

Assessment of Color Vision in Diabetic Patients

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ABSTRACT

AIM: To assess the changes in color vision in diabetic patients in different stages of diabetic retinopathy compared to healthy individuals.

MATERIALS AND METHODS: This cross-sectional comparative study included sixty-eight eyes of 40 diabetic patients, divided into four subgroups (10 patients / group) at different stages of diabetic retinopathy (Eighteen of them had maculopathy) as well as 20 eyes of 10 healthy individuals as controls. Diabetic retinopathy and maculopathy were assessed clinically by direct and indirect fundus examination along with fluorescein fundus angiography, optical coherence tomography. Color vision was assessed quantitatively by Ishihara pseudo iso-chromatic plates test and qualitatively by Farnsworth D-15 test.

RESULTS: Only two control eyes (10%) failed the Ishihara pseudo iso-chromatic plates test, compared to 19 diabetic eyes (27.9%), 14 eyes (20.58%) were suspects. Also just two control eyes (10%) failed the Farnsworth d-15 test while 34 (50%) diabetic eyes failed the test showing; with Tritanopia was the most encountered color vision defect. We find that color vision defects also increases with increasing disease duration, severity of diabetic retinopathy, increased macular thickness and presence of maculopathy, while type of diabetes shows no significant effect.

CONCLUSION: Diabetes mellitus has a clear negative effect upon the color vision in both qualitative as assessed by Farnsworth FD-15 test and quantitative manner as assessed by Ishihara PIP test leading to loss of color vision perception with a varying degree in relation to the type of diabetes and disease duration from patients medical history, degree of retinopathy, presence of maculopathy by Fundus examination+FFA and the increased macular thickness by OCT when compared to normal healthy individuals.

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Key words: Color vision; Diabetes mellitus; Diabetic retinopathy; Maculopathy; Tritanopia; Ishihara PIP; Farnsworth d-15; Color vision defects; Screening

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INTRODUCTION

Diabetes mellitus is one of the most important factors of impaired vision. In 2013, 382 million people developed diabetes; 350 millions of them suffer from type II diabetes^[1,2,3].

Prevalence of diabetic retinopathy (DR) among diabetic patients aged 30 years and above is 54.65%, with the commonest presentation of diabetic retinopathy is mild non proliferative diabetic retinopathy (NPDR) followed by, moderate NPDR, NPDR with cystoid macular edema (CSME), severe NPDR, proliferative diabetic retinopathy (PDR) and finally PDR with CSME^[4].

Many studies reported that screening patients with type I diabetes showed that 56% of them have DR. With 11.2%, suffer sight threatening DR while in type II diabetes, 30.3% of patients have DR and only 2.9% are endangered with sight threatening diabetes^[5].

After initial reports of altered color vision in patients with

diabetes^[6], a number of experimental studies have been conducted to assess this association^[7,8].

This study was carried out in order to evaluate the effect of progression of DR upon the color vision in both quantitative and qualitative manner.

MATERIALS AND METHODS

Sixty-eight eyes of 40 diabetic patients, divided into four subgroups (10 patients/group) at different stages of diabetic retinopathy (Eighteen of them had maculopathy with exclusion of clinically significant macular edema) as well as 20 eyes of 10 healthy individuals as controls. Patients were recruited among those attending the ophthalmology outpatient clinic of Suez Canal University Hospital in Ismailia, Egypt. Diabetic adults aged between 25 and 70 years with clinically diagnosed DR, were included. (The sample size is calculated according to the following equation:

$$N = 2 (Z\alpha + Z\beta)^2 \times p \cdot q / (p^1 - p^2)^2 \quad [1]$$

Where:

n = number per group.

$Z\alpha$ = the value of standard normal distribution for type I error probability for sided test and equals 1.96.

$Z\beta$ = the value of standard normal for the desired statistical power 80% and equals 0.84.

$$p \cdot q = (P^1 + P^2)/2$$

$$q = 1 - P$$

p^1 = prevalence of color vision defects among male diabetic patients = 30 -80 %^[2,3,4,5].

p^2 = prevalence of color vision defects among male controls = 8%^[6].

N = 10 subjects per group.

Total N = 50 Subjects (40 patients in diabetic sub-groups and 10 normal individuals in control group).

For all patients we took detailed history regarding type, onset of diabetes and any visual complaints or previous eye procedures. Then patients were examined for their refraction via retinoscopy, Best corrected visual acuity (BCVA) with Snellen chart, IOP using Goldman applanation tonometer. Anterior segment examination was carried out through Haag Streit -type slit lamp and fundus was examined with +90 D lens as well as indirect ophthalmoscopy.

Patients with known history of congenital color vision defect, previous laser photocoagulation or intravitreal pharmacologic therapy; patients with aphakia, pseudophakia, corneal opacities, amblyopia and clinically significant macular edema were excluded as well as those with BCVA less than 6/60, myopic > 4 diopters or their intraocular pressure (IOP) more than 21 mm Hg.

To classify DR according to ETDRS, we performed color fundus photography and fluorescein angiography for patients with clinical findings of DR. In addition, we utilized spectral domain OCT (Carl Zeiss Meditec, Jena, Germany) for measuring central macular thickness.

Ishihara Pseudo-iso-chromatic plate test was used as a quantitative test for detection of defective color vision test results analyzed as follows:

Plates 1- 15 determine the normality or defectiveness of color vision.

If 4 or less plates are red wrong, colour vision is regarded normal.

If 5-7 plates are red wrong. Patient is a suspect of colour vision deficiency.

If 8 or more plates are red wrong, colour vision is regarded deficient, while Farnthsworth D-15 test was the qualitative test for detection of the type of the color vision deficiency through analysis

of the caps arrangement as follows:

Normal result – No cross-lines.

Protanope – cross-lines parallel to protan axis.

Deutanope – Cross-lines parallel to Deutan axis.

Tritanope – Cross-lines parallel to tritan axis.

Non specific colour vision defect – cross-lines does not obey any axis.

Ethical approval was acquired from the Suez Canal University research ethics committee. An informed consent was taken from every patient participating in the study after complete and detailed discussion of risk and benefits of his/her inclusion in the study in accordance to the declaration of Helsinki.

Data were analyzed with SPSS version 16. A *p* value of <0.05 was considered statistically significant. The normality of data was first tested with one-sample Kolmogorov-Smirnov test.

RESULTS

Diabetic patients in the study had ages between 35 to 72 years, with a mean of 55.5±9.49 years, while controls ranging from 45 to 65 years, with a mean of 54.2±6.59 years with a *p* value of 0.565. 39 (57.4%) were of type II diabetes mellitus. The mean duration of diabetes mellitus was 11.28±4.35 year ranging from 5 to 22 years. Average macular thickness of diabetic patients was 230.71±28.06 μm with a ranging from 115 to 312 μm; with only 26.5% had maculopathy. In the Ishihara pseudo iso-chromatic plates test; only 51% of diabetic patients passed the test, 28% failed and the remaining 21% were suspects, with gradual increase in deficiencies with the progression of DR. In contrary; 90% of controls passed and only 10% (Table 1). Qualitative color assessment showed that 10% of controls failed the Farnsworth D-15 test due to Protanopia, while 50% of the diabetics failed the test, with variable dyschromatopsia mainly Tritanopia and Deutanopia (Tables 2 and 3). The stratification of color vision deficiencies types in different stages of DR showed gradual increase in both Tritanopia and combined color vision deficiency in NPDR with progression of DR stages with total color blindness appearing only in PDR (Table 4). Duration of diabetes due to the relation between Duration and progression of DR and increased macular thickness (Table 5) with *p* value of ≤ 0.001* and presence of maculopathy (Table 6) with a *P* value of 0.001* were found to increase the presence of color vision defects; type of diabetes had no clear effect on color vision (Table 7).

DISCUSSION

Diabetic retinopathy is a potentially sight threatening disease and a major cause of blindness in patients under the age of 60 years. The highly demanding work environment now days makes normal color vision an increasingly essential asset. The increase in diabetes incidence in developing countries, with its possible negative impact on color vision may have its sequel on labor force and daily activities and represents a strong socioeconomic burden. This study was conducted for better understanding for diabetic associated effect upon color vision. Patients were recruited above age of 30 years to enable better correlation to diabetes duration effect upon color vision deficiency as well as the effect of aging as did Lakowski et al and Lombrial et al in their studies^[15,16].

The mean duration of diabetes mellitus was 11.28±4.35 SD year ranging from 5 to 22 years which was longer than the group studied by Klein *et al* with average duration of 7.45 years^[17].

Table 1 Results of Ishihara pseudo iso-Chromatic plates Test with DR stratification.

Item	Control (n=20)		Mild NPDR (n=17)		Moderate NPDR (n=18)		Severe NPDR (n=16)		PDR (n=17)	
	No	%	No	%	No	%	No	%	No	%
Ishihara pseudo iso- chromatic plates										
Pass	18	90	11	64.7	11	61.1	9	56.2	4	23.5
Failed	2	10	3	17.6	3	16.7	5	31.2	8	47.1
Suspect	0	0	3	17.6	4	22.2	2	12.5	5	29.4
X ²	21.67									
p-value	0.008*									

NPDR: Non proliferative diabetic retinopathy; PDR: proliferative diabetic retinopathy; * Statistically significant results.

Table 2 Comparing the Colour vision deficiency types between the control and the diabetic group.

Item	Diabetics (n=68)		Control (n=20)		X ²	P-value
	No	%	No	%		
Color vision defect						
Non	34	50.0	18	90	14.15	0.015*
Tritan	13	19.1	0	0		
Deutan	3	4.4	0	0		
Combined	13	19.1	0	0		
Protan	3	4.4	2	10		
Total	2	2.9	0	0		

* Statistically significant results.

Table 3 Results of Farnsworth D-15 Test with DR stratification.

Item	Control (n=20)		Mild NPDR (n=17)		Moderate NPDR (n=18)		Severe NPDR (n=16)		PDR (n=17)	
	No	%	No	%	No	%	No	%	No	%
Farnsworth D-15 test										
Pass	18	90	11	64.7	10	55.6	7	43.8	6	35.3
Failed	2	10	6	35.3	8	44.4	9	56.2	11	64.7
X ²	13.75									
p-value	0.008*									

NPDR: Non proliferative diabetic retinopathy; PDR: proliferative diabetic retinopathy; * Statistically significant results.

Table 4 Color vision deficiency types in controls and Diabetics with DR stratification.

Item	Control (n=20)		Mild NPDR (n=17)		Moderate NPDR (n=18)		Severe NPDR (n=16)		PDR (n=17)	
	No	%	No	%	No	%	No	%	No	%
Color vision defect										
Non	18	90	11	64.7	10	55.6	7	43.8	6	35.3
TRITAN	0	0	3	17.6	3	16.7	4	25.0	3	17.6
DEUTAN	0	0	1	5.9	1	5.6	0	0	1	5.9
Combined	0	0	2	11.8	3	16.7	4	25.0	4	23.5
PROTAN	2	10	0	0	1	5.6	1	6.2	1	5.9
Total Color blindness	0	0	0	0	0	0	0	0	2	11.8
X ²	27.13									
p-value	0.132									

NPDR: Non proliferative diabetic retinopathy; PDR: proliferative diabetic retinopathy; * Statistically significant results.

Table 5 The relation between the macular thickness and the colour vision deficiency.

Macular thickness	Color vision defect		t-test	p
	Non	Yes		
Mean ± SD	216.35±25.62	245.06±22.75	4.885	≤0.001*
Min-Max	115-256	192-312		

* Statistically significant results.

Table 7 The comparative results of Ishihara pseudo iso-chromatic of the control group and the two types of diabetes mellitus.

Item	Control		IDDM		NIDDM		X ²	p
	No	%	No	%	No	%		
Pass	19	95	14	48.3	21	53.8	17.19	0.002*
Failed	1	5	6	20.7	13	33.3		
SUSPECT	0	0	9	31.0	5	12.8		

* Statistically significant results.

Table 6 Effect of maculopathy on the colour vision in diabetic patients.

Color vision defect	Maculopathy				X ²	p
	Yes		No			
	No	%	No	%		
No	3	16.7	31	62.0	10.88	0.001*
Yes	15	83.3	19	38.0		

* Statistically significant results.

As expected; DR severity increased with both age and duration of diabetes, and this was highly significant from statistical point of view ($P \leq 0.001$). This was documented by many previous studies^[18,19,20,21].

Among diabetics; only 51% passed 21% were suspects and 28% failed. This means that 49% of them were either defective or borderline defective color vision. Mäntyjärvi claimed 62% of diabetic patients got defective color vision the inequality may result from the sampling technique we used in the study intending to equally represent each DR stage equally to other groups while Mäntyjärvi minded the toll of DM with no special care for the stages of DR as we focused in our study^[22].

Ten percent of controls failed Ishihara test. This almost three folds the number reported by Khalaj *et al.* (3.49%) in his studies. The difference may be explained by the fact that Khalaj and his colleagues depended merely on history taking for diagnosing color deficiency while we examined our patients to confirm our findings^[23].

In this work; 10% of controls failed the Farnsworth D-15 test showing Protanopia, while 50% of diabetics did so. Fong^[13] reported similar results, others reported varying results as 30% Lombrial *et al.*^[11] 70% Lakowski *et al.*^[24] and 80% Roy *et al.*^[10], though the varying results they all agree upon the impact of diabetes upon the color vision and the variation is mostly because the varying sampling, inclusion and exclusion criteria, stage of retinopathy and maculopathy.

In this study we found that the most frequent color vision deficiency among diabetics was the Tritan deficiency 19.1%. Color deficiency in the form of Deutan and Protan were equal (3% each), combined color deficiency was found in 19.1% while total color blindness was responsible for 2.9%, showing no observable variations from most of the pre-mentioned studies. Different values yet same arrangement were noticed when comparing type 1 and type 2 diabetes and the presence and absence of maculopathy.

The quality of color vision defects in the diabetic acquired dyschromatopsia was the aim of several studies, Sadiqulla *et al.*^[25] reported a red- green loss pattern prevailing then total color blindness, Shin *et al.*^[26] reported a Blue-yellow loss pattern, the same reported by Patz *et al.* and Ma'ar *et al.*^[27,28] which was further explained by the psychophysical measurements which show that the three cone types red, green and blue are present in the approximate proportion 40:20:1, respectively, in the control retina and are randomly distributed in the cone matrix^[29], leading to early loss of blue color then combined Tritanopia and Deutanopia then Protanopia at last in contrary to congenital color vision deficiency pattern with Protanopia prevailing.

This study included both Type 1 and type 2 diabetes mellitus, while most studies were exclusively to type 1 diabetes only or type 2 diabetes as did Lakowski *et al.*^[15], Bresnick^[30] and Aspinall *et al.*^[12] Our results showed no statistically significant difference between type 1 and type 2 diabetes regarding their effect on color vision impairment. (The results about differences between type 1 and 2 DM were not found in this study) IDDM 48.3% passed and in NIDDM 53.8% (Table 7)

Regarding the different stages of retinopathy, Tritan deficiency was the most frequent, Protan and Deutan were less frequent. It was also found that with increasing severity of retinopathy there was a gradual increase in combined color deficiency while total color blindness was only present in the PDR. Same chronological relation was reported by Marré and Birch *et al.*^[31,32].

The average OCT measured macular thickness of the diabetic patients in this study was $230.71 \pm 28.06 \mu\text{m}$ and ranging from 115-312 μm , while Sadiqulla *et al.*^[25] reported an average of 276 μm

and range of 198-388 μm and Sasaki *et al.*^[33] reported an average of $273.7 \pm 17.8 \mu\text{m}$, Goeble *et al.*^[34] reported an average of 283 μm and Oshima^[35] reported an average of 283 μm . Lower value of the average macular thickness in our study could be due to the criteria of selection excluding diabetic patient with BCVA less than 6/60. Also, the methodology used by Sadiqulla^[25] to include the diabetic patients whom already diagnosed to suffer color vision deficiency which was reported to be correlated with increased average macular thickness on other hands almost all the studies including diabetic patients reported increase in average macular thickness when compared to normal individuals like the results of Goeble *et al.*^[34].

Macular thickness has shown a gradual yet non-significant increase in the stages of diabetic retinopathy as well as a weak positive correlation identified between the average macular thickness and the duration of diabetes which is also reported by Oshima *et al.*^[35] with no studies found to contradict this finding.

In this study we have concluded a highly statistical significance ($P \leq 0.001$) between the increase in macular thickness and in the deterioration of color vision, which is similar to the reports of Sadiqulla *et al.* and Shin *et al.*^[25,26].

In patients with diabetic maculopathy 83.3% have color vision deficiency, while in those free from maculopathy only 38% suffered color vision deficiency. Birch^[36] research raised the percentage to 90% and to even 100% by using the Birch Tritan plates, which explains the higher percentage due to the higher test sensitivity.

In conclusion diabetic retinopathy induce varying degree of color vision defects with a varying degree in relation to the type of diabetes, degree of retinopathy, the duration of illness, presence of maculopathy and the increased macular thickness when compared to normal healthy individuals.

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CONFLICT OF INTERESTS

The author has no conflicts of interest to declare.

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