• Investigation •

The prevalence of red-green color vision deficiency and its related factors in an elderly population above 60 years of age

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Abstract

• **AIM:** To determine the prevalence of red-green (RG) color vision deficiency (CVD) in an elderly population and its related factors.

• **METHODS:** This report is a part of the Tehran Geriatric Eye Study: a cross-sectional population-based study that was conducted on the elderly population (≥60y) of Tehran, Iran using multi-stage stratified random cluster sampling. All study participants underwent complete ocular examination, including the measurement of uncorrected and best-corrected visual acuity, objective and subjective refraction, and slit-lamp biomicroscopy. The color vision was tested using Ishihara plates with the near optical correction in place.

• **RESULTS:** Of the 3791 invitees, 3310 participated in the study. The data of 2164 individuals were analyzed after applying the exclusion criteria. The prevalence of R-G CVD was 3.73% (95%CI: 2.37%–5.09%) in the whole sample; the prevalence of protanomaly, protanopia, and deuteranopia was 1.51%, 1.76%, and 0.45%, respectively. The prevalence of R-G CVD was significantly higher in males than in females. The prevalence of RG CVD increased with advancing age from 2.91% in the age group 60–64y to 5.8% in the age group ≥80y (P=0.070). According to the multiple logistic regression model, male sex, and glaucoma were significantly related to RG CVD. Older age and hypertension also had a marginally significant relationship with RG CVD.

• **CONCLUSION:** Changes in color vision occur in the elderly due to the aging process and some physiological and pathological factors. Since the change in visual perception may affect the person's performance, this aspect of the visual system's function should also be taken into consideration in the examinations of the elderly.

• **KEYWORDS:** color vision; population-base study; protanomaly; protanopia; deuteranopia; elderly

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INTRODUCTION

Color vision deficiency (CVD) is one of the most important visual system disorders that leads to the inability to distinguish between different wavelengths of light[1]. CVD develops as a result of hereditary or acquired factors affecting the number or absorption spectrum of photoreceptors in two forms: red-green (RG) and yellow-blue (YB), with RG being the most common type[2]. Various factors play a role in the development of acquired CVD, which cause problems in the reception and transmission of color signals to the brain by disrupting the visual system[3]. Among these factors are ocular diseases including cataracts[4], refractive errors[5], age-related macular degeneration (AMD)[6], glaucoma[7], and retinal diseases[8], neurological factors[9], metabolic factors[10], chronic diseases such as diabetes mellitus[11], viral diseases such as COVID-19[12], drugs and toxins[13], occupational[14], and aging[15].

Several studies have investigated the prevalence of CVD among different populations and age groups[16-18]; the findings indicated that the prevalence of CVD varies depending on the ethnicity, geographic region, occupation, age and sex distribution of the studied population. In general, the prevalence of CVD is about 8% and 0.4% in men and women, respectively[19]. More specifically, the prevalence of CVD has been reported to be about 4% to 6.5% in China and Japan, 4% in African countries, lower than 2% in USA and Israel, and 5% in Asian countries[20]. Moreover, previous studies showed that the prevalence of acquired CVD is higher in the population above 40 years of age[21]. Few studies in Iran reported the prevalence of CVD between 1.6% and 15.85% depending on demographic factors[18,22-23]. For example, the Shahroud Eye Cohort study reported the prevalence of acquired and congenital CVD as 1.1% and 4.4%, respectively[18]. However, the mentioned study included only a small sample of older adults aged 40 to 64y[18]; so there is a need for additional information on the prevalence of CVD in the Iranian elderly population.

Age-related visual changes in the elderly could affect daily activities, physical health, and quality of life. Although various studies investigated the prevalence of CVD worldwide, there is limited information in this regard in the elderly population[24]. CVD can influence almost all aspects of modern human life. Despite individual differences, a person with CVD may have difficulty in fundamental activities such as occupational performance, education, social and emotional relationships, personal care, and access to entertainment and information. In addition, studies suggested the effects of CVD on the development of self-esteem, personality, challenges and difficulties faced by professionals in the medical field, and difficulties in sports practice. The epidemiological study of CVD in the elderly is important considering the age-related increase in the prevalence of ocular diseases (such as AMD, glaucoma, cataracts, and diabetic retinopathy), the direct effects of age on retinal physiology, and the world population aging. According to the above, the present study aimed to investigate the prevalence and related factors of CVD in an Iranian elderly population aged 60y and above.

SUBJECTS AND METHODS

Ethical Approval Informed consent was obtained from all participants. The principles of the Helsinki Declaration were followed in all stages of the study. The study protocol was approved by the Ethics Committee of the National Institute for Medical Research Development (NIMAD) under the auspices of the Iranian Ministry of Health (grant code: 963660).

The present report is a part of the Tehran Geriatric Eye Study (TGES): a population-based cross-sectional study that was conducted from Jan 2019 to Jan 2020. The target population of TGES was elderly people aged 60y and above living in Tehran, the capital of Iran. The sampling was performed using the multi-stage stratified random cluster sampling method. First, the 22 municipality districts of Tehran city were defined as strata and the population ≥60y in each district was inquired from the National Statistics Center. Next, the block map of each district was prepared and each block was considered a cluster. A total of 160 clusters were randomly selected proportional to size from all 22 districts of Tehran. After identifying clusters, a sampling team was sent to the address of each cluster and the first house was chosen as the cluster head by being located on the southwest side of the selected block. Then, by moving counterclockwise while selecting the next households, all people 60 years of age and above were invited to participate in the study. The goals and steps of the study were fully explained to all invitees and they were assured of the confidentiality of the information. If a person desired to participate in the study, informed consent was obtained and an ID card was issued. Study participants were transferred to the study site (Noor Eye Hospital, Tehran, Iran) on a prescheduled day free of charge. When the sampling team went to the door of the houses in each cluster, if a household was not present, they would return on another occasion (preferably in the evening).

Once the study participants were present at the study site, a preliminary interview was carried out to collect demographic data and medical records. Ocular examinations and imaging were performed in the next step. First, the uncorrected distance visual acuity (UCVA) was measured using an LED visual chart, Smart LC 13 (Medizs Inc., Korea) at 6 m, followed by objective refraction using an auto-refractometer/keratometer (ARK-510A, Nidek Co. 42 LTD, Aichi, Japan). Then, subjective refraction was performed to determine best distance optical correction and best-corrected distance visual acuity (BCVA) was recorded. Appropriate presbyopic addition lens power was also determined using near subjective refraction.

Color vision was tested monocularly using Ishihara plates at 40 cm with the near correction in place. The Ishihara is one of the well-known color vision tests based on pseudoisochromatic plates, which is used to screen for RG (deutan and protan) color vision deficiencies. This test consists of several plates: each plate depicts a circle of colored dots which are randomized in color and size. Within the pattern are dots that form a number or shape clearly visible to individuals with normal color vision, and invisible, or difficult to see, to those with an RG-CVD. Other plates are intentionally designed to reveal numbers only to patients with an RG-CVD, and be invisible to those with normal color vision. Ishihara's 24-plates edition was used in this study and testing was performed in a room with daylight illumination conditions equivalent to

50-foot candle. According to the test instruction, the first 15 plates including the introduction, transformation, vanishing, and hidden-digit plates were presented to the participant and he/she was asked to identify the character inside each plate. The patient was given up to 5s to respond to each plate and six or more errors were considered as the failing criterion or CVD. In case of CVD, the classification pages (pages No.16 and 17) were used to identify the type and the severity of the CVD. Severe disorder was defined as dichromacy (protanopia or deuteranopia) and mild disorder was defined as anomalous trichromacy (protanomaly or deuteranomaly)[2].

Finally, all study subjects underwent anterior and posterior segment ocular health examination by an ophthalmologist using a slit-lamp biomicroscope (B900, Haag-Streit AG, Bern, Switzerland) and a +90 diopter (D) lens. Exclusion criteria were history of ocular surgery and BCVA worse than 6/60.

Statistical Analysis The prevalence and 95% confidence interval (CI) of CVD was reported in the whole sample and by age, sex, and some underlying diseases. The cluster sampling method was taken into account in calculating the standard error. Multiple logistic regression was used to investigate relationships.

RESULTS

Of the 3791 invitees, 3310 participated in the TGES. After applying the exclusion criteria, the final analysis was performed on the data of 2164 individuals. Of these, 1248 (57.7%) were female and the mean age of the analyzed subjects was 68.12±6.26y (range: 60–92y). The overall prevalence of CVD was 3.73% (95%CI: 2.37%–5.09%) in the whole sample. The prevalence of CVD types was as follows: 1.51% protanomaly, 1.76% protanopia, and 0.45% deuteranopia. Table 1 shows the prevalence of CVD by study variables. As seen in Table 1, the prevalence of CVD was higher in men, the odds ratio (OR) of CVD in men were 3.33 times that of women (P<0.001). The prevalence of CVD increased with advancing age from 2.91% in the age group 60–64y to 5.8% in the age group ≥80y (P=0.070). According to the simple logistic regression, there was no statistically significant difference in the prevalence of CVD between diabetics and non-diabetics and between those with and without hypertension. Among ocular diseases, higher OR of CVD were observed only in glaucoma patients (OR=3.04, P=0.002). Based on the multiple logistic regression model, male sex and glaucoma were significantly related to CVD. Older age and hypertension also had a marginally significant relationship with CVD.

Table 1 The prevalence of color vision deficiency by study variables

Parameters	(95%CI) %
Total	3.73 (2.37–5.09)
Gender	
Male	5.67 (3.35–7.99)
Female	1.77 (0.96–2.59)
Age (y)	
60–64	2.91 (1.38–4.44)
65–69	3.49 (2.03–4.95)
70–74	3.70 (1.51–5.89)
75–79	4.70 (1.65–7.75)
≥80	5.80 (1.05–10.55)
Diabetes	
No	3.61 (2.14–5.08)
Yes	4.07 (2.09–6.04)
Hypertension	
No	2.18 (0.55–3.81)
Yes	4.11 (2.59–5.64)
Age-related macular degeneration	
No	3.59 (2.28–4.9)
Yes	4.47 (1.38–7.56)
Diabetic retinopathy	
No	3.71 (2.33–5.1)
Yes	4.02 (-0.70 to 8.74)
Glaucoma	
No	3.43 (2.20–4.65)
Yes	9.74 (2.77–16.72)
Cataract	
No	4.15 (2.34–5.96)
Yes	3.23 (1.75–4.72)
Type of color vision deficiency	
Protanomaly	1.51 (0.88–2.14)
Protanopia	1.76 (0.81–2.71)
Deuteranopia	0.45 (0.14–0.77)

DISCUSSION

The prevalence of CVD was 3.73% in the present study, which is close to the prevalence reported in South Korea (3.9%)[1]. However, the prevalence of CVD in the present study was lower than reported in the study by Jafarzadehpur *et al*[18]. Table 2[1,18,22,25-29] summarizes the findings of various studies regarding the prevalence of CVD among different populations and age groups. In general, it has been suggested that the prevalence of CVD in Asian countries is lower than in European countries such as Switzerland, England, Belgium, Finland, Germany, and France with an approximate prevalence rate of 8%[20]. This variety can be explained by the differences in ethnicity and geographical region[26].

Several studies previously investigated the prevalence of CVD in different cities of Iran, including Mashhad[22], Shahroud[18], and Tehran[25], and reported a higher prevalence compared to the present study. Various causes may contribute to this discrepancy, including differences in the studied population demographics, the sample size, and the test used for color vision screening. In the present study, we used the Ishihara test for CVD screening; this test is suitable for the diagnosis of RG-CVD and is designed for visual defects related to long/medium wave cone photoreceptors[2]. It should be noted that YB is the most common type of CVD in the population

Table 2 Summary of other studies concerning color vision deficiency in worldwide

Studies	Country	Sample size	Age (y)	Color vision test	Total (%)	Male (%)	Female (%)
Modarres *et al*, 1996[25]	Iran, Tehran	2058	12–14	Ishihara	8.18	-	-
Citirik *et al*, 2005[26]	Turkey	941	20–26	Ishihara	-	7.33	-
Reshadat *et al*, 2012[27]	Iran, Kermanshah	28009	22–71	Ishihara	-	2.8	-
Khalaj *et al*, 2014[28]	Iran, Qazvin	1853	10–25	Ishihara	3.49	2.56	0.93
Kim *et al*, 2019[1]	South Korea	2686	19–49	HRR	3.9	6.5	1.1
Jafarzadehpur *et al*, 2014[18]	Iran, Shahroud	5102	40–64	D-15	14.7	16.6	13.3
Alabdulmunem, 2011[29]	Saudi	7467	13–68	Ishihara and D-15	-	-	0.35
Hahsemi *et al*, 2019[22]	Iran, Mashhad	2628	7–90	D-15	13.93	15.85	12.96
This study	Iran, Tehran	2146	60–92	Ishihara	3.73	5.67	1.77

above 40 years old[21]. Considering that the Ishihara test is incapable of identifying short wave cone disorder that plays an important role in acquired CVD[2], these statistical differences among studies could be explained. In the studies conducted in Shahroud on individuals above 40 years of age, the Farnsworth D-15 test was used to precisely screen acquired CVD cases, which could significantly affect the observed results[18]. Other possible factors influencing the differences between the studies include the level of participants' cooperation during the test, a large number of immigrants and the high genetic diversity for random mating, and finally less consanguineous marriage, which pushes the population towards the Hardy-Weinberg equilibrium[30].

The present study showed a significant association between CVD and sex. Congenital CVD is an X-linked recessive disorder, so a higher prevalence is expected in men[31]. In the present study, the prevalence of CVD in men was 3.33 times that of women, which was similar to the reported sex-distribution pattern of the disease in China and Japan[16]. This similarity can be attributed to the large samples with high genetic diversity, and similar geographical locations (Asia). Moreover, the prevalence of CVD in men in the present study was lower compared to those found in northeast of Iran[22]. The prevalence of CVD in men in the present study was also significantly lower than reported in the study by Jafarzadehpur *et al*[18] in older adults 40 to 64 years of age in Shahroud; these differences are probably due to the differences in the age range and race of the studied population as well as type of test used for color vision screening. Jafarzadehpur *et al*'s[18] study used the D-15 test, which can well identify different types of CVD. In addition, some other possible influential factors such as pathological factors may also have influenced the observed findings. The prevalence of CVD in women in the present study was higher than the values presented in the study by Birch[20]; the mentioned study reviewed the reported prevalence of CVD in studies conducted before 2000 and reported the prevalence of CVD in women to be lower than 0.5%[20]. However, two studies conducted in Iran by Hashemi *et al*[22] and Jafarzadehpur *et al*[18] reported a much higher prevalence of CVD in Iranian women than in other parts of the world; the most important difference between the above two studies and the present study is that both studies used the D-15 test for color vision screening, which has the ability to detect different types of CVD.

The increase in CVD prevalence with advancing age is one of the notable findings of the present study. According to the results, the prevalence of CVD in people older than 80y was about twice the prevalence in individuals aged 60–64y. The age-related increase in the prevalence of CVD has also been observed in other studies such as studies by Kim *et al*[1] and Hashemi *et al*[22]. Physiological and pathological changes in the visual system seem to be the main cause of this phenomenon. It is well known that some ocular diseases such as optic neuropathy[32] and drug toxicity[13] are associated with RG-CVD and the prevalence of these diseases increases with age.

One of the controversial findings of the present study is the lack of association between the prevalence of CVD and AMD; a similar finding was also observed in the study by Jafarzadehpur *et al*[18]. However, a group of studies showed changes in color perception toward YB defects in patients with AMD. Vemela *et al*[6] stated that both YB and RG types of CVD were significantly more prevalent in AMD patients compared to healthy people of the same age; the mentioned study uses Color Assessment and Diagnostic Test and relates these defects to choroidal hypoxia and changes in the function of retinal cells. Also, Decleva *et al*[33] in their study found that with using Cambridge Color Test, color vision defects are seen in all three axes of protan, deutan and triran in patients with AMD. Failure to identify YB defects by the Ishihara test is the most important reason for the difference in the results of the present study compared to other studies in this field. However, despite the use of D-15 test, Jafarzadehpur *et al*[18] also did

not find a significant relationship between AMD and CVD in people aged 40 to 64y in Shahroud, Iran.

Acquired CVD occurs secondary to ocular and systemic diseases or side effects of drugs and poisons[34]. The present study showed a significant relationship between glaucoma and the prevalence of CVD. Similar studies have also indicated that glaucoma results in RG-CVD in advanced stages; this disease mainly causes YB and sometimes RG defects[7]. Various studies have shown that changes in color discrimination, even prior to noticeable visual field defects in patients with glaucoma[35]. Therefore, it is important to evaluate color vision in suspected glaucoma patients, especially by using tests that are capable to identify YB anomalies. The noteworthy point is that glaucoma was significantly related to CVD despite the use of the Ishihara test in the present study. So, contrary to the expectation that the majority of glaucoma patients have a YB-CVD[7], glaucoma has led to a RG-CVD in a significant percentage of study participants. Based on the type of CVD, supporting programs can be considered in the treatment and follow-up of patients with glaucoma.

In the present study, no significant association was found between diabetes and diabetic retinopathy with CVD. This is while most previous studies reported CVD in a high percentage of patients with diabetes, whether in the presence[36] or absence of diabetic retinopathy[37]. For example, Tan *et al*[38], observed that one in four patients with diabetes had CVD, with tritanomaly being the most common form of CVD in these patients. The present study differed from other studies in the type of test used; Tan *et al*[38] used the D-15 test, Sharma *et al*[36] used the Mansell 100-Hue test, Wolff *et al*[39] used the color confusion score, and the present study used the Ishihara test. The inability of the Ishihara test to detect YB defects has probably influenced the results obtained in the present study. Therefore, despite the results of the present study, changes in color perception toward YB defects should be carefully evaluated in the assessment of the quality of life and visual requirements of patients with diabetes.

Cataracts had no significant relationship with CVD in the present study, while they were associated with CVD, especially Tritan type in some studies[4]. Mehta *et al*[40] observed that the color discrimination score increased after cataract surgery for all three types of cones, and the greatest changes were related to S-cones. This finding indicates that the presence of cataracts changes color perception and most affected patients develop YB-CVD. In the study by Jafarzadehpur *et al*[18], there was also a direct relationship between cataracts and CVD (detected by the D-15 test). Like other relations above, the type of test used in the present study may have influenced the results.

Based on the type of photoreceptor involved, different types of CVD develop[41]. In the present study, the highest prevalence of CVD was related to protanopia with a prevalence of 1.76%, followed by protanomaly and deuteranopia with a prevalence of 1.51% and 0.45%, respectively. This finding differs from the results of most previous studies in this regard. For example, Shah *et al*[42] reported deuteranomaly as the most common type of CVD. Kim *et al*[1] also reported deutan defect as the most prevalent CVD in the elderly. The dominant finding of previous studies is the higher prevalence of CVD related to the green color photoreceptors[1,42]. The most important reason for this difference is probably the selection of the appropriate screening test based on the studied population's age distribution so that it has led to overestimation of protanomaly or underestimation of deuteranomaly.

Among the limitations we faced in conducting the present study was the impossibility of using other color vision diagnostic tests that require more cooperation, as mentioned in different parts of the text, the Ishihara test can only detect RG color vision defects. It is suggested that in future studies, other color vision tests should be used in a high sample size of the geriatric population, which, in addition to RG defects, can also examine YB defects and the results could properly generalized to the adult's population.

In conclusion, the present study showed color vision changes in the elderly with increasing age and in the presence of some pathological factors. Since the change in color perception could affect the person's performance, it is necessary to pay attention to this aspect of the visual system in the examinations of the elderly. By using a test capable of detecting YB color defects, a broader and better interpretation of color vision status can be obtained in the elderly population.

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CORRIGENDUM

Effects of *Lycium barbarum polysaccharide* on the photoinduced autophagy of retinal pigment epithelium cells

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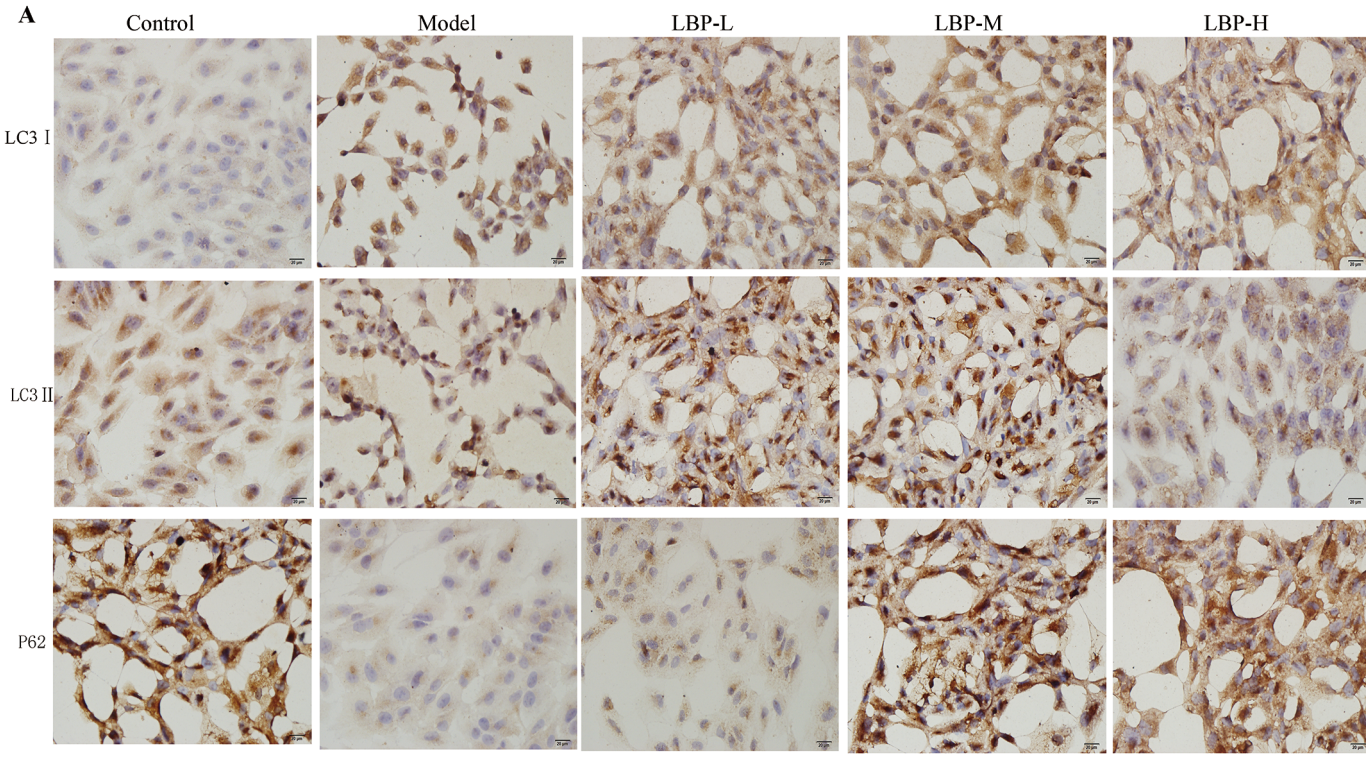
The authors would like to make the following change to the above article:
Part A in Figure 4 on page 27 should be changed as follows.



The authors apologize for any inconvenience caused by this error.