International Journal of Life Sciences, Biotechnology and Pharma Research Vol. 13, No. 10, October 2024 Online ISSN: 2250-3137
Print ISSN: 2977-0122

DOI: 10.69605/ijlbpr_13.10.2024.87

ORIGINAL RESEARCH

Correlation Between Hba1c And Central Macular Thickness In Diabetic Patients With Or Without Diabetic Retinopathy

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Received Date: 23 September, 2024 Accepted Date: 15 October, 2024

ABSTRACT

Aim: To assess the correlation between Hba1c and central macular thickness in diabetic patients with or without diabetic retinopathy. **Material and Methods**: This observational cross sectional study was conducted involving the 50 patients with and without signs and symptoms of diabetic retinopathy who are attending the Outpatient Department of Ophthalmology at Maharishi Markandeshwar Institute of Medical Science and Research. All patients underwent SD OCT, and central macular thickness was assessed regardless of the presence or absence of diabetic retinopathy. The HBA1C test was performed the same day as the ophthalmic examination, and its results were correlated with the central macular thickness. **Results**: The study subjects were divided 66% male and 34% female. The mean CMT was 192.16±10.78, 247.08±13.99, 283.11±22.84, and 289.4±17.82 for the participants with no DR, mild NPDR, moderate NPDR, and severe NPDR, respectively. It was revealed that the mean CMT was highest in individuals with a HbA1c >7 and lowest in those with a HbA1c >7.8%. **Conclusion**: There was a strong positive association found between the levels of CMT and HbA1c. Increased retinal thickness was seen in patients with HbA1c > 8% and longer-term diabetes, as well as in patients with proliferative and severe non proliferative DR.

Keywords: HbA1c, CME, Diabetes, Retinopathy

INTRODUCTION

According to WHO estimations, diabetes is an epidemic risk that the world is currently confronting. It is projected that by 2030, there will be 360 million diabetics globally[1]. Type 1 diabetes mellitus is characterised by primarily impaired insulin production, while type 2 diabetes mellitus is associated with increased resistance to insulin, is associated with a familial history, and is linked to a sedentary lifestyle[2]. There are 47.8 million diabetics in India, according to a recent epidemiological survey done at Aravind Eye Hospital[3].

One in three people with diabetes mellitus will develop diabetic retinopathy, a unique microvascular consequence of the disease. The primary cause of diabetic retinopathy is microangiopathy, a condition in which hyperglycaemia can cause damage to small blood vessels. DR is still the most common cause of vision loss in adults. According to reports, patients with severe cases of DR have lower physical, emotional, and social wellness as well as a lower quality of life[2]. Up to 80% of persons with diabetes who have had the disease for ten years or more may develop diabetic retinopathy[4]. Despite these concerning figures, research indicates that if appropriate treatment and eye control are provided, at least 90% of these new cases may be prevented[5].

Diabetic retinopathy (DR) can be classified into two clinical stages: nonproliferative and proliferative. DR is a progressive illness that primarily damages the integrity of tiny capillaries present in the retina.[6] One of the most severe and vision-threatening complications is macular edema, which is caused by vascular malfunction[7]. According to estimates, 50% of people with proliferative diabetic retinopathy will go blind within five years of diagnosis if they do not receive therapy[8]. Proliferative diabetic retinopathy (PDR) is predominantly responsible for severe vision loss (Best corrected visual acuity of 5/200 or worse) associated with diabetic eye illness, whereas diabetic macular edema is primarily responsible for moderate vision loss (doubling of the viewing angle)[9].

A novel medical diagnostic imaging technique called optical coherence tomography (OCT) can image biological tissues cross-sectionally or tomographically with micrometre resolution[10]. In ophthalmology,

DOI: 10.69605/ijlbpr_13.10.2024.87

optical coherence tomography, or OCT, is now considered as standard diagnostic modality. With a micrometre scale-depth resolution, it offers three dimensional and cross-sectional imaging of the optic nerve head, retina, and anterior segment[11].

Compared to funduscopic or photographic examinations, OCT is more sensitive and can identify structural macular alterations and much early symptoms. For this reason, it may be a useful technique. When using slit lamp bio-microscopy and ophthalmoscopy, shallow changes in retinal thickness of less than 100 microns may not be apparent; however, OCT makes this plainly observable[12]. By assessing macular thickening both before and after laser therapy, OCT is useful in the monitoring and treatment of diabetic retinopathy as well as in tracking the effectiveness of therapeutic interventions.

Long-term exposure to hyperglycaemic levels causes escalating complications with diabetes mellitus (DM), affecting insulin metabolism as well as biological macromolecules such proteins, lipids, carbohydrates, and nucleic acids[13]. Measurements of haemoglobin A1c (HbA1c) on a regular basis can provide insight into the management of hyperglycemia over the long run. Diabetes management and consequences studies have demonstrated that intensive glycaemic control effectively reduces the incidence rate of formation and progression of diabetic retinopathy in both type 1 and type 2 diabetes mellitus[14].

Patients in poor nations such as India typically present later in the disease course, primarily as a result of ignorance. Therefore, early identification of macular alterations in diabetic patients' eyes prior to other clinical indications of retinopathy would be beneficial in starting DR treatment early. By comparing macular thickness in diabetic individuals with or without diabetic retinopathy with changes in Hba1c, this study intends to assess early macular changes in people with diabetes who do not yet have clinical diabetic retinopathy.

MATERIAL AND METHODS

The present cross sectional study was conducted among 50 patients with signs and symptoms of diabetic retinopathy who were attending the Outpatient Department of Ophthalmology at Maharishi Markandeshwar Institute Of Medical Science And Research, Mullana, Ambala, Haryana during January 2023-March 2024.

Inclusion criteria

1. Patients more than 18 years of age
2. Patients of both genders having diabetes with and without Retinopathy
3. Patients prepared to sign consent to participate in the study.

Exclusion criteria

1. Patients less than 18 years of age
2. Patients of other vascular retinopathies
3. Patient not willing to be a part of study
4. Patients who have undergone any intraocular procedure (ppv, intra vitreal injections, cataract surgery, prp etc.)
5. Patients with dense cataracts and corneal opacities (centre involving)

Methods

a. Prior to their admission for the trial, every patient signed a consent form in their native tongue.
b. Patient data was gathered through a piloted proforma, fulfilling the study's objectives through in-person interviews and clinical examinations.
c. The patients were eliminated based on the given data.
d. The study included only patients who met the inclusion and exclusion criteria.
e. A comprehensive clinical history of the patient, including the length of the complaint, was obtained once the patient was chosen for the study.
f. A thorough history was taken, and the patients were then clinically examined in accordance with departmental protocols.
g. The patients' visual acuity was assessed using the Snellen chart. Prior to a thorough examination with a slit lamp, the patient was checked under a torch light.
h. All patients had their intraocular pressure measured. Following this, all patients had a fundus examination using a direct and indirect ophthalmoscope, and the results were recorded.
i. All patients underwent SD OCT, and central macular thickness was assessed regardless of the presence or absence of diabetic retinopathy (figure 1).

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Figure 1: OCT examination of the patient to check the Central Macular Thickness (CMT)

j. The HBA1C test was performed the same day as the ophthalmic examination, and its results were correlated with the central macular thickness. After data was gathered, statistical analysis was performed.

Statistical analysis

A statistician assisted in tabulating the data that was gathered in an excel spreadsheet for statistical analysis, the means and standard deviations of each measurement group were utilised (SPSS 25.00 for Windows; SPSS Inc., Chicago, USA). Anova and the t test were used to calculate the difference between the two groups. A significant threshold of $p < 0.05$ was established.

RESULTS

Male and female comprised of 66% and 34% of the study subjects. Hence there was male dominancy in this study. Maximum subjects were from age group of >60 years (52%) followed by 41-60 years (36%). Only 12% of the subjects were having age between 18-40 years. Mean duration of diabetes was 15.73±6.41 years. Mean HbA1c (%) among the study subjects was 8.29±1.38 with more than 46% of the subjects having HbA1c (%) of >8 (table 1).

Table 1: Gender, age, duration of diabetes and HbA1c distribution among the study subjects

Gender	**N**	**%**
Male	33	66
Female	17	34
Age Group (in years)		
18-40	6	12
41-60	18	36
>60	26	52
Duration of diabetes (in years)		
5-10	9	18
11-15	19	38

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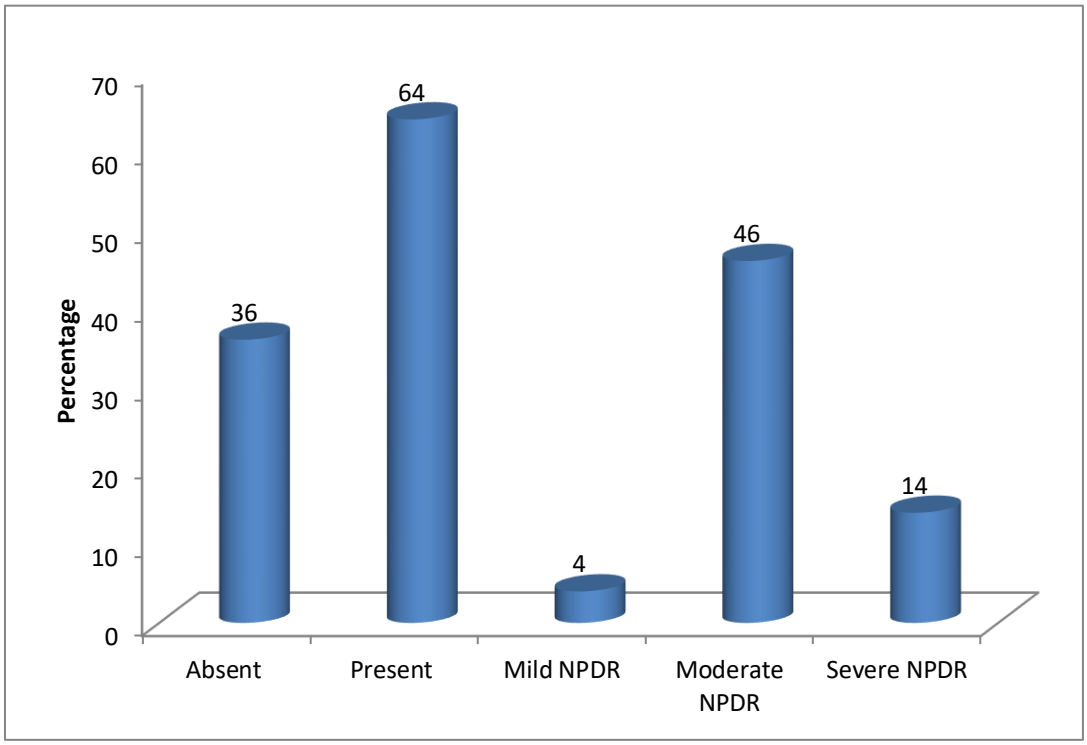
>15	22	44
Mean±SD	15.73±6.41	
HbA1c		
<7	8	16
7-8	19	38
>8	23	46
Total	50	100
Mean±SD	8.29±1.38	

Diabetic retinopathy was present in 64% of the subjects, out of which mild, moderate and severe NPDR was revealed in 4%, 46% and 14% of the subjects respectively (graph 1).



Graph 1: Distribution of study subjects according to DR

Mean CMT among the subjects having no DR, mild NPDR, moderate NPDR and severe NPDR was 247.08±13.99, 283.11±22.84 and 289.4±17.82 respectively. Hence CMT increases with increase in severity of DR with statistically significant difference as $p<0.05$ (table 2).

Table 2: Central Macular Thickness and Degree of DR

DR	Mean CMT	SD	p value
No DR	192.16	10.78	0.004*
Mild NPDR	247.08	13.99	
Moderate NPDR	283.11	22.84	
Severe NPDR	289.4	17.82	

*: statistically significant

Mean CMT was found minimum among subjects with HbA1c <7 and maximum in subjects with HbA1c>8. Hence CMT increases with increase in HbA1c with statistically significant difference as $p<0.05$ (table 3).

Table 3: Central Macular Thickness and HbA1c

HbA1c	Mean CMT	SD	p value
<7	199.9	14.68	0.002*
7-8	253.15	19.04	
>8	302.7	16.52	

*: statistically significant

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Mean CMT was found maximum in subjects with diabetes more than 15 years followed by 11-15 years. Hence CMT increases with duration of diabetes but is not statistically significant as p>0.05 (table 4).

Table 4: Central Macular Thickness and Duration of diabetes

Duration of diabetes (in years)	Mean CMT	SD	p value
5-10	211.89	16.01	0.09
11-15	260.23	18.36	
>15	295.71	17.08	

DISCUSSION

It has been suggested that slight alterations in retinal thickness may place even prior to the onset of clinically severe ME, which may negatively impact visual acuity[15]. Therefore, by comparing macular thickness in patients with diabetic retinopathy, this study was carried out to examine early retinal alterations in patients with diabetes who do not yet have clinical diabetic retinopathy and correlate it with Hba1c levels.

This study had found a male-dominated population. Larsson LI et al.'s[16] and Sachdev N and Sahni A[17] too in their studies revealed male dominancy.

The majority of participants (52%) came from the over-60 age group, with 36% coming from the 41–60 age range. The average age of the research volunteers in a study by Sachdev N and Sahni A[17] was 55.6 ± 7.4 years. Similar age distributions were found in the studies conducted by Vrushabh Ghanshyam Malani et al[15] and Ivone Caroline et al[18].

Sixty-four percent of the participants had diabetic retinopathy, of which four percent had mild, fourty six percent had moderate, and fourteen percent had severe NPDR. According to Al-Bdour MD et al[19], 64.1% of patients had diabetic retinopathy in some capacity; of them, 30.8% had maculopathy, 54.8% had NPDR, and 9.3% had PDR. 33.2% of patients had mild NPDR, 35.6% had moderate NPDR, 10% had severe NPDR, and 21.1% had PDR in the study by Alattas K et al[20].

The individuals with mild NPDR, moderate NPDR, severe NPDR, and no DR had mean CMT values of 247.08±13.99, 283.11±22.84, and 289.4±17.82, 192.16±10.78 respectively. As a result, CMT rises as DR severity increases, with a statistically significant difference at p<0.05. Similar to the current study, Cho A et al[21] found that in diabetic individuals, moving from the no DR to the NPDR stage was linked to increased HbA1c levels. In their study, Vrushabh Ghanshyam Malani et al[15] reported that the proliferative DR and severe nonproliferative DR groups exhibited greater values in the correlation between DR grades and subfield thickness and overall macular volume. This study and this one are comparable.

According to Oshitari et al., the central macula of patients with diabetic retinopathy was noticeably thinner in the early stages compared to controls. This was clarified by the neurological abnormalities brought on by diabetes, such as axonal degradation and retinal ganglion cell loss. It was postulated that in individuals with early-stage diabetes, these neuronal changes occurred prior to vascular problems, hence explaining the reduced macula in diabetic patients. The mean CMT was observed to be gradually rising with increasing DR stage when compared across DR subgroups. Changes in the peri-foveal and macular capillaries' vascular permeability in diabetic eyes can account for the increased macular thickness and steadily worsening retinopathy[22].

The mean CMT was observed to be highest in patients with a HbA1c >8 and lowest in subjects with a HbA1c<7. With a statistically significant difference as p<0.05, CMT rises as HbA1c rises in this study. One significant modifiable risk factor that can impact the course of diabetic retinopathy (DR) and vision loss is glycated haemoglobin (HbA1c). Additionally, a favourable connection between HbA1c and macular thickness and volume was found by Vrushabh Ghanshyam Malani et al.[15]

Long-term hyperglycemia can be effectively monitored with glycosylated haemoglobin, which is an effective metric. It has been noted that a change in OCT measures greater than 10% of the baseline thickness is likely to represent a real change in macular thickness[23-24]. This implies that retinal thickness and function are significantly impacted by effective glycemic control. Uncontrolled HbA1c levels can cause microvascular damage that breaks down the inner Blood Retinal Barrier (BRB), which thickens the macular pigment. A study including 124 patients revealed an inverse relationship between HbA1c levels and central macular thickness in ME patients (r=-0.374, p=0.005). This relationship held true even after controlling for age, sex, the severity of DR, and other metabolic variables (p=0.002)[15].

But according to Jiang J et al[25], only the temporal perifoveal thickness showed a negative connection with the HbA1c level, suggesting that higher HbA1c levels were a factor in the reduction of retinal thickness. Compared to controls, patients with subclinical ME eventually advance to clinically significant ME; the odds of progression rise by 15% for every 10 μm increase in central subfield retinal thickness. As a result, diabetics need to be closely watched in order to identify vision-threatening ME early on and take appropriate action (Bhavsar KV et al[26]).

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Limitation(S) and Recommendations

According to the current study's observations, there may be a higher risk of DME associated with high HbA1c readings. The study's limitation, though, was that it did not evaluate additional risk factors, including nephropathy, insulin use, elevated diastolic blood pressure, and lipid dysfunction. Although studies have established a higher risk of diabetic macular edema with few of the above factors taken in isolation but more comprehensive studies need to be undertaken to fully understand the various complex underlying mechanisms.

CONCLUSION

There was a strong positive association found between the levels of CMT and HbA1c. Increased retinal thickness was seen in patients with HbA1c > 8% and longer-term diabetes, as well as in patients with proliferative and severe non proliferative DR. There is proof that even in the absence of diabetic ME, there is a rise in macular thickness and volume. Therefore, it's imperative to maintain stringent glucose control and routinely check on diabetic individuals in order to stop macular function from declining even before ME is identified clinically. Further investigations are necessary to comprehend the alterations in hemodynamics at the macula.

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