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Original Article

Relationship Between Glycosylated Hemoglobin Levels and Contrast Sensitivity in People with Type 2 Diabetes Mellitus Without Diabetic Retinopathy

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Abstract

Objectives: This study aimed to investigate the relationship between glycosylated hemoglobin (HbA1c) value and contrast sensitivity (CS) in people with Type 2 diabetes mellitus (T2DM) and no diabetic retinopathy (DR) changes.

Materials and Methods: This cross-sectional study was conducted in the endocrinology department of a tertiary hospital and included 120 participants aged 30-40 years with T2DM without DR and with visual acuity of 6/6 in both eyes. Lea CS charts with one symbol size (10M) were used to measure CS. The relationship between HbA1c value and CS was calculated using linear regression analysis.

Results: Of 120 participants with T2DM without DR, 83 (69.2%) were female. Sixty-four participants (53.3%) were in the 36-40 years age group. Mean known duration of diabetes was 3.3±1.65 years. Mean HbA1c value was 10.46±1.48%, with three-fourths of participants having an HbA1c value greater than 8%. Mean CS measured at distances of 1 meter, 2 meters, 3 meters and 4 meters were 164.75±21.12, 122.0±45.08, 93.0±45.37, and 58.67±20.04, respectively. Most participants (n=113, 94.2%) had normal CS (170 at 0.6% contrast) tested at 1 meter. More than half (53.3%) of the participants had reduced CS (40 at 2.5% contrast) at 4 meters. CS measured at 3 meters showed a strong negative correlation with duration of diabetes ($r=-0.855$, $p<0.001$; $R^2=0.731$) and HbA1c values ($r=-0.865$; $p<0.001$; $R^2=0.747$).

Conclusion: CS was inversely associated with diabetes duration and HbA1c values in people with T2DM before any defect in visual acuity or clinical evidence of DR.

Keywords: Contrast sensitivity, HbA1c values, Type 2 diabetes mellitus, diabetic retinopathy

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Introduction

Diabetic retinopathy (DR) is an ocular complication of diabetes mellitus (DM) that causes retinal damage leading to vision impairment and blindness.[1] Vision loss can be prevented in more than 90% of people with diabetes if DR is diagnosed and managed at early stage.[2] Complications from diabetes are strongly related to the type and duration of diabetes and to glycemic control.[3,4] Though vision loss due to DR is preventable through better glycemic control, the prevalence of blindness and vision impairment due to DR is rising in developed and developing countries due to continuous increase in the number of people with diabetes.[5,6]

The prevalence of any type of DR among people with diabetes ranges from 17-22% in India, 17-26% in Pakistan, and 37% in Iran.[7,8,9,10,11] Up to 21% of people with type 2 DM (T2DM) develop DR before diabetes is diagnosed.[12] It is reported that in India, 45% of people with diabetes visit eye clinics for their first eye examination after loss of their vision.[13] Though it is evident that changes in the retinal neurons may be present in people with diabetes without any symptoms of DR, considerable delays in the early detection and treatment of DR are reported.[12,13,14] There is a need for cost-effective testing for people with diabetes to identify people with high risk of DR before the appearance of clinical signs of diabetic eye disease.

In people with DM, the normal function of the retinal neurons is affected by diabetes, and retinal neuronal damage is an early stage of the pathogenesis of DR.[15,16] Visual acuity may not be reduced until 55% of all neuro-retinal channels are affected.[17] One of the functions of the retina is contrast sensitivity (CS), the capacity of the neurological and optical processes to perceive dissimilarity between objects and their surroundings.[18] CS reflects the quality of central vision and may be decreased in people with diabetes despite having normal visual acuity and no signs of DR.[19]

As vision loss caused by DR is irreversible, predictive methods are important to prevent vision loss due to DR through timely intervention.[4] Early evaluation of changes in CS in people with diabetes could assist in the early detection of DR. An understanding of the relationships between glycosylated hemoglobin (HbA1c) values, diabetes duration, and CS may provide information about the usefulness of evaluating CS as a screening tool and predictive measures of retinal dysfunction in people with diabetes. This study aimed to investigate the correlation of HbA1c level and CS in people with T2DM without DR.

Materials and Methods

The study was approved by the Institutional Research and Ethics Committee. Signed inform consent was obtained from each participant. All procedures performed in the study were in accordance with the Declaration of Helsinki.

This cross-sectional prospective study was carried out on participants with T2DM, without DR changes, presenting to the Endocrinology out-patients department in Lady Reading Hospital (a tertiary care hospital) in Peshawar, Pakistan. Using a consecutive sampling method, a total of 120 participants examined from August 15 to November 15, 2019 were included in the study. Inclusion criteria were having T2DM with no signs of DR, age 30-40 years, and best corrected visual acuity of 6/6 in both eyes. Patients over the age of 40 were excluded to avoid age-related changes in CS.[20] Other exclusion criteria were a history of any other eye disease affecting visual acuity and/or CS (e.g., cataract, corneal opacities), refractive errors greater than -3.00 diopters sphere and/or more than ±1.00 diopter cylinder, and mental disability.

Duration of diabetes was determined based on the date of the first blood test that detected diabetes. People with fasting plasma glucose equal or higher than 7.0 mmol/L (126 mg/dL) or 2-h plasma glucose equal or higher than 11.1 mmol/L (200 mg/dL) were included in the study.[21] HbA1c level was measured for each participant at the same visit in the laboratory in the same hospital. HbA1c is a test for people with T2DM that can determine their average blood glucose levels over the previous 3 months.[21]

All participants underwent a detailed ophthalmological examination in the department of ophthalmology in the same hospital. Anterior segment and fundus examination was performed to exclude patients with DR, lens opacification, or any other ocular pathology which reduces visual acuity or CS. The visual acuity of each participant was recorded using a Snellen chart with standard illumination for each eye. Refraction and assessment of CS was performed on each participant by a senior optometrist. Each participant was required to wear their prescribed distance correction before measuring CS.

The contrast of the symbol was defined using the Michelson formula:[22]

$$Contrast = \frac{(Lmax - Lmin)}{(Lmax + Lmin)}$$

Where Lmax equals the luminance on the lighter surface, measured as candelas per square meter, and Lmin equals the luminance on the darker surface.

The ratio is multiplied by 100 and the contrast is expressed as a percentage. CS is expressed as inverse of the contrast. For instance, if the lowest contrast perceived by a person is 0.6%, their CS is 100/0.6=170. Similarly, if the lowest contrast discernable by a person is 1.25%, their CS is 100/1.25=80.

Lea contrast sensitivity charts with one symbol size, 10M, were used. Lea symbols were selected due to the low literacy rate in our society. As most of the participants were illiterate, it was easy for them to match symbols on Lea CS chart. The 10M size was considered appropriate for this study because at the most common testing distance of 1 meter, it corresponds to a visual acuity of 0.1 (20/200, 6/60); at 2 meters, it corresponds to a visual acuity of 0.2 (20/100, 6/30); at 4 meters, it corresponds to a visual acuity 0.4 (20/50, 6/15).[22] The test consists of four shapes: pentagon, square, circle, and apple. The contrast level of the test lines on the Lea contrast sensitivity test chart are 0.6%, 1.25%, 2.5%, 5%, 10%, and 25%. Details about CS on the Lea CS chart is as follows:[22]

Contrast 0.6% = CS 170 (normal CS)
Contrast 1.25% = CS 80 (reduced CS)
Contrast 2.5% = CS 40
Contrast 5% = CS 20
Contrast 10% = CS 10
Contrast 25% = CS 4

CS was measured at four different distances (1, 2, 3, and 4 meters) using standardized room lighting. Each participant was asked to match the shapes on each contrast level and was recorded for the specified four distances for each eye. Patients with CS 170 (who can discern all symbols at 0.6% contrast) were considered normal CS and the patients who could not discern at 0.6% contrast but at 1.25% or higher contrast were classified as having reduced CS.[22]

Statistical Analysis

Statistical analyses of the data were performed using the statistical software SPSS for Windows version 19 (IBM Corp, Armonk, NY, USA). Demographic characteristics were analyzed using descriptive statistics (frequency and percentage). Quantitative variables were expressed as mean ± standard deviation. The relationship between HbA1c value and CS was calculated using Pearson correlation. Taking CS as a dependent variable, linear regression analysis was conducted to measure the strength of the linear relationship between HbA1c values and CS. Statistical significance was accepted at $p<0.05$ within a 95% confident interval (CI).

Results

Of the total 120 participants with T2DM without any DR changes, 37 (30.83%) were male and 83 (69.17%) were female. The male-to-female ratio was 1:2.3. More than half of the participants (n=64, 53.33%) were in the 36-40 years age group. The mean known duration of diabetes was 3.3±1.65 years (range: 0.5-5 years). Most of the participants had a duration of 4-5 years. The mean HbA1c value was 10.46±1.48%, with three-fourths of participants having an HbA1c value greater than 8%. The demographic characteristics and disease profile of the participants are shown in Table 1.

In all participants, CS decreased at greater distance. Mean CS values measured at distances of 1 meter, 2 meters, 3 meters, and 4 meters were 164.75±21.12, 122.0±45.08, 93.0±45.37, and 58.67±20.04, respectively. At 1 meter, 113 participants (94.17%) had normal CS (170, 0.6% contrast) and 7 (5.83%) had reduced CS (80, 1.2% contrast). None of the participants had normal CS (170, 0.6% contrast) at 4 meters. In 64 participants (53.33%), CS fell to 40 (2.5% contrast) at 4 meters. Of 120 participants, none had CS lower than 40 (2.5.% contrast). The results of CS measurement at 1, 2, 3, and 4 meters are given in Table 2.

There was no significant association between the participants' gender and their CS assessed at 0.6% and 1.2% contrast at all distances. Table 3 shows details regarding the association of CS with gender.

Participants in the 36-40 years age group had a higher frequency of reduced CS than the younger age group at all distances. Participants in the 30-35 years age group had normal CS at 1 meter but their CS declined at increasing distances, as shown in Table 4. The difference in CS between the two age groups was statistically significant only at a distance of 1 meter (p=0.01). At longer distances, the difference in CS between the two age groups was not statistically significant, indicating that both groups had a decline in CS as the distance increased.

Pearson correlation analysis was conducted to examine the relationship of diabetes duration and HbA1c values with CS

Table 1. Demographic characteristics and disease profile (n=120)

	Characteristics	Frequency, n (%)
Gender	Male	37 (30.83)
	Female	83 (69.17)
Age	30-35 years	56 (46.67)
	36-40 years	64 (53.33)
Duration of diabetes	<1 year	16 (13.33)
	2-3 years	16 (13.33)
	4-5 years	48 (40.0)
	>5 years	40 (33.33)
HbA1c	<8%	28 (23.33)
	≥8%	92 (76.67)

Table 2. Contrast sensitivity measured at four different distances

Contrast sensitivity (% contrast)	1 meter n (%)	2 meters n (%)	3 meters n (%)	4 meters n (%)
170 (0.6% contrast)	113 (94.17)	56 (46.67)	28 (23.33)	0
80 (1.2% contrast)	7 (5.83)	64 (53.33)	68 (56.67)	56 (46.67)
40 (2.5% contrast)	0	0	24 (20)	64 (53.33)
Total	120	120	120	120

Table 3. Association between gender and contrast sensitivity (CS) measured at four different distances

Distance	Gender	Normal CS (170, 0.6% contrast) n (%)	Reduced CS (80, 1.2% contrast) n (%)	P value
1 meter	Male	35 (94.59)	2 (5.41)	0.89
	Female	78 (93.98)	5 (6.02)	
2 meters	Male	12 (32.43)	25 (67.57)	0.35
	Female	44 (53.01)	39 (46.99)	
3 meters	Male	7 (18.92)	30 (81.08)	0.45
	Female	21 (25.30)	62 (74.70)	
4 meters	Male	16 (43.24)	21 (56.76)	0.616
	Female	40 (48.19)	43 (51.81)	

at different distances. Considering CS of 170 (0.6% contrast) normal and CS of 80 (1.2% contrast) as reduced, the results showed that duration of diabetes and HbA1c values were strong negative correlates of CS in people with T2DM, as shown in Table 5. People who had diabetes for more than 5 years showed more reduction in CS. In addition, CS assessed at 3 meters was more strongly negative correlated with HbA1c values (r=-0.865, p<0.001) than CS measured at 1 meter (r=-0.287, p<0.001) and 2 meters (r=-0.768, p<0.001). Though mean CS assessed at 4 meters was significantly lower than mean CS assessed at 3 meters (58.67±20.04 vs. 93.0±45.37; p<0.001), the negative correlation of HbA1c with CS was slightly stronger when CS was assessed at 3 meters than at 4 meters (r=-0.865 vs. r=-0.813). These findings indicate that CS measured at 3 meters reveals much more about the relationship between HbA1c levels and CS than when measured at distances of 1 or 2 meters.

A bivariate regression analysis was conducted to examine how well HbA1c level could predict reduction in CS. Linear regression analysis showed that Hba1c level accounted for 74.9% of the variance in CS measured at a distance of 3 meters. There was a statistically significant relationship between HbA1c level and CS (p<0.001). The 95% confidence interval for the slope to predict decline in CS from HbA1c level ranged from -23.77 to -29.38. Therefore, for each unit of increase in HbA1c, CS decreased by 23.77 to 29.38 points. Similarly, linear regression indicated that diabetes duration was a strong negative correlate of CS at 3 meters (r=-0.855, p<0.001; R^2= 0.731; CI: -26.05 to -20.86).

Table 4. Association between age and contrast sensitivity (CS) measured at four different distances

Distance	Age (years)	Normal CS (170, 0.6% contrast) n (%)	Reduced CS (80, 1.2% contrast) n (%)	P-value
1 meter	30-35	56 (100)	0	0.01
	36-40	57 (89.06)	7 (10.94)	
2 meters	30-35	26 (46.43)	30 (53.57)	0.96
	36-40	30 (46.88)	34 (53.13)	
3 meters	30-35	16 (28.57)	40 (71.43)	0.20
	36-40	12 (18.75)	52 (81.25)	
4 meters	30-35	26 (46.43)	30 (53.57)	0.96
	36-40	30 (46.88)	34 (53.13)	

Table 5. Correlation of duration of diabetes and HbA1c values with contrast sensitivity

		Contrast sensitivity			
		1 meter	2 meters	3 meters	4 meters
Diabetes duration	rho	-0.257	-0.779	-0.855	-0.779
	p	0.002	<0.001	<0.001	<0.001
HbA1c value	rho	-0.287	-0.786	-0.865	-0.810
	p	<0.001	<0.001	<0.001	<0.001

Discussion

The results of this study demonstrated a statistically significant negative correlation between HbA1c values and CS (p<0.001). CS was affected earlier than any defect in visual acuity or manifestation of DR in people with diabetes. Our findings also indicated a significant association between CS and the duration of diabetes. People having diabetes for more than 5 years showed more reduction in CS. Additionally, reductions in CS were more pronounced when measured at a distance of 3 meters as compared to 1 meter.

We observed a decline in CS with increasing HbA1c values in this study. A similar association between HbA1c values and CS in people with diabetes has been reported in other studies.[23,24,25] Our study shows that people with diabetes who are able to read the 6/6 line on the Snellen chart may have reduced CS despite visual acuity in the normal range. These results are consistent with prior reports indicating that people with diabetes may experience a decline in CS even with no clinical signs of DR.[26,27] These findings suggest that higher HbA1c levels may affect retinal neuronal function in people with diabetes, and previous research has shown that damage to retinal neurons could precede DR.[16,28,29,30] Assessing CS in diabetic people with increased HbA1c values could aid in the monitoring of diabetes-related changes in retinal function.

Complications of diabetes are strongly associated with the duration of diabetes.[24] All 7 participants in this study who showed reduced CS even at a distance of 1 meter had diabetes for at least 5 years. Our results also indicated that participants with diabetes duration of less than 5 years but HbA1c level of 8% or greater had normal CS at 1 meter but reduced CS at longer distances. Similarly, participants aged 30 to 35 years had normal CS at 1 meter and reduced CS at increasing distance, indicating that CS at 3 meters may provide more information about the relationship between CS and HbA1c values than CS assessed at closer distances. These findings suggest that routine assessment of CS in people with a diabetes duration of 5 years or more and/or HbA1c level higher than 8% could be used to complement other diagnostic procedures when assessing the progression of retinal neuronal damage.

Reduced CS in the participants in this study indicates early impairment of retinal function in people with diabetes, as reported in the literature.[15,16,31] Detection of these early changes in retinal function can help in the regular monitoring of retinal function in people with diabetes. Researchers have suggested various types of diagnostic tests that can be used to identify signs of early retinal dysfunction in people with diabetes before anatomical changes appear. They used various types of tests such as retinal sensitivity, optical coherence tomography angiography, and electroretinogram.[20,29,30] These tests are expensive, whereas letter/symbol CS charts are inexpensive and simple to use for screening purposes.

Study Limitations

The limitation of the current study was that we only recruited people with T2DM and did not include a nondiabetic control group. The reason for this was that in the hospital where the study was conducted, laboratory tests are free of charge for people with diabetes but not for nondiabetic people (controls). Due to a lack of funding to cover the cost of laboratory investigations for a control group, we enrolled only people with T2DM.

Conclusion

CS is reduced in association with increased HbA1c values in people with T2DM before any defect in visual acuity or clinical evidence of DR. Findings from this study suggest that periodic evaluation of CS in people with a diabetes duration of 5 years or more and/or HbA1c value greater than 8% could help in the early detection of changes in visual function in people with diabetes.

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Ethics

Ethics Committee Approval: Ethical approval was obtained from the Institutional Research and Ethics Committee.

Informed Consent: Obtained.

Peer-review: Externally and internally peer reviewed.

Authorship Contributions

Concept: M.S., A.F., Y.T., Design: M.S., A.F., Y.T., Data Collection or Processing: M.S., A.F., Y.T., Analysis or Interpretation: M.S., A.F., Y.T., Literature Search: M.S., A.F., Y.T., Writing: M.S., A.F., Y.T.

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