

Original research

Distribution of iris color and its association with ocular diseases in a rural population of Iran

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Abstract

Purpose: To determine the distribution of iris color and its relationship with some ocular diseases in a rural population of Iran.

Methods: Two rural areas of the north and southwest of Iran were selected by a cross-sectional study using multi-stage cluster sampling. After selecting samples, the participants had an eye examination including measuring visual acuity, refraction, and Pentacam imaging. Then an eye examination for individuals was performed by slit-lamp.

Results: Out of 3851 invited people, 3314 participated in this study (participation rate, 86.05%). Dark brown [41.28%, confidence interval (CI) 95% = 31.88–50.68] and blue (0.99%, CI 95% = 0.57–1.41) were the most and the least type of iris colors among participants of this study. Compared to others, people with a dark iris have the biggest anterior chamber depth (ACD), angle and volume while central corneal thickness (CCT), keratometry and pupil were highest among people with a dark brown iris ($P < 0.002$). Considering the dark brown group as a base group, the chances of being afflicted to cataract among people with dark, light brown, green, and blue irises are 1.89 (CI 95% = 1.25–2.86), 1.53 (CI 95% = 1.17–2.01), 4.60 (CI 95% = 2.17–9.71), and 12.17 (CI 95% = 5.05–29.31), respectively. The chance of being afflicted to myopia among people with green irises and to hyperopia among people with blue irises were high (1.60, CI 95% = 1.08–2.36 and 3.20, CI 95% = 1.03–9.97, respectively).

Conclusions: Dark brown was the most prevalent iris color in rural areas of Iran. The index of cornea among people with dark and dark brown iris color is higher than other people, and people with light iris color are at a higher risk of developing eye disease such as cataract, corneal opacity, and refractive error. To determine this relationship and its usage for therapeutic and public health purposes, further studies are recommended.

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Keywords: Iris color; Cornea indices; Ocular disease; Population-based cross-sectional study

Introduction

Iris color as a multifactorial hereditary trait varies depending on the race and ethnicity of people. It has been an object of interest to ophthalmology researchers due to absorption of ultraviolet radiation and protection of ocular tissue.¹

Unlike some genetic characteristics, iris color changes in early childhood. During infancy the iris color is brighter due to

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lack of pigments in the iris. Darkening occurs up to 6 years due to an increase in pigments.² On the other hand, iris color variation has been observed in different races. Blue-gray iris color is more common in most European^{3,4} and American^{5,6} countries, whereas dark and brown iris color are more common among Asians.^{7,8} Although iris color is attributed to the race, the geographical pattern may be due to sunlight.

Quite a few epidemiologic studies about iris color have been carried out.^{6,9–18} The first reason can be the relationship between iris color and eye diseases. The studies have shown that people with dark irises have a high risk for getting cataract, especially nuclear and posterior subcapsular cataract.^{9,13,14,16} In this regard, the risk of age-related macular degeneration is high among people with light irises.^{11,12,17} Even by controlling the effective variable on death, blue or gray irises are a death factor for death from choroidal melanoma.⁶ The relationships between iris color and intraocular pressure,^{10,13,17} myopia,¹⁵ ocular uveal melanoma,¹⁶ and other diseases such as diabetes^{3,19} and blood pressure²⁰ have been reported in other studies. The importance of the relationship between the iris color and the above-mentioned diseases is such that most of them are controllable even if they have a heavy health burden. The other reason for studying iris color is its relationship with the cornea indices as the values of anterior chamber depth (ACD), central corneal thickness (CCT),²¹ and pupil size²² are different for different colors.

Because of the racial, genetic, and geographical diversity that existed in Iran, various studies have been carried out regarding eye diseases in Iran,^{23–25} and only one of them¹³ has pointed to iris color and its relationship with eye diseases. In 2015, a cross-sectional study was conducted in two villages to survey eye problems in deprived rural areas, and delivered the comprehensive information on the condition of eye diseases in these areas. Due to the lack of information about the distribution of iris color in the other areas of Iran, the relationship of iris color with some of the important eye disorders such as refractive error, cornea opacity, and the distribution of corneal index in types of iris color, we aimed to carry out a study to cover these defects in present research.

Methods

Setting and sampling

The present population-based, cross-sectional study was conducted in 2015. First, based on the districts, two districts were randomly selected from the north and the southwest of Iran. These districts consisted of Shahyoun (a suburb of Dezful in Khuzestan province) and Kojur (a suburb of Noshahr in Mazandaran province) (Fig. 1). Then a list of all the villages in each district were prepared, and some villages were selected at random (15 villages for Shahyoun and 5 villages for Kojur). Next, collaborating with the officials of villages, all people residing over 1 year were asked to participate in the study. Permission to participate was obtained for those under 18 years of age from their families. All participants were delivered informed consent.

Collecting demographic information and doing ophthalmic examinations

Demographic information such as age and gender were collected through interviews by means of a form. Then optometry and ophthalmology examinations were taken by two optometrists in a place with standard light.

First, the uncorrected visual acuity was measured at a 6-m distance by means of Snellen chart for all people. Lea Symbols acuity chart was used for children aged 5 and under. In the next step, non-cycloplegic auto-refraction was done through Nidek Ref/Keratometer ARK-510A. Then the result of non-cycloplegic auto-refraction was refined through Heine Beta 200 retinoscope, HEINE Optotechnik, Germany. Subjective refraction was conducted to determine the best corrected vision.

In the next stage, the ocular health examination was performed using slit-lamp biomicroscopy (BM 900, Haag Streit, USA), and finally, all participants over the age of 5 underwent imaging using the latest version (6.03r11) of the Pentacam HR (Oculus, Inc., Lynnwood, WA). In the case of measurement error displayed by the device, imaging was repeated 10 min after instillation of artificial tears. To minimize the impact of diurnal variations, all imaging sessions were held between 9 am and 2 pm allowing for at least 3 h of awake time by the time of the examinations.

Definitions

In the present study, the iris color of the participants was determined by an ophthalmologist (H.M.). The pattern of iris color categorization in this study was consistent with the Tehran Eye Study.¹³ According to Fig. 2, the iris color was categorized into five groups. If the ophthalmologist suspected more than one color, the dominant color was selected as the iris color. If the iris color was different between central and peripheral parts of iris or pupil border, we considered the dominant color that overall reflected the eye's color.

Cataract was determined based on LOCS3 in this study, and spherical equivalent was used to determine the refractive error. Myopia, hyperopia, and astigmatism were defined as <-0.50 , $>+0.5$, and <-0.5 , respectively. In this study, the right eye color was used for analysis.

Analysis

The prevalence of various iris colors and their 95% confidence interval (CI) was determined. ANOVA was used to assess the relationship between the iris color and corneal indices. If ANOVA was significant, Scheffe's-post hoc test was applied for pairwise comparison. Multiple logistic regression was used to evaluate the relationship between the iris color and demographic variables, and simple logistic regression was applied to assess the association of the iris color with diseases (cataract, corneal opacity, refractive errors, and tropia) using the odds ratio (OR) and 95% CI. Cluster effect was applied to

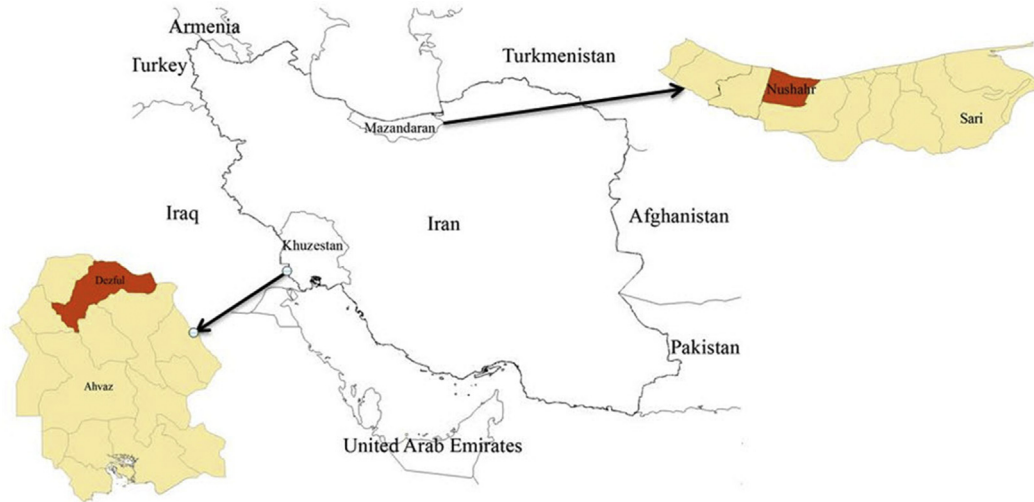


Fig. 1. Position of selected districts of study.

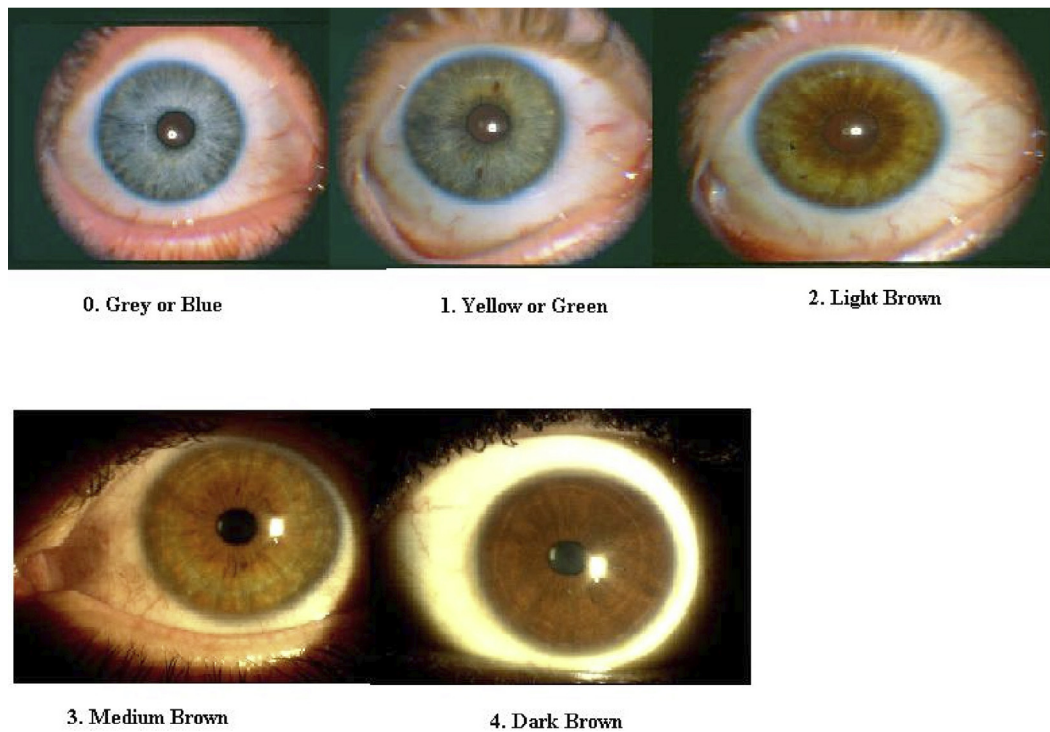


Fig. 2. Iris color definition patterns. (The iris color categorization is similar to the Tehran Eye Study. This figure is adopted from the Tehran Eye Study.¹³).

improve the accuracy of analysis. All analyses were investigated on STATA Software, Version 11, at 0.05 significance level.

Ethical issues

The Ethics Committee of Shahid Beheshti University of Medical Sciences approved the study protocol, which was conducted in accord with the tenets of the Declaration of Helsinki. All participants signed a written informed consent.

Results

Out of 3851 invited people, 3314 participated in this study (participation rate, 86.05%). The mean age of participants was 21.4 ± 37.4 years (range, 2 to 93). 56% (1867 people) were female, and 56.4% (1869 people) lived in rural areas of the southwest.

Table 1 illustrates the distribution of iris color according to age, gender, and place of residence. Accordingly, the highest and lowest kind of iris color among participants studies were

Table 1
Distribution of iris color in terms of age, gender, and place in rural population, Iran, 2015.

		Dark	Dark brown	Light brown	Green	Blue
		% (95%CI)	% (95%CI)	% (95%CI)	% (95%CI)	% (95%CI)
Gender	Total	28.97 (9.20–48.74)	41.28 (31.88–50.68)	20.92 (10.19–31.65)	7.83 (5.56–10.11)	0.99 (0.57–1.41)
	Female	27.20 (7.99–46.40)	44.16 (35.00–53.31)	21.24 (10.02–32.46)	6.95 (5.29–8.61)	0.46 (0.10–0.81)
	Male	31.26 (10.36–52.17)	37.57 (27.93–47.22)	20.51 (10.16–30.87)	8.97 (5.54–12.41)	1.68 (0.77–2.59)
Region	Southern-west	45.80 (32.97–58.63)	33.05 (25.06–41.05)	12.44 (5.97–18.92)	7.33 (4.73–9.93)	1.37 (0.53–2.22)
	North	7.21 (1.24–17.16)	51.92 (45.85–58.00)	31.89 (24.51–39.26)	8.49 (4.55–12.43)	0.49 (0.04–0.95)
Age	≤5	29.35 (11.27–47.42)	46.74 (34.56–58.92)	18.48 (6.81–30.15)	5.43 (0.38–10.49)	0
	6–20	29.81 (13.55–46.08)	46.30 (37.05–55.54)	18.33 (7.39–29.28)	5.56 (2.83–8.28)	0
	21–30	34.82 (15.98–53.66)	41.21 (29.92–52.50)	18.53 (9.36–27.70)	5.43 (1.86–9.01)	0
	31–40	29.39 (9.26–49.53)	43.80 (34.45–53.16)	21.61 (7.40–35.83)	5.19 (2.37–8.01)	0
	41–50	25.41 (6.29–44.53)	44.54 (34.18–54.89)	20.77 (8.33–33.20)	8.74 (5.05–12.44)	0.55 (0.11–0.98)
	51–60	27.41 (2.69–52.13)	41.43 (25.46–57.40)	21.18 (10.99–31.38)	7.79 (3.10–12.48)	2.18 (0.51–3.85)
	61–70	26.09 (1.12–54.01)	28.57 (14.18–42.96)	31.06 (16.51–45.61)	11.18 (2.29–20.07)	3.11 (0.38–5.83)
	>70	27.47 (3.39–51.56)	23.63 (12.18–35.07)	23.63 (12.03–35.22)	20.33 (6.24–34.42)	4.95 (1.03–8.86)

CI: Confidence interval.

dark brown (41.28%, CI 95% = 31.88–50.68) and blue (0.99%, CI 95% = 0.57–1.41), respectively. Dark brown iris color had the highest percentage among women and men, (44.16%, CI 95% = 35–53.31) and (37.57%, CI 95% = 27.93–47.22), respectively. Dark brown was the highest frequent color whereas blue was the lowest frequent color among all age groups except 61–70 and above 70. Other colors are listed in the table.

The results of multiple logistic regression for the association of demographic variables and iris color showed that people living in the north had lower odds of having dark brown iris color as compared to those living in the south of Iran (0.09, 95% CI: 0.2–0.41). The odds of having a dark brown iris decreased with ageing while the odds of having a blue iris increased with ageing (Table 2).

The results in Table 3 show that ACD has a significant difference based on the iris color ($P < 0.001$). In this regard, people with dark irises have deeper ACD than people with blue and green irises. People with blue irises have lower ACD in contrast to the other colors. Keratometry comparison showed that its value varies based on the iris color among the people studied ($P < 0.001$). The dark brown iris group had higher keratometry in contrast to the dark iris group. Similarly,

pupil diameter was different according to iris color ($P < 0.001$). Based on the results of Scheffe's-post hoc, pupil diameter for people with dark irises was lower than those who had light brown and dark brown irises. Angle, CCT, and chamber volume like other corneal indices had significant differences among various groups ($P < 0.002$, all of them). The results of Scheffe's-post hoc are shown in Table 3.

The relationship between some of the eye diseases was analyzed in this study; Table 4 includes the iris color. Assuming the dark brown group as the base group, the chance of being afflicted with cataract becomes high among people with dark, light brown, green and blue irises. Meanwhile, people with blue irises have a high chance of being afflicted with corneal opacity. The chance of being afflicted with astigmatism was high among light brown, green, and blue irises, whereas the chance of being afflicted with myopia was high among people with green irises people and with hyperopia among blue irises.

Discussion

Although iris color is mostly under the influence of genetics and ethnicity, studying the distribution and analyzing its

Table 2
Result of multiple logistic regression between iris color and demographic variables in study population, Iran, 2015.

		Dark	Dark brown	Light brown	Green	Blue
		OR (95%CI)	OR (95%CI)	OR (95%CI)	OR (95%CI)	OR (95%CI)
Sex	(Mal = 1/female = 0)	1.00 (0.8–1.26)	0.83 (0.69–1)	1.10 (0.97–1.25)	1.28 (0.9–1.83)	3.09 (1.22–7.84)
Region	(North = 1/southern-west = 0)	*0.09 (0.02–0.41)	*2.45 (1.65–3.63)	*3.30 (1.71–6.37)	1.07 (0.63–1.82)	0.24 (0.05–1.09)
Age (year)	≤5	1.35 (0.89–2.05)	0.91 (0.72–1.14)	0.85 (0.63–1.14)	0.95 (0.42–2.17)	–
	6–20	1	1	1	1	–
	21–30	1.02 (0.71–1.47)	0.89 (0.63–1.25)	1.20 (0.68–2.12)	1.00 (0.51–1.97)	–
	31–40	1.17 (0.93–1.49)	*0.82 (0.71–0.95)	1.13 (0.84–1.5)	0.94 (0.51–1.74)	–
	41–50	0.86 (0.6–1.23)	0.88 (0.71–1.09)	1.11 (0.85–1.46)	1.65 (0.99–2.74)	1
	51–60	1.24 (0.63–2.45)	0.70 (0.37–1.31)	1.00 (0.56–1.8)	1.44 (0.62–3.32)	4.05 (0.83–19.72)
	61–70	1.65 (0.7–3.89)	*0.34 (0.17–0.71)	1.5 (0.92–2.47)	2.14 (0.72–6.35)	*5.83 (1.11–30.47)
	>70	1.29 (0.63–2.66)	*0.30 (0.15–0.58)	1.14 (0.72–1.8)	4.24 (1.45–12.34)	*9.46 (2.01–44.40)

OR: Odds ratio; CI: Confidence interval.

Base groups = 6–20 Year, * Significance at 0.05.

In dark, dark brown, light brown and green color, age group 6–20 is baseline and in blue color, 41–50 is baseline group.

Table 3
Mean of corneal index in terms of iris color in rural population, Iran, 2015.

Corneal index	Mean \pm SD					P-value	Post hoc
	Dark	Dark brown	Light brown	Green	Blue		
ACD (mm)	3.40 \pm 0.44	3.36 \pm 0.41	3.34 \pm 0.41	3.29 \pm 0.38	2.62 \pm 0.51	<0.001	D > G D > B DB > B LB > B G > B
Keratometry (diopter)	43.31 \pm 1.45	43.61 \pm 1.39	43.49 \pm 1.53	43.43 \pm 1.46	43.51 \pm 2.43	<0.001	DB > D
Pupil (mm)	3.31 \pm 0.73	3.50 \pm 0.76	3.45 \pm 0.74	3.33 \pm 0.70	3.10 \pm 0.41	<0.001	DB > D LB > D
Angle (degree)	35.34 \pm 7.11	34.95 \pm 6.74	34.16 \pm 6.93	33.22 \pm 7.25	27.57 \pm 4.77	<0.001	D > G D > B DB > G DB > B LB > B
Volume (mm)	160.15 \pm 40.36	159.80 \pm 40.25	156.22 \pm 40.00	152.13 \pm 40.59	114.49 \pm 20.65	<0.001	D > B DB > B LB > B G > B
CCT (μ m)	536 \pm 39	538 \pm 37	538 \pm 38	531 \pm 39	513 \pm 36	<0.002	DB > B

ACD: Anterior chamber depth; CCT: Central corneal thickness; D: Dark; DB: Dark brown; LB: Light brown; G: Green; B: blue.

Table 4
Relationship (odds ratio) between some ocular diseases and iris color in rural population, Iran, 2015.

Iris color	Cataract	Corneal opacity	Astigmatism	Myopia	Hyperopia	Tropia
	OR (95%CI)	OR (95%CI)	OR (95%CI)	OR (95%CI)	OR (95%CI)	OR (95%CI)
Dark	1.89 (1.25–2.86)*	1.97 (0.46–8.39)	1.13 (0.86–1.48)	1.01 (0.75–1.34)	1.17 (0.92–1.51)	0.58 (0.30–1.09)
Light brown	1.53 (1.17–2.01)*	3.00 (0.41–22.01)	1.31 (1.03–1.67)*	1.13 (0.88–1.46)	0.99 (0.55–1.79)	0.89 (0.67–1.19)
Green	4.60 (2.17–9.71)*	1.99 (0.28–13.72)	2.29 (1.44–3.64)*	1.60 (1.08–2.36)*	1.51 (0.89–2.56)	0.87 (0.42–1.77)
Blue	12.17 (5.05–29.31)*	33.02 (20.68–52.70)*	4.76 (1.44–15.70)*	0.72 (0.13–3.75)	3.20 (1.03–9.97)*	1.80 (0.33–9.62)

OR: Odds ratio; CI: Confidence interval.

Dark brown is base-line, * Significance at 0.05.

relationship with eye diseases can justify the high outbreak of diseases among various populations. Despite the importance of iris color and its relationship with eye diseases, only one study¹³ has been carried out among the urban population of Iran. Our study is the second to analyze iris color among the Iranian population and the first to study it among the rural population.

A unified category has not been presented by now for iris color, and the studies have used different categories.^{1,4,5,11–13,26,27} In this regard, the literature review has to be

done carefully. Table 5 shows the most prevalent kinds of iris color in various studies. Our participants included 70% dark eyes (dark and dark brown) and 30% light eyes (light brown, green, and blue). The dark brown and blue irises have the highest frequency (41.28%) and the lowest frequency (0.99%), respectively. Hashemi et al.¹³ showed that medium-brown has a higher prevalence among people 40 to 64 years old in Tehran, which was in harmony with our findings, even though this distribution was different for other findings of projects. Sturm⁴

Table 5
The most common iris color in different populations of the world.

Study	Year	Sample size	Age	Place	Most prevalence iris color
Sturm et al. ⁴	2008	3011	12 years old	Northern European	Blue/gray
Tomany et al. ⁵	1990	4926	43–86 years old	America	Blue/gray
Regan et al. ⁶	1999	1162	59–60 years old (average)	America	Blue/gray
Younan et al. ¹⁴	1994	3654	Over 49 years old	Australia	Blue
Nicolas et al. ¹¹	1995	171	52–93 years old	European people in Australia	Blue
Iida et al. ⁷	2009	523	–	Japanese people	Brown
Chang et al. ⁸	2007	401	13–80 years old	Seoul (Korea)	Brown
Iran					
Hashemi et al. ¹³	2010	4200	Upper than 7 years old	Tehran	Medium brown
Current study	2015	3411	Upper than 1 years old	Rural place in north and southeast	Dark brown

studied Europeans, and Tomany⁵ and Regan⁶ studied Americans. They showed that the most frequent iris color was blue/gray (27.7%, 51.6%, and 48%, respectively). Blue Mountains Eye Study¹⁴ in Australia and Nicolas¹¹ studied Europeans residing in Australia and showed that blue irises had the highest frequency (50% and 65.5%, respectively). The difference in iris color distribution can be due to genetic and racial differences.

Our findings showed that residents in the southwest of Iran had darker irises and that residents in the north had lighter eyes (Table 1). Although justifying this difference is complex and environmental factors may have an effect in addition to genetic and ethnic factors, the most important justification can be the difference in the rate of sunlight; that is, due to high sunlight in the southwest of Iran, the eye produces more melanin in order to avoid damaging the retina and interior parts of eye. There is a similar mechanism for skin¹⁵ so that the residents in regions with a high rate of sunlight have darker skin to decrease skin cancer.

Another finding was that iris color changes because of age. The higher age groups had a reduction in darkness of iris color. Likewise, a light iris color increased for the higher age groups. However, these changes were significant only in dark brown and blue iris groups. Iris color becomes darker as age increases, but these changes occur until about 6 years old, after which the iris color remains stable.² Therefore, because of the cross-sectional nature of this study, the relationship between age and iris color can be due to the cohort effect.²⁸

In our study, gender-based iris color frequency did not show a specific pattern so that with the exception of dark brown and light brown, which were higher among women, other colors were prevalent among men. As a result, inter-gender differences were not significant in our study, which was in harmony with other studies.¹³

In this study, we analyzed the relationship between iris color and some of the cornea indices because some of these indices such as CCT, ACD, and pupil size have a relationship with most eye diseases such as glaucoma, corneal diseases, cataract surgery, and intraocular lens implantation.²¹ Meanwhile, various studies have shown the relationship between the iris color and the above-mentioned diseases.^{9,13,29} Therefore, analyzing the relationship between the iris color and the corneal index can be effective in understanding the diseases and their preventive methods.

This study showed that the average ACD, CCT, and pupil size was high among dark-eyed people whereas its value was low among light-eyed people. The lowest value for ACD, CCT, and pupil size was among people with blue irises. Cosar et al.²¹ have confirmed the ACD and the high value of CCT among dark-eyed people, but there is a paradox about the pupil size in the case that some research has not found a difference in the pupil size between dark irises and light irises.^{21,30,31} Richardson²² found a large pupil size among people with lighter iris. For keratometry, a reductionist or holistic pattern has not been found based on iris color whereas the results of the study showed that dark brown-eyed people have a high keratometry value in contrast to brown-eyed-people. Results of other studies do not support this finding.³²

One of the most important findings of our study was the analysis of the relationship between eye diseases and iris color. In this regard, our study showed that people with light eye color such as blue, green, and light brown have a higher chance of being afflicted with cataract, which is in harmony with Hashemi et al.¹³ Bochow³² showed that people with blue irises are at high risk to posterior subcapsular cataract. It seems that because people with dark irises have more melanin, they absorb ultraviolet ray, avoid damaging the lens, and consequently, bring about cataract.⁹ However, other studies represented very paradoxical results, that is, cataract is in higher extent among dark-eyed people^{9,14,16} because dark colors absorb more light. This issue causes the temperature to increase in the eye context, gradually increasing the risk for cataract.⁹ The paradoxes in the above-mentioned studies can be due to the environmental conditions, lifestyle, exposure extent to sunlight, and, most importantly, race and genetics. Therefore, further studies are recommended through stronger designs such as meta-analysis.

According to our findings, the risk of corneal opacity in people with blue irises is 33 times more than people with dark brown irises. Despite our extensive study, a similar study about the relationship between corneal opacity and iris color was not found. Only one study⁸ admitted the impact of the anomalies of the iris on the corneal opacity. Therefore, we can say that this is the first time that the relationship between the colors blue iris and corneal opacity risk is reported.

Another finding of our study was the relationship between iris color and refractive error. In this regard, people with light eyes had a high chance of being afflicted with astigmatism (Table 4). On the other hand, people with green irises had a higher risk for myopia (OR = 1.60; CI 95%: 1.08–2.36), while the chance of hyperopia was high for men with blue irises (OR = 3.20; CI 95%: 1.03–9.97).

It can be inferred that the risk of refractive error is high for people with light-colored irises. Cosar's²¹ results were not in harmony with our findings because he showed that dark-eyed people have more negative spherical equivalence. Studying animal models also showed that dark- and gray-eyed animals have a higher probability of myopia.¹⁵ This relationship, however, can be affected by genetics and the environment. Winn has not found a relationship between eye color and refractive error.³¹

A high sample size, high rate of participation, and careful examination by experts are the strengths of the study. Since the areas and subjects of the study were selected randomly, the sample is a representative of the rural population, and the results can be generalized to the entire rural population of Iran. For using a cross-sectional study, the observed relationship cannot be viewed as a causal relationship. To confirm the observed relationships and determine the possible mechanism, longitudinal studies are recommended. The present study has some limitations which should be taken into account. Failure to consider some factors as exclusion criteria such as uveitis, trauma, and history of surgery was one of major limitations of our study, as these conditions can affect iris color. The other limitation of this study was the lack of repeatability in

determining the iris color by the ophthalmologist. However, the large sample size decreased random error. In summary, we can conclude that dark brown and dark iris colors are the most prevalent in the rural population of Iran. People with dark iris colors have a deeper ACD, larger angle, and more volume than others, while the pupil size, keratometry, and CCT were higher in people with dark brown iris. Since the risk of cataract, corneal opacity, and refractive error is higher among patients with light iris color (blue, green, and light brown), wearing sunglasses and using other preventive measures are recommended.

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