2016) [11,12].

The finding that ADED eyes had FAZ areas exceeding 2.7 mm² indicates extreme capillary dropout and ischemia. This supports earlier work suggesting that ischemic maculopathy may be the strongest predictor of irreversible vision loss in diabetic patients [13].
Interestingly, we observed no significant gender difference in FAZ size, aligning with the findings of Samara et al. (2015) [14].
The utility of OCTA goes beyond visualization — it offers reproducible metrics (e.g., FAZ area) that can serve as **biomarkers** for disease progression and treatment monitoring. Unlike FA, OCTA can be repeated frequently, making it ideal for longitudinal follow-up [15].

5. Clinical Implications

Early Diagnosis: OCTA detects subclinical DR changes, enabling early intervention.
Monitoring: Quantifiable metrics such as FAZ area help monitor response to therapy.
Screening: Ideal for integration into mass diabetic screening programs.

6. Limitations

- Limited sample size for advanced DR stages
- OCTA imaging artifacts in severe disease
- Cross-sectional design limits causality inference
- Some DR features (e.g., leakage) cannot be assessed with OCTA

7. Future Directions

- Larger longitudinal studies are needed to establish FAZ thresholds for DR progression.
- Integration with **AI algorithms** could automate risk stratification.
- Combining OCTA with other biomarkers (e.g., vessel density) may improve diagnostic precision.

8. Conclusion

OCTA is a powerful imaging modality offering both structural and functional insights into diabetic macular disease. This study reaffirms the clinical utility of FAZ area and micro-vascular findings as biomarkers for DR severity. Adoption of OCTA in diabetic eye care can substantially enhance early detection, reduce complications, and improve long-term visual outcomes.

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