

## Digital Retinal Photography Role in Early Detection of Diabetic Retinopathy and Recent Treatment Options for Various Retinopathy Stages

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Type 2 diabetes mellitus (DM) has being a worldwide epidemic with growing number of incidence and prevalence globally, moreover huge impacts of diabetes and its complications have more serious effects on quality of life as well as economically affects budget of government that were illustrated clearly by World Health Organization report (WHO 2016) [1]. Hence, Diabetic Retinopathy (DR) is the leading cause of blindness among diabetic patients due to retinal damage [2], moreover diabetic retinopathy is the first complication that appears early in diabetic patient and occur when hyperglycemic state is lasting for long time which is reflected by presence of high level of glycated hemoglobin (HbA1c) 6.5% (48 mmol/ml) or more that is why American Diabetes Association (ADA) and WHO depend on HbA1c 6.5% as a cutoff point in diagnosis of diabetes mellitus as confirmed by ADA meta-analysis on eye diseases (March 2012), also this study was discussed profoundly prevalence of DR and possible risk factors globally.

### Epidemiology of diabetic retinopathy globally

American Diabetes Association (ADA) had conducted systemic review for 35 studies in DR which was performed worldwide in United State, Europe and some Asians countries (India and China) from 1980 till 2008 in diabetic patients ages 20 - 75 and the total number of participants was 22,896 individuals, so after analyzing these studies the result were significant and estimated that 35% of diabetic patient have DR that means around 130 million of people with diabetes (465 million of individuals are affected with DM confirmed by International Diabetes Federation 9<sup>th</sup> edition [3]), 6.9% have proliferative DR while 10% have Vision threatening diabetic retinopathy (VTDR) and 6,8% have diabetic macular edema.

**Risk factors for diabetic retinopathy:** Based on systemic review of ADA there are many risk factors behind development of DR in diabetic patient which include:

1. Long standing diabetes particularly in those who have uncontrolled glycemc state.
2. Patients with comorbidities like Hypertension and Hyperlipidemia.
3. Diabetic patient with type 1 diabetes at high risk than type 2 diabetes.
4. Cigarette smoking and some psycho- social factors.
5. Pre-existing diabetes in pregnancy.

So, DR is a public health burden that need huge efforts to decrease rate of incidence by early screening techniques and providing adequate management as early as possible [2].

### Screening of diabetic retinopathy in primary and secondary care

Recent guidelines in diabetes treatment recommend doing screening for early detection of DR and prevent progression into blindness, therefore ADA (JAN 2019) illustrated the importance of doing screening for type 1 diabetes after 5 years of diagnosis then annually, but in other hand type 2 diabetes should be screened at time of diagnosis and then every year to follow up retinal condition [2].

In 2005 Somani, *et al.* had applied comparison between old and new technique's in screening of DR and found that Several screening modalities have used to identify DR that used to for long time in the past which include slit-lamp examination and slide film photography, also study showed both of them were sensitive and specific in diagnosis and providing permanent record, but main disadvantages were been requiring high expert and trained ophthalmologists to reduce false positive and negative results and also those modalities have low sensitivity in detecting early stages of DR, particularly early damage of macula and fovea and poor outcome were noticed when monitoring progression of macular edema in DR.

Other hand they found new modality like digital photography through dilated pupil with a nonmydriatic camera has many benefits and superior to old modalities in many parts like:

1. Images can be checked easily at capturing time to assess quality and content of them by ophthalmologist that assist in explaining test result for patient immediately at the same day.
2. Digital images can be transferred through electronic system and transmitted as soft or hard copy that help in monitoring patients through registry system and easy for health authorities to make policies and planning to control DR in the future.
3. Detection of macular degeneration especially early and intermediate drusen changes in macula with specificity rate 97%, while low result in detecting large drusen with 90% sensitivity and 50% specificity respectively.
4. Identifying pigmentary changes as early features of macular degeneration with sensitivity 76% and high specificity rate 92% [4].

In 2018 Pilot study was conducted to confirm effectivity of combination of both digital retinal photography with Spectral Domain Optical Coherence Tomography (SD-OCT) in screening process of DR, 105 patients were participating in the study and most of them were having type 2 diabetes (55 person) rather than type 1 (50 patients), and each patient received digital imaging combined with SD-OCD and also checked by indirect ophthalmoscopy to compare the effectivity of each techniques, finally the result was obtained and showed in high accuracy rate graded by 81% (85/105) in diagnosis of retinopathy by using combination method of imaging with SD-OCT, in case of Macular Edema either cystoid or diffuse was confirmed in 42 patients by SD-OCT while in instrumental methods only 20 patients were identified, while in diagnosis of sever retinopathy that means grade 3 or more, the imaging methods had higher sensitivity (87.3%) than ophthalmoscopy methods by examiner (76.4%), while same result obtained in specificity (96%) versus (100%) respectively [5].

Meta-analysis also conducted 2011 by Peter and his team, they collected 20 studies from 9 countries and found that using of digital retinal photography with camera in case of dilated pupil or not by expert examiner or ordinary worker in screening of DR were unlikely to miss any case as well as having high accuracy rate when compared with direct eye examination or ophthalmoscopy by expert examiner [6].

So nowadays imaging by digital retinal photography in screening of DR is recommended by many guidelines and performed globally as first line (ADA 2019), in gulf region we follow this recommendation, so that ministry of health are trying to provide modern devices for

imaging of retina with low cost in secondary care settings.

### Case study

AMIRA, 25 years old with type 1 diabetes, attends our diabetes clinic for retinopathy screening, unfortunately ophthalmologist report demonstrated that background retinopathy in her left eye and proliferative retinopathy in the right eye, so that AMIRA come and asking about management options of her condition.

Management plan of this patient include many points that will be discussed by details.

**First point:** Explaining retinopathy screening report with simple language for AMIRA.

I will tell her about what does it mean these words (background –proliferative retinopathy), based on American Academy of ophthalmology (OCT 2019) report that explaining DR with simple language and clarifying firstly diabetic retinopathy as damage of retinal blood vessels due to high blood sugar for long time then retinal blood vessels leak and swell or may be close and reduce blood supply, sometimes new blood vessels are formed and may be leaked and causing small bleedings and continual bleeding damage retina and end by vision loss, usually diabetic patients are unaware of this changes until specific features appear like:

1. Seeing many flutters and look like blurry vision.
2. Changes in night vision and seeing dark color in field of vision [7].

Then we look for exact cause of these features by screening for DR as you did already, by the way, there are 2 stages of DR:

1. Non proliferative diabetic retinopathy (NPDR): The earliest stage of NPDR and start when retinal blood vessels swell and leak, so many patients have it, and medically we categorize it into, background retinopathy or mild NPDR as confirmed in the left eye and based on Scottish Grading Protocol of retinopathy, this stage should be rescreened after 12 months, while moderate NPDR is more advanced (more than 4 blot hemorrhages in one hemi field) that must be rescreened after 6 months, then sever NPDR that is most advanced one (more than 4 blot hemorrhages in 2 hemi field and presence of venous beading) so that should be referred for specialist for second opinion.
2. Proliferative diabetic retinopathy (PDR): Which means (new vascular formation, vitreous hemorrhage or retinal detachment) as established in the right eye screening report, PDR case should be referred immediately for specialist to start treatment.
3. Macular damage: As separated finding and presented in the form of macular edema or ischemia that end with vision loss if damaged totally [8].

**Second point:** Treatment options of diabetic retinopathy, in 2002 United Kingdom Prospective Study (UKPDS) was published and stated that (retinopathy, nephropathy and possible neuropathy are benefited from glyceimic control that means keeping HbA1c around 7%, and overall microvascular risk was decreased by 25%) [9], also ADA 2019 emphasize that most important treatment options for microvascular complication of diabetes is glyceimic control and reducing blood glucose level that is established by many Randomized Control Studies such as UKPDS, Japanese study, DCCT and Stockholm Diabetes intervention Study. Therefore, ADA 2019 guideline recommend the flowing for DR treatment:

1. Optimize glyceimic control and HbA1c around 7 - 8%.

2. Encourage lifestyle changes (diet, exercise, loss of weight and stop alcohol or smoking).
3. Keep blood pressure within normal range (not more than 130/80).
4. Normalize lipid profile and keep blood cholesterol in low level.
5. Photocoagulation therapy: Strong evidence emphasize the effectivity of photocoagulation surgery, in 1978 strong large trials was performed and most important 2 are Diabetic Retinopathy Study (DRS) in patients who have PDR and showed high benefits from using pan retinal photocoagulation and reduced vision loss of PDR if left untreated from 15.9% to 6.4% in treated cases especially of DR complicated by vitreous hemorrhage and disc neovascularization, Early Treatment Diabetes Study (ETDS) one of major study that illustrated the efficacy of panretinal LASER therapy (Light Amplification by Stimulated Emission of Radiation) in patients with Macular Edema, moreover LASER therapy have approved for treatment of sever and moderate stage of PDR with high therapeutic effect in 1985.
6. Anti-Vascular Endothelial Growth Factor treatment (Anti-VEGF) current data from many studies support the use of intravitreal injection of Anti-VEGF showed high beneficial effect in PDR with different stages similar to those who treated with panretinal laser therapy, fortunately 3 drugs now is available and one of them is Ranibizumab approved by the Food and Drug Administration (FDA) in 2017 [2]. In 2013 Barot and his team performed study that discussed many types of promising therapies for DR, and found 3 types of Anti-VEGF (Bevacizumab, Ranibizumab and Pegaptinip sodium) with great benefits particularly ranibizumab because it is more safe and effective if combined with photocoagulation therapy with rapid improvement in DR conditions within 24 months of treatment duration and these significant improvement include: A-Improvement in visual acuity (patient ability to read 15 additional letters), B-inhibition of abnormal growth of new blood vessels inside the retina retinal neovascularization rate reduced to 4% after giving 0.5% of ranibizumab, C- vitreous hemorrhage reduced by rate 3.2% in dose group given ranibizumab, by the way from side effects lists of Anti-VEGF are costly, should be taken monthly for 12 months then at regular intervals by intravitreal injections that is why many patient do not like to take it and finally ocular side effects such as raised intraocular pressure, retinal detachment, traumatic cataract and bacterial infection. Also, Barot and his colleagues suggested many other options of treatment but still not approved by international guidelines and these options include:
7. Long acting corticosteroids: many studies are still working to assess affectivity of long acting steroids in treatment of diabetic macular edema like: dexamethasone and triamcinolone acetonide.
8. Protein Kinase C inhibitors (PKC inhibitors) still under research.
9. Anti-Oxidants medications like some vitamins and compounds but unfortunately not confirmed as effective as other options [10].

## **Conclusion**

DR once identified cannot be reversed but we can prevent its incidence by tight glycemic control and regular screening and when DR detected we can treat it well and prevent progression into vision loss as the end outcome of advanced stage of DR.

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