Relationship of diabetic macular oedema with glycosylated Haemoglobin-OCT based approach

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Abstract: Purpose To evaluate the correlation between glycosylated haemoglobin (HbA1c) and central foveal thickness as measured by optical coherence tomography (OCT) in patients with diabetes. Methods Observational study of central foveal thickness measured by OCT and laboratory data of glycosylated haemoglobin. HbA1c was compared with foveal thickness measured by OCT within the preceding 3 months. Clinically significant macular oedema (CSME) was diagnosed if central foveal retinal thickness was greater than 325 µm in OCT. Results One hundred and two eyes of 102 patients were included in this cross-sectional study. The analysis revealed that the CSME diagnosed by OCT in diabetes was statistically significant with sex, right or left eye, DM duration > 10 years or not, and AC sugar level (> 140 or not). The HbA1c level (≥8) and age (≥50) showed a significant (P = 0.005 and 0.006, respectively) and positive association with macular thickness in OCT. A trend towards higher risks was seen for factors of age ≤50 and HbA1c ≥8%. Conclusions Patients with HbA1c of ≥8 had an increase in macular thickness in type 2 diabetic eyes and there was a statistical significant correlation between younger age, shorter DM duration and thicker macular thickness. Strict sugar control decreased the risk of diabetic macular retinopathy, and OCT could be an excellent detector of early diabetic macular oedema.

Keywords: central foveal thickness, HbA1c, diabetic macular oedema, optical coherence tomography

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I. Introduction

Diabetic Macular oedema is defined as retinal thickening within 2 disc diameters of the centre of the macula, causing leakage of plasma constituents into the surrounding retina due to microvascular changes in the blood retinal barrier and ultimately leading to retinal oedema. CME is a cause of severe visual loss that occurs in a variety of pathologic conditions, such as age-related macular degeneration, diabetic retinopathy, branch or central retinal vein occlusion, epiretinal membrane or vitreomacular traction, and as a complication of intraocular surgery. CME is a pathologic definition with two components: abnormal collection of extracellular fluid and cystoid-space formation. Diabetic macular edema is classified in focal and diffuse types and this is important because the treatments of the two types are different. Focal edema is caused by leakage from microaneurysms and is associated with hard exudates rings. Diffuse edema is caused by leakage from retinal capillaries and arterioles. Two types of laser treatment for DMO are focal and grid. Focal laser treatment is used to treat focal diabetic macular edema; the purpose is to close the leaking microaneurysms. Grid laser is used to treat diffuse macular edema and is applied in areas of retinal thickening with diffuse leakage. The Wisconsin Epidemiology Study of Diabetic Retinopathy (WESDR) in 1995 showed that there is an increase in diabetic macular edema in patients with increase HbA1c.

Diabetic macular oedema increases with the duration of diabetes, and the prevalence is 5% within the first 5 years after diagnosis and 15% at 15 years. 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 DME quantitatively. With the advent of OCT, several investigators have classified DME on the basis of the retinal map and cross-sectional appearance of the retina on OCT. Spectral domain (SD) OCT allows for better characterization of the retinal morphology. The morphological patterns of DME on OCT are generally classified into diffuse retinal thickening, cystoid macular edema (CME), subretinal detachment, and vitreomacular interface abnormalities. OCT, first described by Huang et al. in 1991, is an imaging modality capable of providing high-resolution cross-sectional images of the neurosensory retina. As OCT is noninvasive, it was quickly adopted by clinicians for the assessment of patients with CME. In part, because of the relative ease with which they can detect CME, many clinicians now prefer OCT over FA for its detection. OCT has gained increasing popularity as an objective tool to measure retinal...
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Periodic glycosylated haemoglobin (HbA1c) measurements can reflect the long-term control of hyperglycaemia. Intensive glycemic control had been proved to be effective in decreasing incidence rate of development and progression of DR in type 1 and type 2 diabetic mellitus as demonstrated by the diabetes control and complications trials\textsuperscript{13} and the United Kingdom Prospective Diabetes Study\textsuperscript{14}.

II. Materials and methods

It is an observational study conducted in 102 patients attending the ophthalmology OPD between August 16-May 18. Inclusion criteria: (1) received complete ophthalmic evaluation; (2) had HbA1c measured by specific high-pressure liquid chromatography methods; and (3) received OCT examination (TOPCON) within 3 months preceding HbA1c measurement. OCT was performed in both eyes, but the eye with thicker macular oedema was used for statistical analysis. OCT images of few patients of CSME are shown in fig1,2,3. Exclusion criteria included patients who received intraocular surgery (cataract surgery, pars plana vitrectomy, intravitreal injection of triamcinolone or Bevacizumab), subtenon injection, or photocoagulation therapy within 1 year of evaluation and severe vitreous haemorrhage or vitreous opacity that would interfere with the OCT examination. Clinically significant macular oedema (CSME) was defined as central retinal thickness >325 µm in OCT\textsuperscript{15}.

Statistical analysis—Pearson’s correlation coefficient was used to find out the relationships between age, duration of diabetes, HbA1c level, AC sugar level, central foveal thickness. P value <0.05 was considered statistically significant. All patients were divided into 2 groups with no CSME and those with CSME.

III. Results

One hundred and two eyes of 102 patients were included in this cross-sectional study. 63 patients were male and 39 were female. The mean age±SD was 62.3±8.1 years (range, 40–77 years). The mean DM duration was 11.2±5.5 years (range, 1–30). The mean value of HbA1c was 7.8±1.4% (range: 5.1–12.1%). The mean central retinal thickness was 257.1±79.3 mm (range, 151–526 mm) shown by Table 1.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Observation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of included</td>
<td>102</td>
</tr>
<tr>
<td>Male : female ratio</td>
<td>1.61:1</td>
</tr>
<tr>
<td>Mean age (years)</td>
<td>62.3±8.1</td>
</tr>
<tr>
<td>Mean DM duration (years)</td>
<td>11.2±5.5</td>
</tr>
<tr>
<td>Mean HbA1C (%)</td>
<td>7.8±1.4</td>
</tr>
<tr>
<td>Mean central retinal thickness (µm)</td>
<td>257.1±79.3</td>
</tr>
</tbody>
</table>
Table 2 shows the distribution of possible risk factors for CSME diagnosed by OCT among patients with diabetes and results of our study.

<table>
<thead>
<tr>
<th>Factor</th>
<th>Definition</th>
<th>No CSME (OCT=325 μm) No. (%)</th>
<th>CSME (OCT=325 μm) No. (%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>≥50</td>
<td>81(95.3)</td>
<td>12(70.6)</td>
<td>0.006*</td>
</tr>
<tr>
<td></td>
<td>&lt;50</td>
<td>4(4.7)</td>
<td>5(29.4)</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td>Male</td>
<td>52(61.2)</td>
<td>11(64.7)</td>
<td>0.78</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>33(38.8)</td>
<td>6(35.3)</td>
<td></td>
</tr>
<tr>
<td>Laterality</td>
<td>Left</td>
<td>49(57.6)</td>
<td>11(64.7)</td>
<td>0.59</td>
</tr>
<tr>
<td></td>
<td>Right</td>
<td>36(42.4)</td>
<td>6(35.3)</td>
<td></td>
</tr>
<tr>
<td>DM duration</td>
<td>&lt;10</td>
<td>26(30.6)</td>
<td>8(47.1)</td>
<td>0.18</td>
</tr>
<tr>
<td></td>
<td>≥10</td>
<td>59(69.4)</td>
<td>9(52.9)</td>
<td></td>
</tr>
<tr>
<td>AC sugar</td>
<td>&lt;140</td>
<td>28(40.6)</td>
<td>4(26.7)</td>
<td>0.315</td>
</tr>
<tr>
<td></td>
<td>≥140</td>
<td>41(59.4)</td>
<td>11(73.3)</td>
<td></td>
</tr>
<tr>
<td>HbA1c</td>
<td>&lt;8</td>
<td>56(65.9)</td>
<td>5(29.4)</td>
<td>0.005*</td>
</tr>
<tr>
<td></td>
<td>≥8</td>
<td>39(54.1)</td>
<td>12(70.6)</td>
<td></td>
</tr>
</tbody>
</table>

This study revealed that the CSME diagnosed by OCT in diabetes was not statistically significant with sex (P=0.78), right or left eye (P=0.59), DM duration over 10 years or over (P=0.18), and AC sugar level (over140 or not) (P=0.315). The HbA1C level (8 or over) and age (50 or less) showed a significant (P=0.005 and 0.006, respectively) and positive association with macular thickness in OCT.

IV. Discussion

The inclusion of HbA1c in the screening protocol has gained significant importance, not only in the diagnosis and management of DM, but also in the onset and progression of DR [16]. It has been seen that compared to the measurement of glucose levels, HbA1c assay is at least as good in defining the level of hyperglycemia at which the prevalence of DR increases [17,18]. Glycation of tissue proteins is a well-known patho-physiological mechanism in the complications related to diabetes leading to the formation of advanced glycation end products and HbA1c [19]. Tight glycemic control, as measured by these factors, is strongly associated with a decreased prevalence of micro-vascular complications related to DM like retinopathy [20-23]. Anitha et al. also found an association of advanced glycation index (AGI) with the severity of DR [24].

Figure 1- OCT 3D WIDE image showing subretinal fluid collection around macula with hard exudates (CME).
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References


Figure 2 and 3 –OCT 3D MACULA showing increase in central macular thickness due to subretinal fluid collection (cystic spaces) around macula.

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