Correlation of Color Vision Impairment and Capillary Blood Glucose in Diabetic Patients without Retinopathy vs. in those with Mild Non-Proliferative Diabetic Retinopathy

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ABSTRACT

Objective: To compare the frequency and severity of color vision defects between diabetes mellitus (DM) patients without retinopathy and those with mild non-proliferative diabetic retinopathy (NPDR), and to evaluate the relationship between these color vision defects and capillary blood glucose (CBG) levels.

Methods: This was a cross-sectional, hospital-based study conducted over a seven-month period at the Ophthalmology Outpatient Department of Cardinal Santos Medical Center. Thirty-five (35) DM patients (70 eyes) aged 50 to 75 years with best-corrected visual acuity of ≥20/50 and no more than mild NPDR were included. Patients with moderate or severe NPDR, macular edema, optic nerve pathology, or significant cataracts were excluded. All participants underwent visual acuity testing, fundus examination, and color vision assessment using the Ishihara pseudoisochromatic plates and Farnsworth D-15 tests conducted under standardized lighting conditions. CBG was measured using the finger-prick method. Main outcome measures included the proportion and type of color vision defects, their association with DR classification, and CBG levels. Statistical analyses included descriptive statistics, the Fisher exact test, the Mann-Whitney U test for the Farnsworth D-15 Color Confusion Index (CCI), and Spearman correlation between CBG and CCI.

Results: Tritan-type defects were the most common, accounting for 36.2%. Color vision defects were observed in 91.3% (64 eyes) of patients with no DR, while defects were seen in all eyes (100%) with mild NPDR (5 eyes). However, this difference was not statistically significant (p = 1.000). There was no significant correlation between CBG levels and color vision scores. Mean CCI scores were similar between groups (p = 0.394), indicating no substantial difference in defect severity.

Conclusions: Color vision defects may be more prevalent in early NPDR compared to no DR, but this difference was not significant in this sample. No correlation was found between CBG levels and color vision performance. Color vision testing may serve as a useful adjunctive screening tool for early diabetic retinal changes; however, further studies with larger sample sizes are necessary.

Keywords: Color vision defects; diabetic retinopathy; Farnsworth D-15 test; capillary blood glucose; tritan deficiency

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Diabetes mellitus (DM) is a growing global health concern, with projections indicating an increase in its prevalence over the coming decades. The Philippines is not spared in the increasing burden of this disease. The International Diabetes Federation (IDF) reported that one in five Filipinos have DM. Although not in the top ten countries with high DM prevalence rate, the Philippines was projected to rise to 9th place by 2030, with an estimated 7.8 million Filipinos affected.[1,2] This rise in diabetes prevalence has directly contributed to a corresponding rise in diabetic complications, in particular, diabetic retinopathy (DR), a leading cause of preventable blindness globally according to the National Eye Institute and Center for Disease Control and Prevention.[3,4]

In developing countries like the Philippines, limited access to eye care results in missed opportunities for early detection, timely treatment, and patient education, all of which contribute to accelerated progression of DR and increased risk of vision loss. DR is often asymptomatic in its early stages. Availability of easily accessible and affordable screening tests are critical to identify the disease is its early form. One potential screening tool that meets these criteria is color vision testing. Color vision tests have been shown to detect subclinical visual dysfunction in DM individuals before structural retinal changes become apparent.[5]

The Early Treatment Diabetic Retinopathy Study (ETDRS) highlighted that up to 50% of DM patients exhibited impaired hue discrimination, with tritan-type (blue-yellow) defects being most common.[6] Further studies have supported that color vision impairment correlates not only with disease duration but also with DR severity.[7] Gella *et al.* reported that color vision abnormalities detected with Farnsworth D-100 test were prevalent even in DM patients without retinopathy, suggesting the presence of early neurodegenerative changes in the retina.[8] These studies suggest that color vision testing can serve as a non-invasive and time-efficient screening method to detect early diabetic retinal dysfunction.

Additionally, reports have suggested a relationship between capillary blood glucose (CBG) levels and visual function abnormalities. Acute hyperglycemia has been shown to impair visual function, including contrast sensitivity and color vision, even prior to the onset of the clinical signs of DR.[9,10] Fluctuations in blood glucose levels may cause functional changes in the retina, highlighting the importance of measuring CBG levels when assessing visual changes in diabetics, regardless of the presence of DR. Incorporating CBG measurements may enhance the utility of color vision testing as a marker for early retinal dysfunction.

This study assessed the frequency and type of color vision defects among DM patients without DR and with mild NPDR. It also determined the relationship between CBG levels and color vision scores. Lastly, it explored the potential use of color vision testing with the Farnsworth D-15 as an early, adjunctive screening tool for DR.

METHODS

This was a single-center, hospital-based, cross-sectional study conducted from March to September 2013 at the Outpatient Department Ophthalmology Clinic of Cardinal Santos Medical Center, San Juan City, Metro Manila, Philippines. Patients with DM aged 50 to 75 years old, with BCVA of at least 20/50 in each eye were enrolled in the study in a consecutive manner. Patients with DR worse than mild, diabetic macular edema, glaucoma, optic neuropathy, optic neuritis, congenital color vision defects and uncontrolled hypertension were excluded from the study. Phakic patients with Lens Opacity Classification System III (LOCS) grading of nuclear opalescence and nuclear color (N) N4 or worse were also excluded.

All study participants underwent random CBG testing using the *OneTouch Select* blood glucose monitoring system (LifeScan, Milpitas, CA, 2012) on the same day as the eye examination.

Each study participant underwent a full ophthalmologic examination by two ophthalmologists (resident trainee and a consultant) which included: monocular visual acuity testing in distance and near using the Snellen chart and Jaeger chart, respectively and best-corrected visual acuity measurement in both far and near distance. Color vision testing was performed using the Ishihara pseudoisochromatic 16-color plates. Patients who made three mistakes or more in the Ishihara pseudoisochromatic 16-color plates were removed

from the study. The Ishihara test was performed first to exclude patients with preexisting color vision defects.

After completing the pseudoisochromatic test places, the patients underwent the Farnsworth D-15 color confusion test. Both color vision tests were both done monocularly, under illumination with an 80-watt fluorescent bulb at a distance of 30 cm with their subjective near refraction placed in a trial frame beginning with the right eye followed by the left eye. Both tests assessed color confusion, which identify individuals with red-green defects and those with protan-deutan anomalies.

The patients then underwent slit lamp biomicroscopy examination, applanation tonometry, and a dilated fundus examination by a retina specialist to assess DR status.

This study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki. Ethical approval was obtained from the institutional review board of the institution, and written informed consent was secured from all participants prior to enrollment.

Statistical Analysis

Microsoft Excel (Microsoft Corporation, USA) was used for data entry and figure and graph plotting. Statistical analysis was performed using the SPSS v.16 software (SPSS Inc, Chicago Il, USA). Descriptive statistics were used for reporting age, gender distribution, and types of color vision defects. Fisher exact test was used to compare the proportion of color vision defects between the "no DR" and "mild NPDR" groups.

For statistical analysis of the Farnsworth D-15 results, participants' qualitative answers were converted into numerical scores using the Color Confusion Index (CCI)[11]. The CCI is a quantitative measurement of the panel color vision tests results. It is the ratio of the total error scores of the subject over the total error scores color of normal trichromats. A person who does a perfect arrangement has a CCI of one.

The Mann–Whitney U test was used to compare the Farnsworth D-15 CCI scores between the "no DR" and "mild NPDR" groups. Lastly, Spearman correlation was used to assess the relationship between CBG levels and the Farnsworth D-15 scores.

RESULTS

Thirty-five (35) patients (70 eyes) with type 2 DM were included in the study. The mean age of participants was 61.4 years (range: 53–74, SD 53 yrs). Majority (31) was female (88.6%). There were 65 eyes without diabetic retinopathy (92.8%) and 5 eyes (7.2%) with mild NPDR. All eyes (70) had normal Ishihara color vision scores (100%)

Using the Farnworth D-15 test, 6 eyes (8.7%) had normal color vision, the rest (91.3%) had abnormal color vision. Among these, tritan-type (blue-yellow) color vision defect was the most common, accounting for 36.2 % of all abnormalities (25 eyes). The other types of defects are near normal 5.8% (4 eyes), mild defect 10.1% (7 eyes), medium defect 23.2% (16 eyes) and strong defect 11.6% (9 eyes) [**Figure 1**].

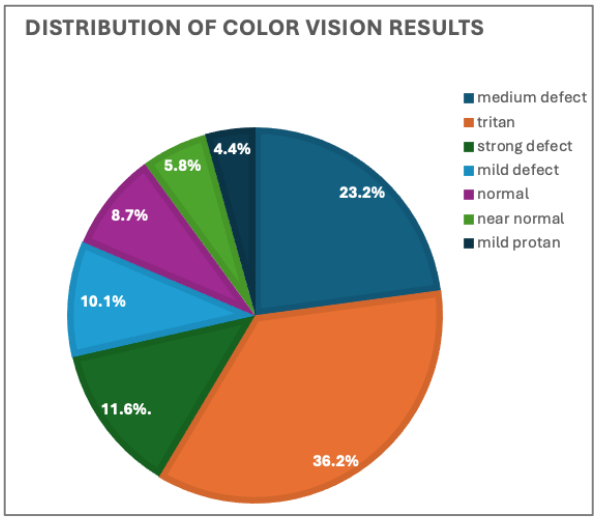

Figure 1. Pie chart illustrating the distribution of color vision anomalies among the study participants. Tritan was the predominant color defect (36.2%).

Color Vision Defects by DR Classification

When the eyes were categorized according to their DR grade, color vision scores using the Farnsworth D-15 test revealed that only 9.2% (6 eyes) had normal color vision in the "no DR" group.

The most common color defect identified in the "no DR" group was medium defect at 24.6% (16 eyes). This was followed by strong tritan (15.4%, 10 eyes), mild tritan (12.3%, 8 eyes), strong defect (10.8%, 7 eyes), medium tritan (9.2%, 6 eyes), mild defect (7.7%, 5 eyes), near normal (6.2%, 4 eyes), and mild protan (4.6%, 3 eyes).

In the "mild NPDR" group, comprising of five eyes, there was no predominant color vision defect type as two eyes showed mild defect, while another two eyes were mild tritans and one eye has strong defect.

The results showed no statistically significant association between retinopathy stage and the presence of color vision defects using the Fisher Exact Test (OR = ∞, p =1.00).

Farnsworth D-15 scores vs. Capillary Blood Glucose (CBG)

Figure 2 shows a scatter plot comparing CBG levels with the CCI. The trendline is flat; as the CBG levels increase, there is no change in color confusion index suggesting no correlation between the two. The Spearman rho's correlation also showed no statistically significant correlation between acute glycemic state and color vision performance (p = 0.516).

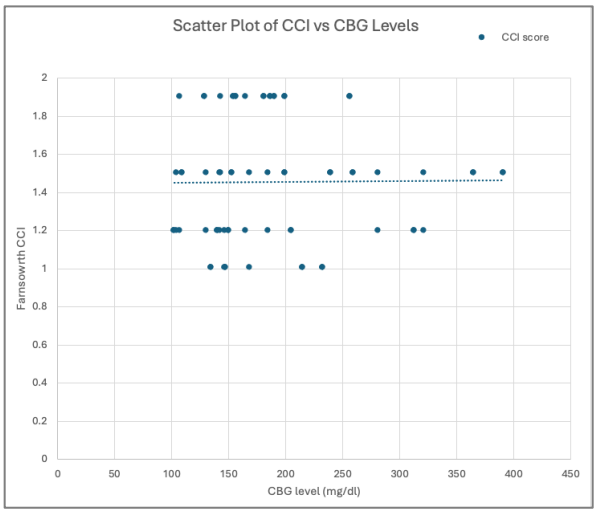

Figure 2. Scatter plot demonstrating a flat trendline suggesting no relationship between Farnsworth D-15 CCI and capillary blood glucose (CBG) levels.

A Mann-Whitney U test was conducted to compare Farnsworth D-15 CCI between patients with "no DR" and those with "mild NPDR". The results showed no statistically significant difference in the color confusion index between the two groups (p = 0.394). This suggests that early-stage diabetic retinopathy may not be associated with significant changes in color vision as measured by the Farnsworth D-15 test.

Table 1. DM Retinopathy Classification and CCI

DR Group	Count	Mean CCI	Median CCI	Standard Deviation	Min	Max	Mann-Whitney U	p-value
Mild NPDR	5	1.34	1.2	0.31304952	1.2	1.9	199	0.3936457
No DR	65	1.46461538	1.5	0.32231136	1	1.9		

DR – diabetic retinopathy; NPDR – nonproliferative diabetic retinopathy; CCI – color confusion index

DISCUSSION

This study investigated the relationship between color vision deficits and early diabetic retinal changes. It evaluated whether color vision testing with the Farnsworth D-15 can serve as an early adjunctive screening tool in diabetic patients with no signs of DR or mild NPDR. Published studies have suggested a strong link between color vision impairment and diabetic retinopathy. [7,8,12] Our study revealed that even in diabetics without retinopathy or with only mild NPDR, color vision changes were present ranging from subtle to marked. Notably, only six of the 70 eyes had normal Farnsworth results, and all of these belonged to the "no DR" group.

Frequency and Type of Color Vision Defects

Majority of the eyes in this study showed color vision changes (64 eyes out of 70), suggesting the presence of color vision impairment in the early stages of DR as 65 eyes of the patients enrolled had no signs of diabetic retinopathy. This may imply that color vision changes can occur early in the course of the disease without obvious clinical retina features of diabetic retinopathy. This aligns with the works of Feitosa-Santana *et al.*, Roy *et al.*, and Tan *et al.*, who reported higher rates of tritan-type (blue-yellow) deficiencies in diabetic populations even in the absence of DR.[5,10,13] The predominance of tritan defects in our cohort supports the hypothesis that the S-cone system is particularly vulnerable to metabolic and vascular compromise in diabetes.

Correlation Between CBG and Color Vision

Our study showed no significant correlation between acute glycemic state and color vision performance. The scatter plot analysis demonstrated a flat trendline, indicating that short-term glucose levels are not predictive of visual dysfunction. This is consistent with findings by Ng *et al.* (2008) and Safi *et al.* (2019), which stated that short-term glycemic fluctuations are less impactful on visual function than chronic glycemic exposure.[14,15]

Association Between DR Classification and Severity of Color Vision Error

The color vision performance using the Farnsworth D-15 test revealed that 59 of the 65 eyes in the "no DR" group showed color vision defects and all five eyes in the mild NPDR group exhibited color vision defects. Eyes with mild NPDR in this study did not have normal color vision. This corroborates the study of Tan *et al.*, which found a progressive increase in CCI scores with worsening DR.[13] However, our study did not show statistical significance. A possible explanation is that we only included patients with early NPDR or no DR and excluded patients with more advanced DR and macular edema. Moreover, our small sample size in the mild NPDR group may have affected the results. In addition, the Farnsworth D-15's sensitivity has its limitations compared to more sophisticated color discrimination tests such as the Cambridge Colour Test or the Lanthony D-15 desaturated version.

Utility of the Farnsworth D-15 as a Screening Tool

Our findings suggest that the Farnsworth D-15 test can detect subclinical color vision changes in diabetic patients, including those without retinopathy. This supports its potential as a quick, non-invasive adjunctive screening tool for early retinal dysfunction in diabetes, as previously recommended.[5, 8, 14, 15] However, further studies with larger sample sizes are warranted to establish its diagnostic value and cost-effectiveness in routine screening.

This study has several limitations. The sample size was small and included only patients with no DR and mild NPDR, without a healthy control group for comparison. The study groups were also imbalanced, being predominantly female, and largely composed of patients in the no DR group. While age-related lens changes were controlled by excluding patients with cataracts worse than LOCS III grading, subclinical blue-yellow color changes from cataracts cannot be totally ruled out. As such, the conclusions of this study cannot be used as preliminary evidence to support immediate policy changes on using color vision for early screening in DR. However, the results are encouraging. Future studies should aim to recruit participants that more equally represent both groups, include a healthy control group for comparison, and ensure that the required sample size, based on power calculations, are met to provide more robust and generalizable results. Moreover, the cross-sectional design restricted the analysis to associations at one point in time. For a better study, longitudinal investigations should be done in the future to better evaluate the progression of color vision changes in DM, recognizing the degenerative nature of the disease.

Lastly, CBG was utilized as the marker for diabetic control in this study because of its ease of use, affordability and accessibility. However, it is not an ideal marker as it may be affected by meals and physical activities – factors that were not taken into consideration in this study. Glycosylated hemoglobin would be a better marker for future studies.

While our study showed the increased frequency of color vision defects in early DR, it did not find a statistically significant difference in CCI scores between no DR and mild NPDR groups. These findings highlight both the potential clinical use and limitations of the Farnsworth D-15 as a screening tool.

The Farnsworth D-15 test serves as a quick, low-cost screening tool for early detection of functional retinal changes in diabetic patients. In resource-limited settings, primarily where access to retinal imaging is constrained, using color vision testing as an adjunct examination of diabetic eye evaluations could facilitate earlier interventions and potentially reduce the risk of irreversible vision loss. Future studies with larger and more balanced samples, as well as more sensitive color discrimination tests, may further elucidate its role in DR screening.

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