*Med & Health Aug 2024; 19(2): 560-572* https://doi.org/10.17576/MH.2024.1902.16

ORIGINAL ARTICLE

# Contrast Sensitivity, Color Discrimination and Visual Acuity as Risk Factors for Visual Dysfunction in Non-Proliferative Diabetic Retinopathy

SOORYANARAYANA SP[1,2], HAIROL MI[1]

[1]*Centre for Community Health Studies, Faculty of Health Sciences, Universiti Kebangsaan Malaysia, Jalan Raja Muda Abdul Aziz, 50300 Kuala Lumpur, Malaysia*
[2]*School of Optometry, Faculty of Medicine & Health Sciences, UCSI University, 56000 Kuala Lumpur, Malaysia*

*Received: 31 Jan 2024 / Accepted: 23 May 2024*

## *ABSTRAK*

*Diagnosis retinopati diabetik (DR) biasanya bergantung pada tanda-tanda klinikal yang ditemui semasa pemeriksaan fundus. Walau bagaimanapun, DR pra-klinikal mungkin mengalami perubahan neurodegeneratif yang berpotensi dikesan melalui penilaian fungsi penglihatan. Kajian ini bertujuan untuk membandingkan fungsi visual pada pesakit diabetes mellitus (DM) jenis 2 pada pelbagai tahap retinopati diabetes bukan proliferatif (NPDR) dan menentukan jika tahap NPDR yang lebih teruk mempunyai risiko kemerosotan fungsi visual yang lebih tinggi. Sejumlah 56 subjek DM dewasa (purata usia: 40.41 ± 7.281 tahun) dikelaskan kepada DM tanpa DR, NPDR ringan dan NPDR sederhana-teruk. Akuiti visual (VA), diskriminasi warna (CV) dan sensitiviti kontras (CS) dinilai menggunakan carta logMAR, ujian FM100, dan carta Pelli-Robson. Kumpulan NPDR sederhana-teruk menunjukkan VA paling teruk berbanding kumpulan lain dengan kemerosotan signifikan CV ($p<0.05$) dan CS yang berkurang [$F(2,107)=22.898$, $p<0.001$]. Analisis regresi logistik multinomial menunjukkan kumpulan NPDR sederhana-teruk berisiko 24.4% lebih tinggi untuk kemerosotan CS berbanding DM tanpa DR (OR:0.756, 95% CI: 0.627-0.913, $p=0.004$). Kesimpulannya, NPDR sederhana-teruk mempunyai CS dan CV yang merosot, dengan risiko yang lebih tinggi untuk kemerosotan CS berbanding pesakit dengan DM tanpa DR. Inklusi parameter-parameter ini ke dalam program saringan optometri DR yang sedia ada boleh mengurangkan perkembangan NPDR dan meningkatkan hasil penglihatan jangka panjang pesakit.*

*Kata kunci:* *Akuiti visual; diabetis melitus; diskriminasi warna; retinopati diabetis; sensitiviti kontras*

**Address for correspondence and reprint requests**: Mohd Izzuddin Hairol. Centre for Community Health Studies, Faculty of Health Sciences, Universiti Kebangsaan Malaysia, Jalan Raja Muda Abdul Aziz, 50300 Kuala Lumpur, Malaysia. Tel: +603-9289 7499 Email: izzuddin.hairol@ukm.edu.my

## ABSTRACT

Diabetic retinopathy (DR) diagnosis relies on clinical signs visible during dilated fundus examinations. However, pre-clinical DR may have neurodegenerative alterations that are only apparent through visual function assessments. This study compared visual functions in type 2 diabetes mellitus (DM) patients at various non-proliferative diabetic retinopathy (NPDR) stages and determined the risks of reduced visual functions. A total of 56 adult DM participants (mean age: 40.41 $\pm$ 7.281 years) were classified into DM without DR, mild NPDR, and moderate-to-severe NPDR. Visual acuity (VA), colour vision discrimination (CV) and contrast sensitivity (CS) were assessed using logMAR chart, FM100 Hue test, and Pelli-Robson chart, respectively. The moderate-to-severe NPDR group exhibited poorest VA than other groups, with reduced CV discrimination (all parameters $p<0.05$) and reduced CS [$F(2,107)=22.898$, $p<0.001$]. An adjusted multinomial logistic regression model revealed a 24.4% higher risk of reduced CS in the moderate-to-severe NPDR group compared to DM without DR group (OR:0.756, 95% CI: 0.627-0.913, $p=0.004$). In conclusion, moderate-to-severe NPDR had reduced CS and CV, with higher risks of reduced CS compared to those without DR. Incorporating these parameters into current DR optometric screening programs can mitigate NPDR progression and enhance long-term visual function outcomes of the patients.

Keywords: Colour discrimination; contrast sensitivity; diabetic retinopathy; diabetes mellitus; visual acuity

## INTRODUCTION

The most prevalent and early microvascular consequence of diabetes mellitus (DM) is diabetic retinopathy (DR), which is the main global cause of acquired vision loss in middle-aged, economically active individuals. In Malaysia, DR is the most common cause of visual loss among adults of working age. Less than 5% of patients will have retinopathy upon diagnosis; ten years later, the frequency increases up to 50% after a decade. After 20 years, nearly all patients with type 1 diabetes (T1DM) and more than 60% of patients with type 2 diabetes (T2DM) have some degree of retinopathy (World Health Organisation 2005).

Thus, it would be very helpful to be able to monitor visual function in addition to morphology to monitor the progression of diabetic retinopathy. Visual loss in many cases of DR could be prevented by early detection of the condition through screening which makes early treatment possible (Antonetti et al. 2012). It must be emphasised that DR is an asymptomatic condition in its early stage when it is easiest to be treated. Therefore, delayed presentation of DR patients for treatment can severely hamper blindness prevention (Chen &

Gardner 2021).

The current clinical diagnosis of DR is only made upon the manifestations of the clinical signs during the ophthalmological examination, often upon pupillary dilation. The Early Treatment of Diabetic Retinopathy Study (ETDRS) classification of DR is being used by clinicians worldwide and has become the gold standard for many years (Yang et al. 2022). Currently, traditional DR diagnosis depends on the severity of microvascular changes observed with increasing severity over the different stages of the disease. These signs are then ranked on a stepwise scale starting with no retinopathy and progressing through several stages of non-proliferative or pre-proliferative disease to advanced proliferative disease (Wong et al. 2018).

At times, the more invasive test is recommended for diabetic patients who have ocular symptoms, which appear when DR has progressed to a very advanced and irreversible level. These symptoms include a progressive decline in visual acuity (VA), metamorphopsia and a sudden loss of vision in one eye. In certain cases, specific techniques such as Optical Coherence Tomography (OCT) may be useful in the presence of macular edema and intravenous fluorescein angiography (IVFA) may be warranted (Chen & Gardner 2021; Safi et al. 2018), although it is an invasive examination.

Apart from the clinical signs noted on the fundus examination, VA is commonly measured in clinics for assessing DR severity. However, several studies have revealed retinal neurodegenerative changes occur in diabetic patients with or without DR before the signs are seen through fundus examinations and deterioration in VA (Chen & Gardner 2021; Karson et al. 2020; Safi et al. 2018), which would be beneficial in assessing the quality of life of DR patients (Pawar et al. 2021). A recent study has also shown the importance of correlating retinal structure and functional outcome data for understanding vision loss in DR (Sheskey et al. 2021). Thus, functional vision evaluation, such as colour discrimination and contrast sensitivity, could be better at detecting retinal neuropathy changes in DR's early stages (Gella et al. 2015). Furthermore, a study explored and proposed the use of visual function measures, combined with traditional statistical methods and machine learning, to identify the severity of DR (Wright et al. 2023).

Colour discrimination can be impaired by retinal neurodegenerative processes that occur in diabetes and the pre-clinical stage of DR (Gella et al. 2015; Sokol et al. 1985). The severity of colour discrimination impairment becomes more pronounced with the increase of retinopathy severity and the occurrence of diabetic macula edema (Shin et al. 2014). It also correlates with other functional and structural retinal abnormalities (Neriyanuri et al. 2017). Additionally, CS changes were found in diabetic patients even with those showing normal VA (Sokol et al. 1985), which could be due to disturbance of neural function in the retina and visual pathway (Wong et al. 2008). Various studies reported a reduction in CS for DM patients even without retinopathy (Gualtieri et al. 2013) and for those with

different stages of retinopathy (Gella et al. 2015). Although these earlier studies documented significant CS reductions in different stages of DR, it is not clear how CS and colour discrimination could be used as one of the risk factors to monitor different stages of non-proliferative DR.

Thus, the study compared visual function status (VA, colour discrimination and contrast sensitivity) between DM patients without DR, DM patients with mild non-proliferative diabetic retinopathy (NPDR), and DM patients with moderate-to-severe NPDR, and to determine if any of these groups had significantly higher risks for having reduced visual functions. It was hypothesised these functions would reduce further as the NPDR stage progressed and could be used to predict the risks for DR development.

## MATERIALS AND METHODS

This cross-sectional prospective study involved Type II diabetes mellitus (DM) patients who attended biochemical check-ups at least quarterly a year at the Outpatient Department of Kuala Lumpur Health Clinic and Endocrinology Clinic of HKL. Using purposive sampling, a total of 56 participants (32 males and 24 females) were recruited in this study.

Using G*Power, based on one-way ANOVA analysis, a sample size of 56 in three groups would give the study a power (1-β error) of 80% with a large effect size $f^2$=0.43) and  error of 0.05. However, we had our number of participants varied across the groups with the most being in the DM without DR group, followed by half of the participants in both mild NPDR and moderate-to-severe NPDR group.

All participants were between 20 to 50 years old, with refractive error not exceeding 6.00DS and 4.00DC as moderate to high myopia could affect the retinal function and impair the CS function (Stoimenova 2007). They underwent comprehensive eye examinations and had their fundus photographed by two medical retina specialists and were categorised into three groups based on clinical findings on the ETDRS grading system: those with DM without DR, DM with mild NPDR, and DM with moderate-to-severe NPDR. Participants were excluded from the study if they had chronic neurological diseases, were on medications affecting visual functions (such as ethambutol, amiodarone, Plaquenil, and vigabatrin), had congenital colour deficiencies, had a history of ocular diseases, had undergone any types of eye surgery, and had received treatment for DR such as laser photocoagulation and intravitreal anti-VEGF injections.

All the visual function measurements were done within the same room to control the effect of surrounding illuminations. VA was assessed in each participant's eye with their best refractive correction using the ETDRS Original Series Chart R from Goodlite at a 4-meter viewing distance. The chart was trans-illuminated with a lightbox (The ESV3000 ETDRS Illuminated Cabinet) that maintained chart luminance at 85 cd/$m^2$. VA was recorded in a logarithm of the minimum angle of resolution (logMAR)

units.

Monocular assessment of colour discrimination was conducted using the Farnsworth-Munsell 100 (FM 100) Hue test. It was done within the FM 100 Hue viewing booth with the illumination of 100 lux at 50 cm while the participants wore their near correction. This test consisted of four boxes containing 85 different coloured caps with a diameter of 1.2 cm that subtended an angle of 1.4 degrees. The colour of the caps differed from the adjacent caps in small steps and represented the entire colour circle. Participants were required to arrange all the coloured caps in each box in a perceptually proper hue arrangement. The colour sequence spanned from red to yellowish-green in the first box, yellowish-green to turquoise green in the second, turquoise-green to bluish-purple in the third, and bluish-purple to red in the fourth. All participants were given a video demonstration on how to perform the test. This was done before the actual test to ensure they understood the procedure and to remove learning effects. The test was administered from the first box to the fourth box in sequence. Participants were encouraged to complete the test without long delays. Colour discrimination parameters were analysed based on two methods. The first method, also called the classical method, gave the Total Error Score (TES) only, which represented the magnitude of error that the patient made when arranging the coloured caps. This TES were compared with the age-matched normal values provided by Kinnear & Sahraie (2002) which was computed automatically by the web-based scoring software used in the entire colour vision data analysis. This was created by Torok B (http://www.torok.info/ colourvision / dir_for_use.htm). The second method was the moment of inertia method (Vingrys & King-Smith 1988), which included the following parameters: (i) Major and minor radii - These parameters were derived from colour difference vectors plotted based on individual participant's cap arrangements; (ii) TES - computed from the square roots of the sum of squares of the major and minor radii; (iii) Angle - This parameter represented the colour confusion's primary axis; (iv) Selectivity index (S-index) - This parameter used the major-to-minor radii ratio to quantify the degree of polarity or lack of randomisation in the cap arrangement; (v) Confusion index (C-index) - This parameter, which was calculated by dividing the length of the subject's maximum radius by the maximum radius obtained for a perfect cap arrangement, quantified the degree of colour loss relative to the perfect arrangement of caps.

CS in each participant's eye was evaluated using the Pelli-Robson CS chart at a viewing distance of 1 meter and the best refractive correction was worn. The test was performed under the illumination of 85 cd/m$^2$ as recommended by the developers of the chart. CS was represented in log contrast sensitivity (log CS) units.

## Ethical Approval

This study has obtained ethical clearance from the Universiti

Kebangsaan Malaysia's Research Ethics Committee (UKMREC). The study code number was JEP-2018-292 and the ethics approval number was UKM/PPI/111/8/JEP-2018-292. In compliance with the current Medical Research and Ethics Committee (MREC) and National Institute of Health (NIH) of the Ministry of Health (MOH), research guidelines, and applicable research guidelines, the research protocols were also reviewed and approved by the Clinical Research Centre (CRC) of HKL. The research ID number filed in MREC is NMRR-18-2581-41114. Informed consent was obtained from all the participants before the commencement of data collection.

### Statistical Analysis

All data were sorted in Microsoft Excel and then analysed with the Statistical Package for Social Science (SPSS) software version 22. Analysis of variance (ANOVA) was used to compare continuous parametric variables among three groups. In the cases where ANOVA indicated significant differences among groups, post hoc tests with Bonferroni correction were conducted to identify specific pairwise differences. The assumptions of homogeneity of variances within the groups were not violated for the ANOVA test.

Multivariate logistic regression analysis was performed to assess the simultaneous influence of multiple independent variables on the presence and stages of DR. The predictor variables that produced a p-value of 0.05 or below in the ANOVA analysis were included in the multinomial logistics regression analysis. Odds ratios (OR) with 95% confidence intervals (CI) were determined, both unadjusted and adjusted for confounding variables. The OR represented the probability of getting mild NPDR and moderate to severe NPDR relative to having DM without DR (i.e., the reference group). The significance level, α, was set at 0.05 for all statistical tests.

## RESULT

Most participants had similar stages of the DR in both eyes. Five participants with unequal NPDR stages between right and left eyes were included in the group based on the worst eye. The DM without DR had the lowest mean age (38.91 $\pm$ 7.804 years), while the moderate-severe NPDR had the highest (43.33 $\pm$ 6.814 years). However, the mean age difference between the three groups was not statistically significant [$F(2,52)=1.910$, $p=0.158$]. Table 1 summarised the participants' characteristics.

### Best-corrected Visual Acuity (BCVA)

The DM without DR group had a better BCVA with a mean of -0.012 $\pm$ 0.08 logMAR. The mild NPDR group had a slightly lower mean BCVA of -0.001 $\pm$ 0.461 logMAR, while the moderate-to-severe NPDR had the poorest mean BCVA of 0.033 0.496 logMAR. One-way ANOVA revealed that the difference in the mean BCVA for the three groups was not statistically significant [$F(2,107)=2.070$, $p=0.131$].

TABLE 1: Study participants' characteristics based on DR categories

| Characteristics | DM without DR (n = 33) | Mild NPDR (n = 11) | Moderate-to-severe NPDR (n = 12) |
|---|---|---|---|
| Age (year) | 38.91 ± 7.80 | 41.73 ± 5.10 | 43.33 ± 6.81 |
| DM duration (year) | 4.02 ± 3.46 | 6.55 ± 4.52 | 6.55 ± 4.53 |
| Ethnicity | | | |
| Malay | 22 | 8 | 6 |
| Chinese | 8 | 3 | 6 |
| Indian | 3 | 0 | 0 |
| Gender | | | |
| Male | 16 | 7 | 9 |
| Female | 17 | 4 | 3 |
| Comorbidities | | | |
| DM only | 19 | 6 | 2 |
| DM with hypertension & hypercholesterolemia | 14 | 5 | 10 |

DM: diabetes mellitus; DR: diabetic retinopathy; NPDR: non-proliferative diabetic retinopathy

The mean BCVA values for the three participant groups were close to the Snellen equivalent of 6/6, indicating that VA was not significantly affected in DM patients with NPDR compared to those with DM without DR.

## Colour Vision Discrimination

When analysed with the classical method, the DM without DR group had the best colour discrimination, with a total error score (TES) of 85.03 ± 38.517, followed by the mild NPDR group (97.25 ± 48.882). The moderate-to-severe NPDR group produced the highest TES (119.27 ± 46.721). However, the difference in mean TES between the three groups was not significantly different [F(2,53)=2.717, p=0.075].

When analysed with the moment of inertia method, the DM without DR group had the lowest TES (5.09 ± 0.837) compared to the mild NPDR group (5.48 ± 1.253). The moderate to severe NPDR group had the highest TES (5.99 ± 1.044). The difference in the TES based on this method of analysis between the groups was significantly different [F(2,53)=3.665, p=0.032].

For the major radius parameter, DM without DR group showed the lowest major radius (4.150 ± 0.762), followed by the mild NPDR group (4.475 ± 1.176) and moderate-to-severe NPDR group (4.991 ± 0.962). These differences were statistically significant [F(2,55)=3.669, p=0.032].

For the Colour Confusion Index (CCI) parameter, the mean CCI was lowest for the DM without DR group (1.64 ± 0.302), followed by the mild NPDR group (1.77 ± 0.460) and the moderate-to-severe NPDR group (1.98 ± 0.381). The difference in CCI between the three groups was statistically significant [F(2,53)=3.782, p=0.029].

A post-hoc analysis using Bonferroni corrections demonstrated that the DM without DR group had better colour discrimination than the moderate-to-severe NPDR group, with significantly lower means for TES, Major Radius, and CCI (all $p<0.05$). However, the mean values for these parameters. were not significantly different between DM without DR and the mild NPDR group, as well as between the mild NPDR and the moderate-to-severe NPDR group (all $p>0.05$). The other colour discrimination parameters (angle, minor radius, and SI) were not significantly different between the three groups (all $p>0.05$). Table 2 summarised the results for the colour vision status.

## Contrast Sensitivity Status

The DM without DR participants had the highest CS, with a mean of 1.61 $\pm$ 0.077 log CS. The mild NPDR group had a mean score of 1.56 $\pm$ 0.759 log CS, while the moderate-to-severe NPDR group had the lowest mean

TABLE 2: Color vision parameters measured in the study participants

| **Variable** | Mean $\pm$ SD |
|---|---|
| TES (classical method) | 85.030 $\pm$ 38.517 |
| DM without DR | 97.250 $\pm$ 48.882 |
| Mild NPDR | 119.273 $\pm$ 46.721 |
| Moderate to severe NPDR | |
| TES (moment of inertia method) | |
| DM without DR | 5.088 $\pm$ 0.837 |
| Mild NPDR | 5.483 $\pm$ 1.253 |
| Moderate-to-severe NPDR | 5.991 $\pm$ 1.044 |
| Angle | |
| DM without DR | 61.994 $\pm$ 11.106 |
| Mild NPDR | 67.575 $\pm$ 13.719 |
| Moderate-to-severe NPDR | 57.018 $\pm$ 48.961 |
| Major Radius | |
| DM without DR | 4.150 $\pm$ 0.762 |
| Mild NPDR | 4.475 $\pm$ 1.176 |
| Moderate-to-severe NPDR | 4.991 $\pm$ 0.962 |
| Minor Radius | |
| DM without DR | 2.947 $\pm$ 0.423 |
| Mild NPDR | 3.183 $\pm$ 0.619 |
| Moderate-to-severe NPDR | 3.282 $\pm$ 0.483 |
| SI | |
| DM without DR | 1.406 $\pm$ 0.140 |
| Mild NPDR | 1.408 $\pm$ 0.120 |
| Moderate-to-severe NPDR | 1.512 $\pm$ 0.164 |
| CCI | |
| DM without DR | 1.642 $\pm$ 0.302 |
| Mild NPDR | 1.767 $\pm$ 0.460 |
| Moderate-to-severe NPDR | 1.980 $\pm$ 0.381 |

DM: diabetes mellitus; DR: diabetic retinopathy; NPDR: non-proliferative diabetic retinopathy; SI: selectivity index; CCI: color confusion index

score of 1.47 ± 0.973 log CS. The difference in the CS score between the three groups was highly significant [F(2,107)=22.898, p<0.001]. Post-hoc analysis with Bonferroni corrections showed that CS was significantly lower in the moderate-to-severe NPDR group compared to the DM without DR group (p<0.01) and the mild NPDR group (p=0.02).

### Colour Discrimination Parameters and CS as Predictors for NPDR in Participants with DM

In the unadjusted multinomial logistic regression model, the predictors (TES, Major Radius, CCI, and log contrast sensitivity) were individually analysed. Relative to the DM without DR participants, those with moderate-to-severe NPDR were 2.39 times more likely to have a higher TES score (OR: 2.389, 95% CI: 1.160-4.921, p=0.028), a larger major radius (OR: 2.554, 95% CI: 1.173-5.558, p=0.018), a higher CCI (OR: 11.043, 95% CI: 1.545-78.948, p=0.017), and less likely to have a high CS (OR: 0.764, 95% CI: 0.641-0.910, p=0.003).

The multinomial logistic regression models were adjusted by including participants' comorbidity and DM duration as the covariates. In the adjusted model, only CS was a significant predictor, where the moderate-to-severe NPDR group had an odds ratio of 0.756, which meant that the group had a 24.4% chance of having lower contrast sensitivity, relative to the DM without DR group (OR: 0.756, 95% CI: 0.627-0.913, p=0.004). The fit of the model with the predictor variables was given by [$\chi$2(6, N = 56) =21.882, Nagelkerke R2=0.386, p=0.001]. Table 3 summarised the findings of the multinomial logistic regression analysis for the unadjusted and adjusted models.

## DISCUSSION

We reported BCVA to be not significantly different among the three groups even though it worsens slightly as the DR progresses, similar to earlier results reported in previous studies (Lupión Durán et al. 2021; Scanlon et al. 2008). Thus, BCVA alone is a very poor indicator in DR, it only becomes significant as the disease progresses into severe stages classified as vision-threatening DR as reported by previous studies (Lupión Durán et al. 2021; Scanlon et al. 2008; Shi et al. 2020). The results are not surprising, as VA in a generally healthy population and those with well-controlled diabetes remains relatively stable until the age of 65 (Panda-Jonas et al. 1995; Saftari & Kwon 2018). Therefore, relying on BCVA as a sole measure for monitoring the progress of visual function in the early stages of DR is not suitable and must be accompanied by other measurements of visual functions, such as colour discrimination and contrast sensitivity. Nevertheless, diabetic patients with older age and more severe DR stages should be monitored closely for prompt treatment when vision loss occurs (Lent-Schochet et al. 2021).

CS test has proven to be a sensitive tool in assessing neurodegenerative changes in diabetic patients, even

TABLE 3: Multivariate logistic regression for NPDR status outcome with color vision parameters and contrast sensitivity as predictors

| Predictor | Group | Unadjusted model | | | Adjusted model[1] | | |
|---|---|---|---|---|---|---|---|
| | | Odds ratio (OR) | p-value | 95% CI | Odds ratio (OR) | p-value | 95% CI |
| Total Error Score (moment of inertia method) | Moderate-severe NPDR | 2.389 | 0.018* | 1.160-4.921 | 2.043 | 0.085 | 0.907-4.605 |
| | Mild NPDR | 1.419 | 0.412 | 0.675-2.983 | 1.347 | 0.431 | 0.642-2.826 |
| | DM without DR | 1 | - | - | 1 | - | - |
| Major radius | Moderate-severe NPDR | 2.554 | 0.018* | 1.173-5.558 | 2.192 | 0.079 | 0.913-5.262 |
| | Mild NPDR | 1.402 | 0.412 | 0.625-3.144 | 1.339 | 0.478 | 0.597-3.002 |
| | DM without DR | 1 | - | - | 1 | - | - |
| Color confusion index (CCI) | Moderate-severe NPDR | 11.043 | 0.017* | 1.545-78.948 | 7.954 | 0.068 | 0.858-73.774 |
| | Mild NPDR | 2.292 | 0.427 | 0.296-17.769 | 2.107 | 0.477 | 0.270-16.440 |
| | DM without DR | 1 | - | - | 1 | - | - |
| Contrast sensitivity | Moderate-severe NPDR | 0.764 | 0.003* | 0.641-0.910 | 0.756 | 0.004* | 0.627-0.913 |
| | Mild NPDR | 0.947 | 0.257 | 0.861-1.041 | 0.920 | 0.141 | 0.824-1.028 |
| | DM without DR | 1 | - | - | 1 | - | - |

[1]Model adjusted with DM duration and comorbidity as covariates. *Significant p<0.05

in those with normal VA. Reduced contrast in diabetics, including those without diabetic retinopathy, could be attributed to disturbances in the retina and visual pathways (Wong et al. 2008). This emphasises the potential value of CS as an early indicator of visual dysfunction in diabetes. Our results support this notion by revealing a highly significant CS difference between the DM without DR group and the moderate-to-severe NPDR group. The DM without DR group had the highest contrast sensitivity, while the moderate-to-severe NPDR group had the lowest. This finding suggests that CS can indeed serve as a sensitive indicator of early visual dysfunction in diabetic patients. When CS was adjusted with comorbidity and duration of DM as the confounding factors, it was found that the moderate-to-severe NPDR group had a 24.4% chance of having lower contrast sensitivity, compared to the DM without DR group. The result suggests that CS reduction may occur even before the clinical manifestation of diabetes. Reduced CS has also been reported in patients who were pre-diabetic compared to non-diabetic healthy controls (Chande et al. 2020;

Safi et al. 2018), and also in patients who are glaucoma suspects (Othman et al. 2023).

Wolff et al. (2015) reported impaired colour discrimination (i.e. colour confusion score, CCS) in both their DM without DR and DM with DR patients, compared to those without DM. The study, however, did not find statistically significant differences in CCS scores between their DM without DR and DR with DR patients. This could be that they did not segregate their CCS score based on DR severity, although they did report that colour vision abnormalities were more frequent if the DR involved areas within 4.5 degrees of the fovea, that is, the more severe stage of DR. In the present study, on the other hand, found that those with moderate-to-severe NPDR had significantly higher total error scores for colour discrimination, in addition to the significantly different major radius and colour confusion index, compared to those with mild NPDR and those with DM without DR. Indeed, longer duration of DM, as those with moderate-to-severe NPDR, is associated with impaired colour vision (Tan et al. 2017). Tan et al. (2017) used the Farnsworth D15 test while Wolff et al. (2015) used the Adam desaturated D15 test to screen and measure colour discrimination of their patients. Our use of the Farnsworth-Munsell 100 Hue test allowed better discrimination of colour vision impairment between participants with different categories of NPDR, thus adding to the knowledge that colour discrimination would become more impaired as NPDR progresses.

In addition, aging is known to influence colour discrimination, even when other characteristics such as visual acuity are not impaired (Ichikawa et al. 2021). However, it is unlikely that the reduction in colour discrimination in the moderate-to-severe NPDR group in this study is due to the normal ageing process that is different from the other participant groups as they were mostly in their fourth decade of life. An earlier study reported that patients with prediabetes have colour vision changes that could be measured in the retina before a diabetes diagnosis is made (Karson et al. 2020). However, the current study found that when adjusted for comorbidity and DM duration, the risks for having more severe colour discrimination parameters were not significantly different for the moderate-to-severe NPDR group compared to the DM without DR group. These results suggest that changes that may occur on the retina in patients with different NPDR stages may depend on their existing comorbidities and the duration of their DM, which warrants further investigation. In addition, including a colour discrimination test would require cost-effectiveness evaluation (Tan et al. 2017), especially when colour discrimination among older patients can also be influenced by changes in the colour and clarity of the ocular media (Nguyen-Tri et al. 2003).

Thus, CS seems to be an excellent indicator of neurodegeneration in pre-clinical DR patients. Hence, we highly recommend that healthcare providers such as optometrists, ophthalmologists,

medical doctors, and trained nurses incorporate CS assessment as part of their current DR screening strategy to rule out and predict the risk of NPDR progression among pre-clinical DR patients. CS can be measured by using various methods from a simple Pelli-Robson test to the most sophisticated software-based computer programs. However, the technical aspects and reproducibility of certain computer programs need to be given attention. The Pelli-Robson chart is sensitive in detecting CSF loss among pre-diabetic patients as noted by Chande et al. (2020). In addition, Ngah et al. (2020) stressed the need for strategies to improve follow-up and screening for DR in Malaysia. Identification of retinal neurodegenerative indicators in pre-clinical DR will certainly help to work on the screening strategies for DR, which in turn lessen the burden of visual loss.

The present study has several limitations. First, the moderate and severe NPDR had to be combined as a group due to the limited number of patients who were willing to participate. These two groups might have different visual functions that should be investigated further. Second, the DM duration was based on the medical record when the patient was first diagnosed. Some of them might have had late diagnoses and thus had longer DM duration than expected.

## CONCLUSION

Moderate-to-severe NPDR had lower CS and colour discrimination, with significantly higher risks of having reduced CS than patients with DM without DR. Thus, CS testing should become a standard clinical measurement when monitoring the progression of NPDR, starting in patients with DM who do not have clinical manifestations of NPDR.

## ACKNOWLEDGEMENT

The author thanked all the participants of the research, and the staff at the Clinic. A special thanks to Dr. Nor Azita Ahmad Tarmidzi and Dr Hamisah Ishak from Hospital Kuala Lumpur.

## REFERENCES

Antonetti, D.A., Klein, R., Gardner, T.W. 2012. Diabetic retinopathy. *New England J Med* **366**(13): 1227-39.

Chande, P.K., Raman, R., John, P., Srinivasan, S. 2020. Contrast-sensitivity function and photo stress–recovery time in prediabetes. *Clin Optom* **12**(2): 151-5.

Chen, X.D., Gardner, T.W. 2021. A critical review: Psychophysical assessments of diabetic retinopathy. *Surv Ophthalmol* **66**(2): 213-30.

Gella, L., Raman, R., Kulothungan, V., Pal, S.S., Ganesan, S., Sharma, T. 2015. Impairment of colour vision in diabetes with no retinopathy: Sankara Nethralaya Diabetic Retinopathy Epidemiology and Molecular Genetics Study (SNDREAMS- II, Report 3). *PLoS ONE* **10**(6): e0129391.

Gualtieri, M., Feitosa-Santana, C., Lago, M., Nishi, M., Ventura, D.F. 2013. Early visual changes in diabetic patients with no retinopathy, measured by colour discrimination and electroretinography. *Psychol Neurosci* **6**(2): 227-34.

Ichikawa, K., Yokoyama, S., Tanaka, Y., Nakamura, H., Smith, R.T., Tanabe, S. 2021. The change in colour vision with normal aging evaluated on standard pseudoisochromatic plates Part-3. *Curr Eye Res* **46**(7): 1038-46.

Karson, N., Smith, J., Jones, M., Datta, A., Richdale, K., Harrison, W.W. 2020. Functional retinal outcomes in patients with prediabetes and type 2 diabetes. *Ophthalmic Physiol Opt* **40**(6): 770-7.

Kinnear, P.R., Sahraie, A. 2002. New Farnsworth-

Munsell 100 hue test norms of normal observers for each year of age 5-22 and for age decades 30-70. *British J Ophthalmol* **86**(12): 1408-11.

Lent-Schochet, D., Lo, T., Luu, K.Y., Tran, S., Wilson, M.D., Moshiri, A., Park, S.S., Yiu, G. 2021. Natural history and predictors of vision loss in eyes with diabetic macular edema and good initial visual acuity. *Retina* **41**(10): 2132-9.

Lupión Durán, T., García-Ben, A., Rodríguez Méndez, V., Gálvez Alcázar, L., García-Ben, E., García-Campos, J.M. 2021. Study of visual acuity and contrast sensitivity in diabetic patients with and without non-proliferative diabetic retinopathy. *Int Ophthalmol* **41**(11): 3587-92.

Neriyanuri, S., Pardhan, S., Gella, L., Pal, S.S., Ganesan, S., Sharma, T., Raman, R. 2017. Retinal sensitivity changes associated with diabetic neuropathy in the absence of diabetic retinopathy. *Br J Ophthalmol* **101**(9): 1174-8.

Ngah, N.F., Muhamad, N.A., Asnir, Z.Z., Aziz, R.A.A., Kassim, Z.M., Sahar, S.A., Ahmad Tarmidzi, N.A., Chan, L.Y., Uthman, R., Satar, N. et al. 2020. Descriptive assessment on diabetic retinopathy screening in an awareness programme in Malaysia. *Int J Ophthalmol* **13**(11): 1808-13.

Nguyen-Tri, D., Overbury, O., Faubert, J. 2003. The role of lenticular senescence in age-related color vision changes. *Invest Ophthalmol Vis Sci* **44**(8): 3698-704.

Othman, S.K.O., Sandragasu, T. & Hairol, M.I. 2023. Comparison of contrast sensitivity and central corneal thickness in primary open angle glaucoma suspects and visually normal participants. *Malays J Med Health Sci* **18**(2): 112-8.

Panda-Jonas, S., Jonas, J.B., Jakobczyk-Zmija, M. 1995. Retinal photoreceptor density decreases with age. *Ophthalmol* **102**(12): 1853-9.

Pawar, S., Parkar, A., Menon, S., Desai, N., Namrata, D., Dole, K. 2021. Assessment of quality of life of the patients with diabetic retinopathy using National Eye Institute Visual Functioning Questionnaire (VFQ-25). *J Healthc Qual Res* **36**(4): 225-30.

Safi, H., Safi, S., Hafezi-Moghadam, A., Ahmadieh, H. 2018. Early detection of diabetic retinopathy. *Surv Ophthalmol* **63**(5): 601-8.

Saftari, L.N., Kwon, O.S. 2018. Ageing vision and falls: A review. *J Physiol Anthropol* **37**(1): 11

Scanlon, P.H., Foy, C., Chen, F.K. 2008. Visual acuity measurement and ocular co-morbidity in diabetic retinopathy screening. *Br J Ophthalmol* **92**(6): 775-8.

Sheskey, S.R., Antonetti, D.A., Rentería, R.C., Lin, C.M. 2021. Correlation of retinal structure and visual function assessments in mouse diabetes models. *Invest Ophthalmol Vis Sci* **62**(10): 20.

Shin, Y.J., Park, K.H., Hwang, J.M., Wee, W.R., Lee, J.H., Lee, I.B., Hyon, J.Y. 2014. A novel colour vision test for detection of diabetic macular edema. *Invest Ophthalmol Vis Sci* **55**(1): 25-32.

Shi, Q., Dong, X.M., Zhang, M., Cheng, Y.H., Pei, C. 2020. Clinical studies of early diabetic macular morphology and visual function changes. *Int Eye Sci* **20**(9): 1519-23.

Stoimenova, B.D. 2007. The effect of myopia on contrast thresholds. *Invest Ophthalmol Vis Sci* **48**(5): 2371-4.

Sokol, S., Moskowitz, A., Skarf, B., Evans, R., Molitch, M., Senior, B. 1985. Contrast sensitivity in diabetics with and without background retinopathy. *Arch Ophthalmol* **103**(1): 51-4.

Tan, N.C., Yip, W.F., Kallakuri, S., Sankari, U., Koh, Y.L.E. 2017. Factors associated with impaired color vision without retinopathy amongst people with type 2 diabetes mellitus: A cross-sectional study. *BMC Endocr Disord* **17**: 1-8.

Vingrys, A.J., King-Smith, P.E. 1988. A quantitative scoring technique for panel tests of colour vision. *Invest Ophthalmol Vis Sci* **29**(1): 50-63.

Wolff, B.E., Bearse, M.A., Schneck, M.E., Dhamdhere, K., Harrison, W.W., Barez, S., Adams, A.J. 2015. Color vision and neuroretinal function in diabetes. *Doc Ophthalmol* **130**: 131-9.

Wong, T.Y., Sun, J., Kawasaki, R., Ruamviboonsuk, P., Gupta, N., Lansingh, V.C., Maia, M., Mathenge, W., Moreker, S., Muqit, M.M.K., et al. 2018. Guidelines on Diabetic Eye Care: The International Council of Ophthalmology Recommendations for screening, follow-up, referral, and treatment based on resource settings. *Ophthalmology* **125**(10): 1608-22.

Wong, R., Khan, J., Adewoyin, T., Sivaprasad, S., Arden, G.B., Chong, V. 2008. The ChromaTest, a digital colour contrast sensitivity analyzer, for diabetic maculopathy: A pilot study. *BMC Ophthalmol* **8**(1): 1-6.

World Health Organization. 2005. *Prevention of blindness from diabetes mellitus*. Geneva: WHO.

Wright, D.M., Chakravarthy, U., Das, R., Graham, K.W., Naskas, T.T., Perais, J., Kee, F., Peto, T., Hogg, R.E. 2023. Identifying the severity of diabetic retinopathy by visual function measures using both traditional statistical methods and interpretable machine learning: A cross-sectional study. *Diabetologia* **66**(12): 2250-60.

Yang, Z., Tan, T. E., Shao, Y., Wong, T. Y., Li, X. 2022. Classification of diabetic retinopathy: Past, present and future. *Front Endocrinol* **13**: 1079217.