

Research Article

Correlation between Diabetic Macular Edema and Peripheral Retinal Ischemia in Saudi Arabia

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Received: August 19, 2015; Accepted: October 01, 2015; Published: October 08, 2015

Abstract

Evaluation of the correlation between Peripheral Retinal Ischemia (PRI) and Diabetic Macular Edema (DME) in Saudi patients using Ultra-Wide Field Fluorescein Angiography (UWFA) and Spectral domain Optical Coherence Tomography (OCT) imaging techniques.

Subjects and Methods: A prospective non-randomized cross sectional study of 90 eyes of 58 Saudi Diabetic Retinopathy (DR) patients (36 Males and 22 Females aged from 22-80 years old) were examined using diagnostic UWFA (Optos 200Tx imaging system), in the late phase of Fluorescein Angiography (FA) to assess the presence of PRI. Based on OCT and early/ mid phases of FA using Topcon camera, patients were classified as either having DME or not. Chi-square test was used to assess the correlation between DME and PRI. The level of statistical significance was set at (P= 0.05).

Results: This study included 90 eyes from 58 DR patients (36 Males and 22 Females) who underwent diagnostic UWFA. DME was detected in 69 eyes (76.7%) of those eyes. Eyes diagnosed with DME were divided into four types: diffuse 36 eyes (40.0%); focal 23 eyes (25.6%); combined 6 eyes (6.7%) and cystoids, 4 eyes (4.4%). Out of these 90 eyes, 63 (70.0%) demonstrated PRI.

PRI was detected in 32 eyes with diffuse DME (64.0%), 12 eyes with focal DME (24.0%), 4 eyes with combined DME (8.0%), and 2 eyes with cystoids DME (4.0%).

In this study, there was a statistically significant relationship between the presence of PRI and DME in diabetic eyes, especially the diffuse type (P value= 0.013). There was median correlation (0.394) between PRI and DME types.

Conclusion: There is a significant correlation between DME and PRI. UWFA is a useful tool for detecting PRI which may have direct implications in the diagnosis, follow-up and treatment such as targeted peripheral photocoagulation.

Keywords: Peripheral retinal ischemia; Diabetic macular edema; Ultra-wide field fluorescein angiography; Optical coherence tomography; Diabetic retinopathy

Introduction

Diabetic Macular Edema (DME) is the most common cause of visual loss in patients with Non-Proliferative Diabetic Retinopathy (NPDR) [1]. According to the Wisconsin Epidemiologic Study of Diabetic Retinopathy (DR), the prevalence of DME after 15 years of diagnosed diabetes is around 20% in patients with type 1 diabetes, 25% in patients with insulin-dependent type 2 diabetes, and 14% in patients with non-insulin dependent type 2 diabetes [2].

The conventional Fundus camera provides good photographs of optic nerve and posterior pole but with a limited view of the retinal periphery. The invention of Ultra-Wide Field Fluorescein Angiography (UWFA) in 2000 overcomes this limitation. It is capable to image 200 internal degrees field of view. An ellipsoid mirror is used to image the retinal periphery. A red (633 nm) and green laser (523 nm) was utilized to scan the retina and obtain the images. In addition, high-resolution Fluorescein Angiography (FA) images of the retinal periphery obtained by Optos are clinically useful in eyes with retinal

vascular disease [3].

Optical Coherence Tomography (OCT) is a non-invasive and non-contact diagnostic method for detection of various retinal diseases. It uses infrared light reflections to obtain reliable, reproducible, and objective cross sectional images of the retinal structures and the vitreoretinal interface and allows quantitative measurements of retinal thickness [2].

The aim of this cross sectional study is to assess the correlation between Peripheral Retinal Ischemia (PRI) and DME in Saudi DR Patients using UWFA and Spectral domain OCT imaging techniques.

Subjects and Methods

This study was a prospective non-randomized cross sectional study. 90 eyes of 58 Saudi DR patients (36 Males and 22 Females aged from 22-80 years old at King Khaled Eye Specialist Hospital (KKESH) were enrolled in the study (from January to June 2013). They were examined using diagnostic UWFA (Optos 200Tx imaging system) in

Table 1: DME was detected in 69 eyes of the total eyes.

Diabetic Macular Edema (DME)	Frequency	Percent
Present	69	76.7
Absent	21	23.3
Total	90	100.0

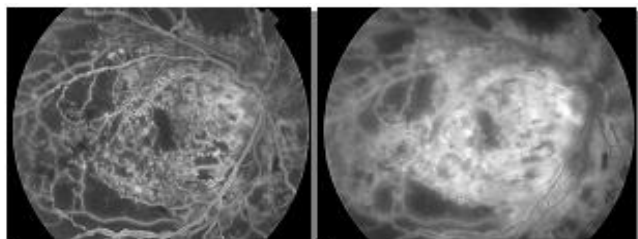


Figure 1: Early/Mid phase of diffuse leakage on FA by Topcon camera.

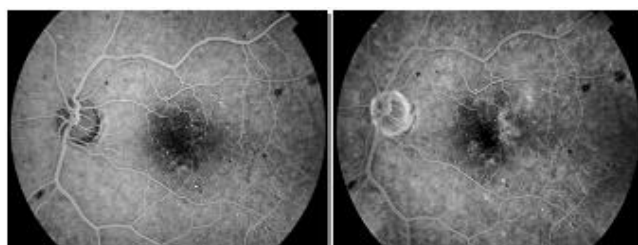


Figure 2: Early/Mid phase of focal leakage on FA by Topcon camera.

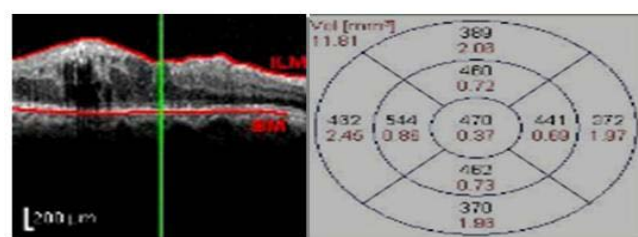
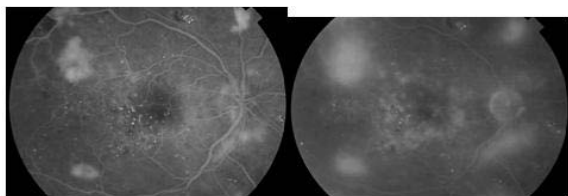
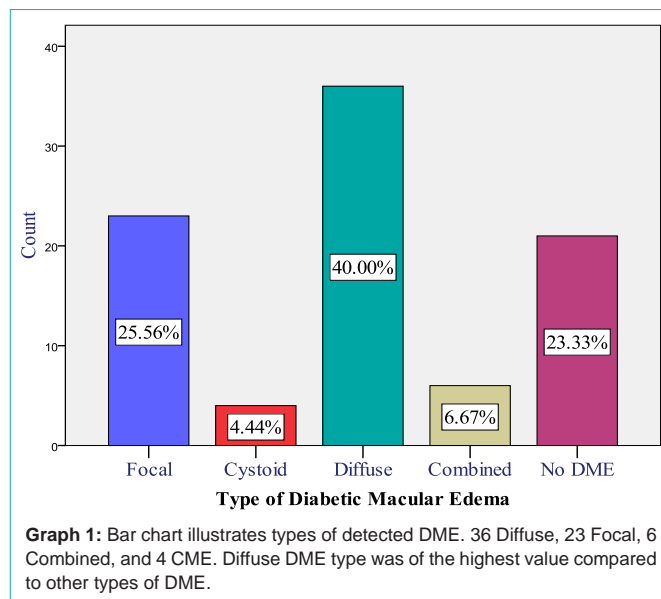


Figure 3: Combined pattern on FA and OCT.

the late phase of FA to assess the presence of PRI. Based on OCT and early / mid phases of FA using Topcon camera, patients were classified as either having DME or not.

Different types of DME were differentiated according to the pattern of leakage related to the vascular abnormalities within or adjacent to the Fluorescein dye leakage areas. Focal macular edema was defined by the presence of localized areas of retinal thickening associated with focal leakage of micro aneurysm/s. Diffuse macular edema was identified by a more generalized form of edema, visualized as widespread macular leakage and pooling of dye in cystic spaces. CME was diagnosed by accumulation of dye in the perifoveal region



Graph 1: Bar chart illustrates types of detected DME. 36 Diffuse, 23 Focal, 6 Combined, and 4 CME. Diffuse DME type was of the highest value compared to other types of DME.

in a petalloid pattern [2]. DME in OCT scans was discriminated by diffuse thickening of the neurosensory retinal and loss of the foveal depression, cystic retinal changes, which manifested as areas of low intraretinal reflectivity; and serous retinal detachment, alone or combined [2].

Inclusion criteria of the DR patients were more than 18 years old and able to understand instructions.

Exclusion criteria are patients with a history of focal, pan-retinal laser photocoagulation or retinal surgeries. In addition, patients with history of vascular occlusions, uveitis, sickle cell retinopathy, retinal scars, intraocular tumors, significant media opacity, vitreous hemorrhage and ptosis were excluded.

The research followed the tenets of the Declaration of Helsinki that informed consent was obtained from the subjects after explanation of the nature and possible consequences of the study. The research was approved by the appropriate Institutional Review Board (IRB).

The selected patients were injected by 5 cc of sodium Fluorescein dye (10%). The images were captured first by Topcon camera followed immediately by UWFA. It provides high resolution images of about 82.5 % of the total retinal surface area in a single capture [4]. All captured images were compressed in to high quality jpeg files, and transferred to Adobe soft-ware for review [5]. V2 vantage Pro contains a set of applications that monitor and manage the quality of images. Each eye was evaluated for presence or absence of PRI in Optos images.

OCT images were analyzed to reveal the presence or absence of DME in those eyes. Macular thickness and volume were measured by Heidelberg Eye Explorer Soft Ware.

Chi-square test depending on the frequency values was used to assess the correlation between DME and PRI. The level of statistical significance was set at (P= 0.05). Frequency and percentage were calculated for categorical variables like: DME (present or absent), type of DME and PRI. Finally, SPSS version 16 system was used to do all statistical parts in this study.

Table 2: Frequency table shows the number and percentage of eyes with and without PRI.

Peripheral retinal Ischemia	Frequency	Percent
Present	63	70.0
Absent	27	30.0
Total	90	100.0

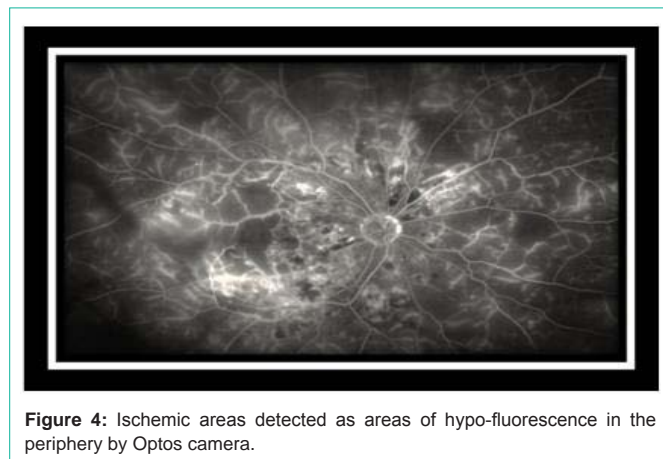


Figure 4: Ischemic areas detected as areas of hypo-fluorescence in the periphery by Optos camera.

Results

A total of 126 eyes of 63 diabetic patients were examined by UWFA at photography department of KKESH in Kingdom of Saudi Arabia (K.S.A). Thirty six eyes were excluded according to the exclusion criteria. This study included 90 eyes 200Tx imaging from 58 DR patients (36 Males and 22 Females) who underwent diagnostic UWFA.

DME was detected in 69 eyes (76.7%) of those eyes (Table1). Eyes diagnosed with DME were divided into four types: diffuse (Figure 1) 36 eyes (40.0%); focal (Figure 2) 23 eyes (25.6%); combined (Figure 3) 6 eyes (6.7%) and cystoids 4 eyes (4.4%) (Graph 1).

Out of the 90 eyes, 63 eyes (70.0%) demonstrated PRI (Table 2) and (Figure 4). PRI was detected in 32 eyes with diffuse DME (64.0%), 12 eyes with focal DME (24.0%), 4 eyes with combined DME (8.0%), and 2 eyes with cystoids DME (4.0%).

In this study, there was a statistically significant relationship between the presence of PRI and DME in diabetic eyes, especially the diffuse type of DME (P value= 0.013). There was median correlation (0.394) between PRI and DME types (Table 3).

Discussion

In DR, Ischemic changes lead to the production of Vascular Endothelial Growth Factor (VEGF) [6], which can cause the breakdown of blood-retinal barriers, and increased retinal vessel permeability producing DME. The successful effect of anti-VEGF

therapy in the management of DME may support the idea that retinal ischemia and DME are correlated [7]. But assessment of PRI using conventional retinal imaging modalities is challenging. UWFA has become a valuable tool for detection of PRI [8-10]. Since first described by Friberg and Forrester in 2004 [11], UWFA has proven to have favorable sensitivity and specificity compared to other traditional methods including 7 standard fields (7SF) [12,13]. Recent comprehensive study showed the good ability of UWFA imaging system in detection of diabetic pathology [10]. The same study found that 7SF has failed to detect either ischemia or neovascularization in 10% of eyes. Visualization of up to 200 degrees or more of the peripheral retina captured in a single frame can be obtained using UWFA imaging system [10].

In this study, PRI was detected in 70%of the examined eyes. This was almost equal to what conducted by Mackenzie PJ when they examined the sensitivity and specificity of the Optos Opto map for detection of peripheral retinal lesion in (2007) [13].

In our study, DME types were detected by both imaging systems (FA and OCT). This is because there is a discrepancy between OCT and FA outcomes that was mentioned in Ozdek et al. [14]. In their study, diabetic CME was detected with Stratus OCT in 30 eyes (15.4%) but not confirmed by FA in 63.3% of these cases. 3D-OCT is more sensitive and reproducible than FA for the detection of CME type [13]. In addition, OCT is superior in evaluating foveal changes that are not evident in diabetic eyes angiographically [15]. In contrast; OCT cannot detect the abnormal vessels and abnormal blood flow which can be imaged by FA only [16].

In our study, FA and OCT showed 76.7% of the examined eyes with DME and 23.3% of eyes showed no evidence of DME. There is a variation in time between capturing Fluorescein images and OCT images. This may affect the Fluorescein leakage patterns especially in the diffuse type. We recommend a one machine combining both FA and OCT in order to help in a specific definition of pathophysiology (FA) and morphologic (OCT) retinal changes related to DME. This agreed with the recommendations of Bolz et al. [16].

Witmer et al., compared Optos Optomap with Heidelberg Spectralis OCT. They are UWF imaging devices. Optos Optomap was found to be effective in imaging the temporal and nasal retina compared to OCT which was superior in evaluating the superior and inferior retina to farther point [8].

The limitations in our study were the duration was only 3 months, and it was a random study including DR eyes existed in outpatient clinics in KKESH.

Conclusion

There is a significant correlation between DME and PRI. UWFA is a useful tool for detecting PRI which may have direct implications

Table 3: Shows the relationship between PRI and DME types with median correlation between them which equals to 0.394.

Peripheral Retinal Ischemia (PRI)	Type of DME				Total 69(100.0%)	Pearson Chi-Square	Correlation	Significance
	Diffuse 36(52.2%)	Focal 23(33.3%)	Combined 6(8.7%)	Cystoid 4(5.8%)				
Present	32(88.9%)	12(52.2%)	4(66.7%)	2(50.0%)	50(72.5%)	10.725	0.394	0.013*
Absent	4(11.1%)	11(47.8%)	2(33.3%)	2(50.0%)	19(27.5%)			

in the diagnosis, follow-up and treatment such as targeted peripheral photocoagulation.

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