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CORRELATION OF SERUM HBA1C LEVEL,AGE OF PATIENT & DM DURATION WITH CENTRAL MACULAR THICKNESS BY OCT IN DIABETIC MACULAR EDEMA

Ophthalmology

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ABSTRACT

Purpose To evaluate the correlation between glycosylated haemoglobin (HbA1c) and central macular thickness as measured by optical coherence tomography (OCT) in patients with diabetes.Methods Observational study of central macular thickness as measured by OCT and laboratory data of glycosylated haemoglobin. HbA1c was compared with central macular thickness measured by OCT within the preceding 3months. Clinically significant macular edema (CSME) was diagnosed if central macular retinal thickness was greater than325 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 not 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 risk 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 macular thickness,HbA1c, diabetic macular oedema,optical coherence tomography.

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[1]. 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[2]. CME is a pathologic definition with two components: abnormal collection of extracellular fluid and cystoid-space formation[3]. 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 micro aneurysms 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 isused to treat focal diabetic macular edema; the purpose is to close the leaking micro aneurysms. Grid laser is used to treat diffuse macular edema and is applied in areas of retinal thickening with diffuse leakage.[1]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[4].

Diabetic macular edema increases with the duration of diabetes, and the prevalence is 5% within the first 5 years after diagnosis and 15% at 15 years.[5]Flourescein angiography is indicated in guiding treatment of macular oedema[6]. 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[7].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[8].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)(fig1), subretinal detachment, and vitreomacular interface abnormalities[9].

OCT, first described by Huang et al[10] 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[11].OCT has gained increasing popularity as an objective tool to measure retinal thickness and other aspects associated with macular edema[12]. An advantage of using OCT is its quantitative assessment, rather than the qualitative evaluation performed with photography or biomicroscopy7. 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[13] and the United Kingdom Prospective Diabetes Study[14].

II. Materials and methods

A total of 102 patients of either sex suffering from diabetes were evaluated and randomly divided into two groups (group A and group B) were included in this study conducted in the Department of Ophthalmology, Maharani Laxmi Bai Medical College, Jhansi, Uttar Pradesh, India over a period of 17 months from Jan 2017 to may 2018. The procedures followed were in accordance with the Ethical Standards Committee on Human Experimentation (institutional or regional) and with the Helsinki Declaration of 1975, as revised in 2000. The necessary permission from the Ethical and Research Committee was obtained for the study.

Group 'A' included patients who had no CME and group B included patients who had CME . CME was confirmed by the fundus fluorescein angiography. The serum HbA1c levels were measured by liquid chromatography and the central macular thickness (CMT) were measured by OCT. OCT was performed in both eyes,but the eye with thicker macular oedema was used for statistical analysis. Inclusion criteria comprised of all patients with diabetes having diabetic retinopathy, the presence of clinically significant macular oedema in the fundus examination, the presence of fluroscein angiographically confirmed diabetic macular oedema, the presence of CME and serous macular detachment documented by OCT . Exclusion criteria comprised of non diabetics with macular oedema, patients having undergone vitreoretinal surgery in past, eyes that had received previous grid laser photocoagulation,the presence of epiretinal membrane or vitreo-macular traction documented by OCT, the presence of dense media opacity or pre-retinal haemorrhage that might prevent OCT examination, eyes with previous intraocular surgery or vitreo-retinal pathology other than diabetic retinopathy, cataract, glaucoma, problem in follow-up or documentation.

The patients underwent complete ophthalmic examination, including best- corrected VA measurement were done as per logMAR, slitlamp biomicroscopy and fundus examination done with a 78/90 diopter noncontact lens and , OCT(fig3) and FFA(fig2) were done. OCT and FFA examinations and collection of venous blood samples were performed on the same day. The central macular thickness was measured automatically using the topography software built into the OCT device.

The patients were followed up for measuring HbA1c level, FFA, OCT for each eye at 3 month, 6 month, 9 month respectively. Clinically significant macular oedema (CSME) was diagnosed according to central macular retinal thickness >325 µm in OCT15.

Statistical analysis- Pearson's correlation coefficient was used to find out the relationships between age, duration of diabetes, HbA1c level, AC sugar level,central macular retinal thickness. P value <0.05 was considered statistically significant.

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 Table1. Table 2 shows the distribution of possible risk factors for CSME diagnosed by OCT among patients with diabetes and results of our study. 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.

Table 1 Demographic & clinical data of study population

Parameters	observation
Total number of included	102
Male : female ratio	1.61:1
Mean age (years)	62.3±8.1
Mean DM duration (years)	11.2±5.5
Mean HbA1C (%)	7.8±1.4
Mean central retinal thickness (µm)	257.1±79.3

Table 2- Analysis of risk factors associated with OCT-based CSME in diabetic eyes

Factor	Definition	No CSME (OCT<325 µm) No. (%)	CSME (OCT≥325 µm) No. (%)	P value
Age	>50	81(95.3)	12(70.6)	0.006*
	≤50	4 (4.7)	5(29.4)	
Sex	Male	52(61.2)	11(64.7)	0.78
	Female	33(38.8)	6(35.3)	
Laterality	Left	49(57.6)	11(64.7)	0.59
	Right	36(42.4)	6(35.3)	
DM duration (years)	<10	26(30.6)	8(47.1)	0.18
	≥10	59(69.4)	9(52.9)	
AC sugar (mg/100 ml)	<140	28(40.6)	4(26.7)	0.315
	≥140	41(59.4)	11(73.3)	
HbAlc	<8	56(65.9)	5(29.4)	0.005*
	≥8	29(34.1)	12(70.6)	

IV. Discussion

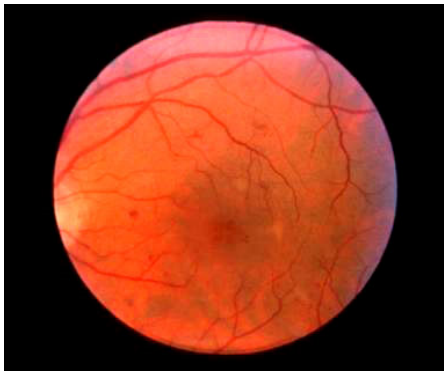
The inclusion of HbA1c in the screening protocols has gained significant importance, not only in the diagnosis and management of DM, but also in the on set and progression of DR [16]. It has been seen that compared to the measurement of glucoselevels,HbA1c assay is atleast as good in defining the level 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].

Our results were also consistent with the finding of Michael Larsen, Maria Wang et al, (2005) 25 did a prospective study of twelve eyes in 12 patients aged 39 to 78 years (mean age 57) with fovea-involving diabetic macular edema and 14 eyes in 7 healthy volunteers aged 30 to 70 years (mean age 57). Ling Yeung, Chi-Chin Sun, Wan-Chen Ku(2009)26 had also found the mean age of diabetic patients is 62.2 years in his study. Our study shows significant correlation between the reduction of HbA1c level and also decrease the CMT measured by OCT, that findings is consistent with Neil H. White, Wanjie Sun(2010)27, clearly demonstrated in his study that the benefits of intensive diabetes therapy aimed at lowering blood glucose and HbA1c (A1C) as near to the normal range as safely possible. Ong Ming Jew, Mohammadreza Peyman, Tan Chen Chen, Subrayan Visvaraja (2012)28 also demonstrate in his study that the HbA1c and total cholesterol are the two most important risk factors associated with CSME in patients with NPDR. Cho TH et al (2008) 29 also clearly showed in his study that the strict sugar control decreased the risk of diabetic macular retinopathy, and OCT could be an excellent detector of early diabetic macular oedema.Studies have shown that the reduction of (CMT) by using various treatment modalities and the CMT finding is consistent with Kiyoshi Suzuma et al (2011)30. LingYeung et al (2009) 31 found in his study that linear regression chronic HbA1c level also showed reduction in mean CMT. Our study is not consistent with Demir M et al (2013)32. His study showed the no statistically significant relationship was found between CMT, HbA1c, and fasting plasma glucose level in either group(p=0.05).

V. Conclusion

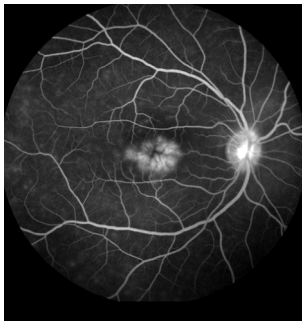
Elevated HbA1c is a well-known risk factor for diabetic macular edema. Prolonged hyperglycemia is known to significantly increase the rate of macular edema, while reduction of HbA1c levels with strict glycemic control decreases the rates of clinically significant macular edema, cystoid macular edema, serous macular detachment and other microvascular complications and also noticed the reduction of central macular thickness.

Figure-1



FUNDUS PHOTOGRAPH OF CYSTOID MACULAR EDEMA

Figure-2



FLUROSCEIN ANGIOGRAPHY IN CYSTOID MACULAR EDEMA

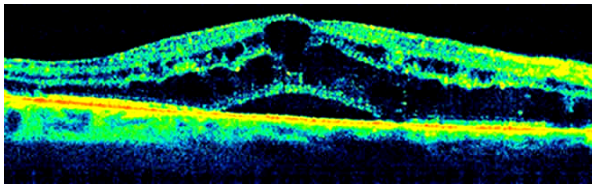


Figure-3

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