Research Article

Correlation between central foveal thickness as measured by OCT and HbA1c level in diabetes retinopathy

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Abstract

Objectives: To evaluate the correlation between Glycosy lated Haemoglobin (HbA1c) level and central foveal thickness measured by Optical coherence tomography (OCT) in patients with type 2 diabetes mellitus. **Materials and methods:** This was a retrospective single center study of 6 month duration including patients of pre-proliferative stage of type 2 diabetes mellitus. Clinically significant macular oedema (CSME) was diagnosed by using OCT. OCT examination by 'RT optovue, Fremont, CA' and HbA1c measured by specific high-pressure liquid chromatography methods. If patient have both eye macular oedema, eye with thicker macular oedema was used for statistical analysis. Exclusion of patients who received intraocular surgery, cataract surgery, pars plana vitrectomy, Severe vitreous haemorrhage, etc. **Results:** One hundred four eyes of 104 patients were included in this cross-sectional study. The mean Age ±SD was 62.3±8.1 years (range, 40–77 years). Mean value of HbA1c was 7.8%±1.4% (range, 5.1%–12.1%). Mean DM duration was 11.2±5.5 years (range, 1–30 years). Mean central retinal thickness was 257.1±79.3 μm (range, 151–526 μm). Univariate analysis was significant with HbA1C level (7 or over) (P=0.005). Not statistically significant with Sex (P=0.78), Right or left eye (P=0.59). **Conclusion:** Patients with HbA1c of 7% or above had an increase in macular thickness as measured by OCT in shorter DM duration (< 10 years). Its association with macular oedema is statistically significant. Good sugar control decreased the risk of diabetic macular oedema.

Key word: Clinically significant macular oedema, Diabetes mellitus type 2, Glycosylated Haemoglobin, Macular oedema, Optical coherence tomography.

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Introduction

Diabetic retinopathy (DR) is the leading cause of blindness among working aged adults around the world [1]. Despite the significance of this problem, and the rising prevalence of diabetes notably in emerging Asian countries such as India and China [1], there are few precise contemporary estimates of the worldwide prevalence of DR, particularly severe vision-threatening stages of the disease, including proliferative DR (PDR) and diabetic macular oedema (DME) [1]. In the past, DME was diagnosed by ophthalmoscope as Clinical Significance Macular Oedema (CSME). Fluorescein angiography is indicated in guiding treatment of macular oedema. With the help of optical coherence tomography (OCT), it is now possible to measure the macular thickness objectively and to follow the progression of diabetic macular oedema quantitatively [2].

Risk factors associated with diabetic retinopathy in type 2 diabetes is divided in two groups one is non modifiable and other is modifiable. Most important non modifiable risk factors is duration of diabetes and modifiable risk factor include hyperglycemia, hypertention, the rennin-angiotensin system, dyslipidemia, anemia, and smoking [3].

Manuscript received 26th April 2016
Reviewed: 10th May 2016
Author Corrected: 24th May 2016
Accepted for Publication 7th June 2016

It is well know that hyperglycemia is one of the most important determinants of diabetic microvascular complications [1,3,4]. like a diabetic macular oedema (DME). In these patients Periodic glycosylated haemoglobin (HbA1c) measurements can reflect the long-term control of hyperglycaemia.

The diabetes control and complications trial (DCCT) [5] for type 1 and UK prospective diabetes study (UKPDS) [6] for type 2 diabetes have demonstrated that intensive glycemic control (HbA1c <7%) reduced both the development and progression of diabetic retinopathy (DR)with the beneficial effects of intensive glycemic control persisting for up to 10 to 20 year .

Optical Coherence Tomography (OCT) now plays a vital role in the diagnosis and management of retinal diseases.

By producing detailed cross-sectional images of the retina, ophthalmologists can visualize changes in the anatomy caused by DME and monitor the response to treatment [7].

OCT is a specific instrument that use light rays and can capture detailed cross-sectional images of retina without changing its architecture, and give image like histopathological examination of dead tissue .

In Indian scenario there is no study which directly correlates DME toHbA1c. We therefore conducted a study to evaluate the correlation between Glycosylated hemoglobin (HbA1c) level and central foveal thickness measured by Optical coherence tomography (OCT) in patients with type 2 diabetes mellitus.

Materials and Methods

Study type– Retrospective study (randomized)
Study design– Cross-sectional study
Study period– Six months patients data analyzed

We included only one eye of patients. If both eyes have diabetic macular oedema (DME) we include eye which have high foveal thickness. Eligible subjects had to meet all of the following criteria Clinically significant macular oedema (CSME)/diabetic macular oedema (DME) was diagnosed according to central macular retinal thickness greater than 300 micron in OCT.

Inclusion Criteria

- Received complete ophthalmic evaluation;
- Had HbA1c measured by specific high pressure liquid chromatography methods.
- Received OCT examination for measurement of DME [figure 1 and figure 2] with the help of 'Stratus OCT by RT optovue, fremont, CA' within 3 months preceding HbA1c measurement.
- Pre-proliferative stage of type 2 diabetes.
- Less than 30 year duration.
- Age between 40-70 year.

Exclusion Criteria

1. Patients who received intraocular surgery
2. Cataract surgery
3. Pars plana vitrectomy
4. Intravitreal injection of triamicinolone or Bevacizumab
5. Sub tenon injection, or photocoagulation therapy within 1 year of evaluation .
6. Severe vitreous haemorrhage or vitreous opacity that would interfere with the OCT examination.

Result

One hundred and four eyes of 104 patients were included in this cross-sectional study. As described in Table 1, Sixty two patients were male and 42 were female. The mean Age ±SD was 62.3±8.1 years (range, 40–77 years). The The mean value of HbA1c was 7.8±1.4% (range, 5.1–12.1%).

The mean DM duration was 11.2±5.5 years (range, 1–30 years). The mean central retinal thickness was 257.1±79.3 μm (range, 151–526 μm). Table 1 shows the distribution of possible risk factors for DME diagnosed by OCT among patients with diabetes and results of the univariate analysis.

Univariate analysis revealed that the DME diagnosed by OCT in diabetes was not statistically significant with age (P-value 0.06) sex (P-value 0.78), right or left eye (P-value, 0.59), DM duration over 10 years or over (P-value, 0.18), The HbA1C level (7 or over) showed a significant (P-value 0.005) and positive association with macular thickness in OCT [figure 3]. A positive correlation also present if patient duration of diabetes was less than 10 year and he have poor glycemic control more chances of increase foveal thickness.

Table1: Univariate logistic regression analysis of factors associated with OCT-based DME in diabetic eyes.

Factor	Definition	No DME (OCT <300Um)	DME (OCT >300 Um)	Univariate analysis (P-value)
Age (40 -70 year)	>60 year	80(76.92%)	13(12.50%)	0.06
	<60 year	5(4.80%)	6(5.76%)	
Sex	Male	51(49.03%)	11(10.57%)	0.78
	Female	35(33.65%)	7(6.73%)	
Laterality	Right	34(32.69%)	6(5.76%)	0.59
	Left	52(50.00%)	12(11.53%)	
DM duration (<30 years)	<10 year	27(25.96%)	8(7.69%)	0.18
	> 10year	59(56.73%)	10(9.61%)	
HbA1c (5.1%-12.1%)	<7%	57(54.80%)	5(4.80%)	0.005*
	>7%	29(27.88%)	13(12.5%)	

Abbreviations: DM, diabetic mellitus. HbA1c, hemoglobin A1c.
*Indicates statistically significant (<0.05).

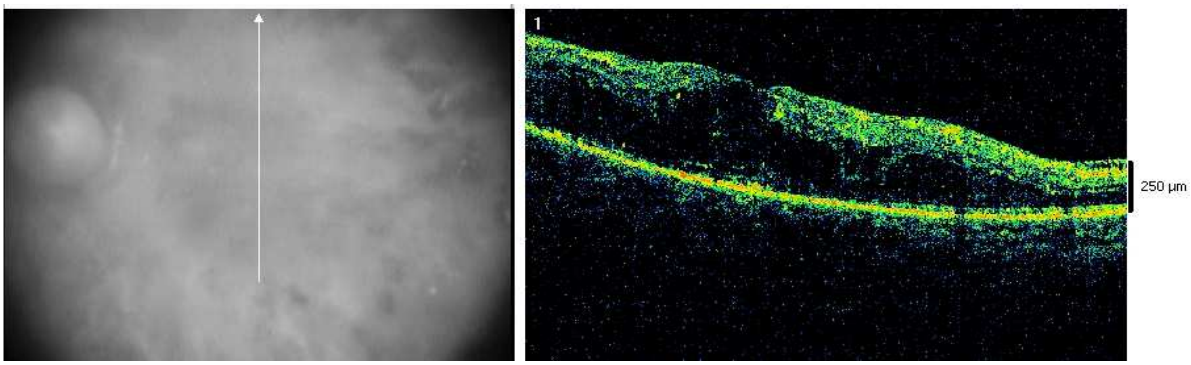

Figure-1: Increase foveal thickness in DME

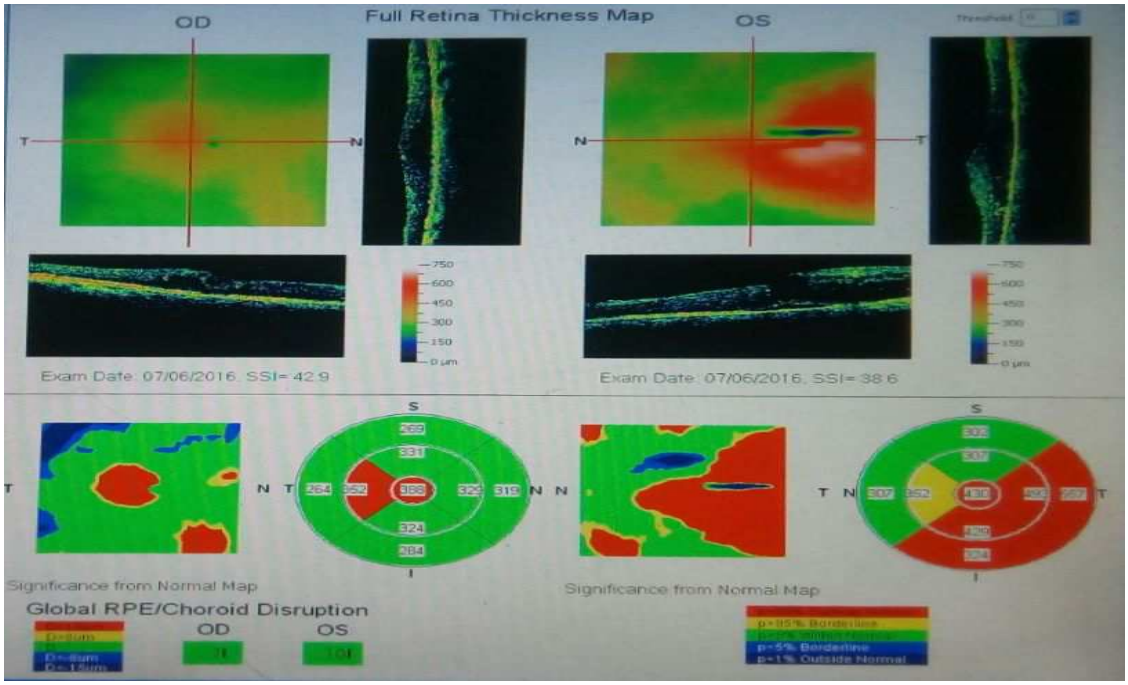

Figure-2: Stratus OCT, increase foveal thickness (right eye 386 u, and left eye 430u,)

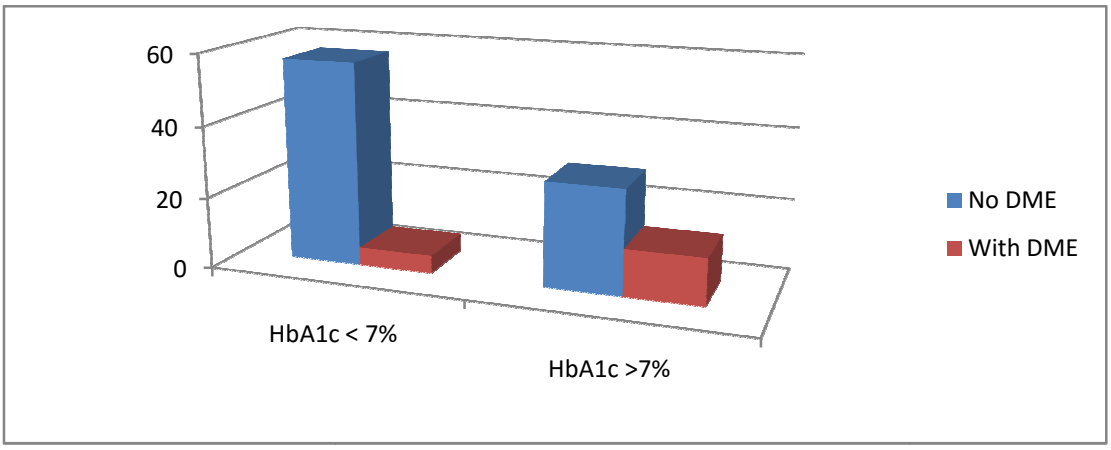

Figure-3 : Correlation between HbA1c and DME

Discussion

Earlyepidemiological studies have shown showed a consistent relationship between Glycosylated hemoglobin (HbA1c) levels and the incidence of DR [3,7]. Various randomized clinical trials like the diabetes control and complications trials (DCCT) [5] and the epidemiology of diabetes interventions and complications (EDIC) study in T1D [8] and the UK prospective diabetes study (UKPDS) in T2D [6] have described at the association between hyperglycemia and diabetic retinopathy and the importance of glycemic control in reducing the incidence of retinopathy .

Retinopathy included many signs and symptoms but most problematic symptom for the patient is visual disturbances which is mostly because of diabetic macular oedema (DME) and proliferative diabetic retinopathy (PDR). Thus, we reach the conclusion that DME is the most important parameter to diagnose and to determine progression of DR. In the CRUES eye study [4], a linear trend of increase in prevalence of DR with increasing HbA1c (trend Chi^2 =51.6,p,0.0001) was observed.

The CRUES [4] subjectswere categorized into two groups according to duration of diabetes, i.e. those with diabetes duration < 10 years and those with diabetes duration > 10 years and regression analysis was done using DR as dependent variable and tertiles of HbA1c as independent variable. The risk for DR in subjects with duration of diabetes <10 years and HbA1c level 9.5% was 3.4 times (p <0.001), whereas this risk increased seven fold (p<0.001) in subjects having duration of diabetes >10 years showing the additive effect of increased disease duration and hyperglycemia on the risk for DR.

The benefits of intensive therapy were greater in patients with shorter duration of diabetes. In patients with no retinopathy at baseline (primary prevention cohort), intensive treatment (median HbA1c 7.2%) reduced the risk of the development of DR by 76% and in the secondary prevention cohort, intensive treatment slowed the DR progression by 54% relative to conventional treatment (median HbA1c 9.1%) (p<0.001) [5].

The epidemiology of diabetes interventions and complications (EDIC) has shown that the benefit of early tight control on the progression of DR was maintained, despite subsequent equalization of the HbA1c values between the groups, a concept of “metabolic memory” [8].

The UKPDS [6] also studied the impact of tight control versus conventional control for T2D on the microvascular (DME) and macrovascular complications of diabetes. After 6 year of follow-up, the intensive treatment group had significantly lower rate of the two-step progression DR. UKPDS showed a 25% risk reduction in microvascular endpoint, including the need for retinal photocoagulation. The result of the DCCT and UKPDS showed that while intensive therapy does not prevent retinopathy completely, it reduces the risk of the development and progression of DR.

Two study, the action to control cardiovascular risk in diabetes (ACCORD) eye study[9], and the action in diabetes and vascular disease: preterax and diamicron MR controlled evaluation (ADVANCE) retinal measurements study (AdRem) [10], examined the effect of more aggressive blood glucose lowering (HbA1c<6.5%) in patients with T2D.

However, there are some reports that intensive glycemic control can have some adverse effects including hypoglycemia and a worsening of DR that may be attributable to a rapid reduction of plasma glucose levels [11].

Good metabolic control (<7%) is important to prevent and delay progression. Microaneurysm turnover has been validated as a prognostic biomarker of development of clinically significant macular oedema (CSME). HbA1c remains the only confirmed systemic prognostic biomarker of DR progression [12].

Good glycemic control right from the time of diagnosis of diabetes is beneficial in preventing the onset of DR as well as in delaying the progression of the retinopathy. Targeting an HbA1c level of <7% is recommended for slowing down the progression of DR [9].

In our study, only mild-to-moderate DR was included, It explain that the shorter DM duration (<10 years) with poor control of diabetes is more associated with macular. Other reported risk factors of DME, including: Increased diastolic blood pressure, Insulin use, Nephropathy, Cataract surgery, Panretinal photo-coagulation, were not analyzed in our study. Further prospective study may be indicated for evaluation.

Conclusion

In patients with HbA1c of 7% or above had an increase chances of macular thickness (DME) as measured by OCT, is statistical significant and in shorter DM duration (<10 years) with poor glycemic control is associated with macular oedema. Good sugar control decreased the risk of diabetic macular oedema.

Funding: Nil, **Conflict of interest:** None initiated.
Permission from IRB: Yes

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How to cite this article?

Parashar H, Shastri A, Goel S, Thakur S, Sitaraman C, Sharma. Correlation between central foveal thickness as measured by OCT and HbA1c level in diabetes retinopathy. *Int J Med Res Rev* 2016;4 (6):924-929doi: 10.17511/ijmrr.2016.i06.10.

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