Distribution of Iris Colors and its Association with Ocular Disorder in the Tehran Eye Study

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Abstract

Purpose: To determine the distribution of iris colors in the population of Tehran and to assess possible associations between iris color and Ocular disorder

Methods: Through a stratified random cluster sampling approach, 160 clusters were selected in different municipality districts of Tehran, and the approached households were invited to a clinic. After the initial interview, all participants had complete eye examinations and their iris color was categorized as grey/blue, yellow/green, light brown, medium brown, and dark. Distributions were determined in percentages and possible correlations with race, refractive errors, visual impairment, cataracts, age-related macular degeneration (AMD). Intraocular pressure (IOP) was also examined.

Results: Out of 4230 participants aged 7 years or more, the iris color was determined in 4200 people; in 54.09% [95% confidence interval (CI) 51.74% to 56.44%] the iris color was medium brown as the most prevalent color, and in 1.96% (95% CI: 1.43% to 2.48%) the color was grey/blue as the least prevalent color. The inter-gender difference in iris color was not statistically significant (P=0.288). AMD showed the highest prevalence in light brown iris colors (P<0.001). Nuclear cataract and posterior subcapsular cataract (PSC) was significantly correlated with iris color, with higher risks of cataract among medium brown, light brown and yellow/green iris colors (P<0.001).

Conclusion: The most prevalent iris color in the population of Tehran was medium brown. In light of the observed correlation between the iris color and certain conditions such as cataract and AMD with lighter eye colors, further studies are recommended to investigate the probable associations.

Keywords: Iris Color, Ocular Disorder, Cross-Sectional Study

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Introduction

Eye color as a hereditary trait, has long been an object of interest to researchers in the fields of genetics, anthropometry, and ophthalmology.[1,2]

Some studies have addressed that the iris color may change by the age of 6. It has even been reported that nonpigmented iris presented during infancy but pigmentation may develop slowly over time. Not only the iris color may change progressively during early childhood, but physiological changes have also been reported to affect the index. Pregnancy, puberty, and even some traumas are among the probable causes.[3]

As a genetic factor, the iris color is indicative of certain races, and some reports have discussed its role in some eye diseases.[1,4-8] Iris color has also been suggested as a protective factor in the occurrence of some eye conditions.[8-10] The Blue Mountains Eye Study for instance, found a significant correlation between this variable and the intraocular pressure (IOP),[11] and its role in the occurrence of cataract, specially nuclear cataract which is more prevalent in dark brown irises than light blue ones.[12] Age-related macular degeneration (AMD), has been shown to be more prevalent among people who have blue and bright eyes.[4,13] Another association has been reported by Regan et al[7] and Saornil[14] who found a higher prevalence of ocular melanoma among light colored eyes. Here we present our findings in the Tehran Eye Study (TES) concerning the distribution of iris colors in the population of Tehran and the correlation between iris color and common eye conditions in a population in the Eastern Mediterranean region.

Methods

The TES was conducted as a population-based, cross-sectional study. The TES detailed protocol has been published elsewhere.[15] Here we present a brief review of the methodology.

The sampling strategy of the study followed a stratified cluster sampling procedure with proportional allocation within strata. The stratification of the sample according to the 22 municipal districts of Tehran was incorporated in the sampling process. A total of 160 clusters were randomly selected based on block enumeration of the national census of 1996 by the Statistical Center of Iran. For each cluster, a team consisting of two interviewers (one male and one female) approached the first household. They introduced themselves by their identification cards. Then they described the project to the members of the household who were present. At the end, all household members were invited for a complete eye examination at Noor Vision Correction Center. Enumeration was continued for 10 neighboring households by proceeding systematically in a clockwise direction from the initial household within the cluster.

All subjects included in this study were informed about the project and the procedures in their native language before being enrolled. The participant's agreement for examination was obtained verbally.

Examinations

All TES participants had complete eye examinations including manifest, subjective and cycloplegic refraction, uncorrected visual acuity (UCVA), best corrected visual acuity (BCVA), presenting visual acuity, color vision tests, IOP measurement, the slit-lamp exam, and fundoscopy.

Refraction examination, visual acuity (VA) measurement, and color vision test were done by an optometrist. IOP measurement, fundoscopy and other eye examinations were performed by an ophthalmologist.

The main index for cataract was all lens changes defined as all participants with a history of cataract surgery or the presence of a gradable cataract in either eye. A gradable cataract was defined as LOCS III grade of three or more in cortical and/or Nuclear and/or a grade of two or more in Posterior subcapsular. IOP was measured using a Goldmann applanation tonometer. Then all participants underwent a retinal examination first using direct ophthalmoscopy followed by indirect ophthalmoscopy. The retina was examined systematically to ensure that no lesions are missed. The examiner inspected the optic disc assessing disc size, color, vascularity, and degree of cupping. AMD was defined by the presence of the following abnormalities in the macular area: soft drasen or hypo- or hyperpigmentation of the retinal pigment epithelium (RPE) associated with drasen in

the absence of AMD, or as the presence of either geographic atrophy or neovascular AMD.

In the interview, participants were asked about their personal details, history of ocular disease or trauma, diabetes, high blood pressure, and previous eye examinations.

Iris color

To determine the iris color, the participant's iris and undilated pupil was illuminated with a penlight. The color was compared to standards developed in accordance with the Beaver Dam Eye Study.[16]

Iris color definition pattern is presented in Figure 1. The definitions of "yellow or green", "gray or blue", "light brown" colors were based on Beaver Dam eye study. Furthermore, based on iris color of the country's population, we add two other medium and dark brown colors to the study color pattern.

The amount of pigment in the iris was taken into account rather than the actual color. When an iris has more than one color, the grade is assigned based on the color which is 50% or more.

Statistical analyses

The prevalence of each eye color and their confidence intervals (CI) were determined. In calculating standard errors and 95% CI, the cluster sampling design was taken into account. Rates were directly standardized for age and gender according to the 1996 Tehran population using data from the Iranian Statistics Center. We used logistic regression tests to assess associations between iris color and other potential factors and report odds ratios (OR). In the regression model, iris color was analyzed as a dummy variable, and "dark" was set as the comparison basis for other colors.

Because of some reports about the changes of the iris color by the age of 6, the individuals under the age of 7 were excluded from the study.[3]

Results

During the study period from July to November 2002, a total of 6,497 people were selected through a stratified cluster sampling approach, and 4565 eligible samples took part in the study (response rate, 70.3%). Of 4,565 eligible samples, 335 participants aged lower than 7 years were excluded from analysis. The mean age of the participants was 32.13±17.94 (range, 7 to 96) years, and 41.3% (1747 people) of them were male. In terms of ethnicity, 80.6% were Persian, 16.2% were Turk, 1.4% were Kurd, 0.3% were Arab, 0.4% were Afghan and 1.1% were from other ethnic groups. Iris color was determined in 4,200 of the 4,230 participants.

The iris color was "medium brown" in 54.09% (95% CI: 51.74% to 56.44%) as the most prevalent color, and "grey or blue" in only 1.96% (95% CI: 1.43% to 2.48%) as the least prevalent one. The prevalence of "dark", "light brown", and "yellow or green" iris colors was 31.74 (95% CI: 29.02% to 34.45%), 9.60% (95% CI: 8.30% to 10.91%), and 2.56% (95% CI: 2.03% to 3.10%), respectively. The inter-gender differences in iris color were not statistically significant (P=0.288). Table 1 demonstrates the distribution of iris color in Tehran by ethnicity and their associations.

Logistic regression model results have also been presented in the table 1. As the analysis of the logistic regression shows, the distribution of the "dark" color among other people was less than Persians and the distribution of "yellow or green" and "light brown" was higher among Turks.

Assessment of the association between iris color and AMD is summarized in Table 2. The prevalence of AMD was highest among "light brown" irises with a rate of 3.97% (95% CI: 2.13% to 5.80%), and lowest among grey or blue with a rate of 0.91%. Using "dark" as the comparison basis in the logistic regression model demonstrated that "light brown" eyes are at a significantly higher risk of AMD than darker eyes (P<0.001).

Table 3 shows the prevalence of cataract among different iris color groups. The prevalence of cataract was highest among "yellow/green" irises with a rate of 9.40% (95% CI: 4.20% to 14.60%), and lowest among "grey/blue" eyes. The odds of cataract were significantly higher among "yellow/green" and "medium brown" iris colors compared to "dark" eyes (P<0.001). Assessment of cataract types showed that the prevalence of nuclear cataract in "dark" eyes was 1.91%, and the prevalence rates among "light brown", "medium brown", and "yellow/green" iris colors were significantly higher (P<0.001). Table 3 demonstrates the distribution of different types

of cataract among iris color groups. We found no significant association between iris color and cortical cataract. Posterior subcapsular cataract (PSC) was least prevalent among "dark" eyes, and most prevalent in "yellow/green" eyes. In the regression model, the odds of PSC in "yellow/green" eyes were significantly higher than in "dark" eyes (P<0.001).

Figure 2 shows the mean IOP in iris color groups. The highest IOP was found among "grey/blue" eyes and people with "yellow/green" eyes had the lowest IOP (14.65 and 14.10 mmHg, respectively). In the analysis of variance, the inter-group differences in IOP were statistically significant (P<0.001).
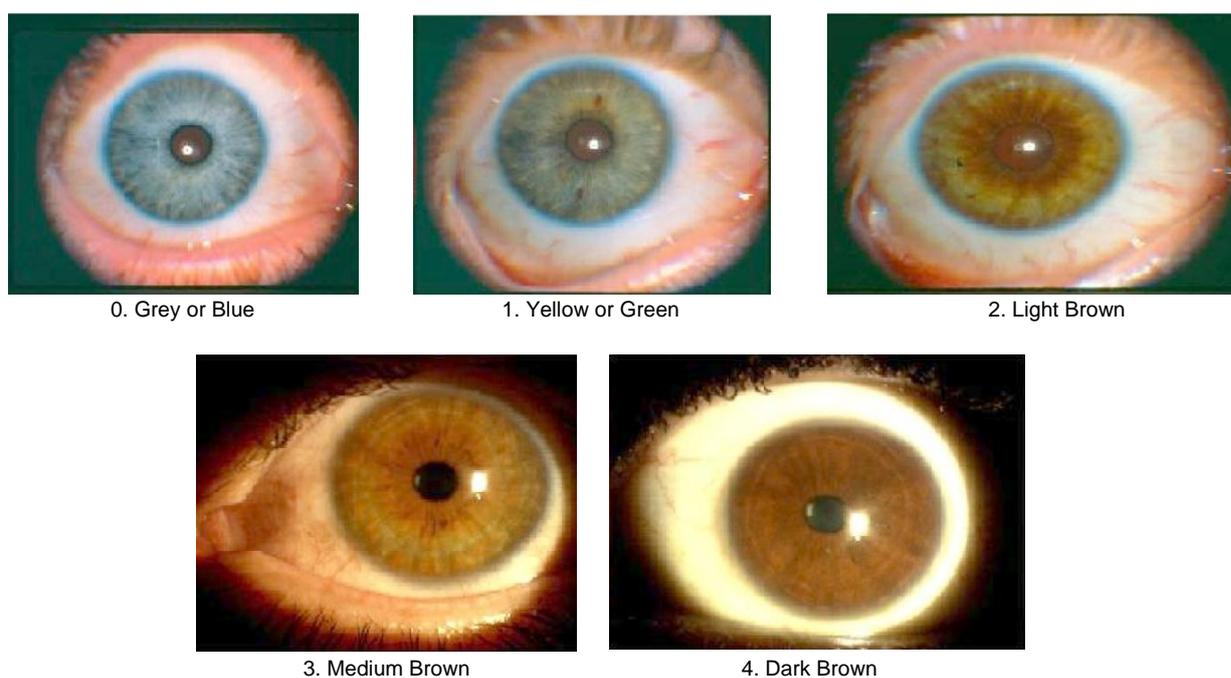

0. Grey or Blue   1. Yellow or Green   2. Light Brown

3. Medium Brown   4. Dark Brown

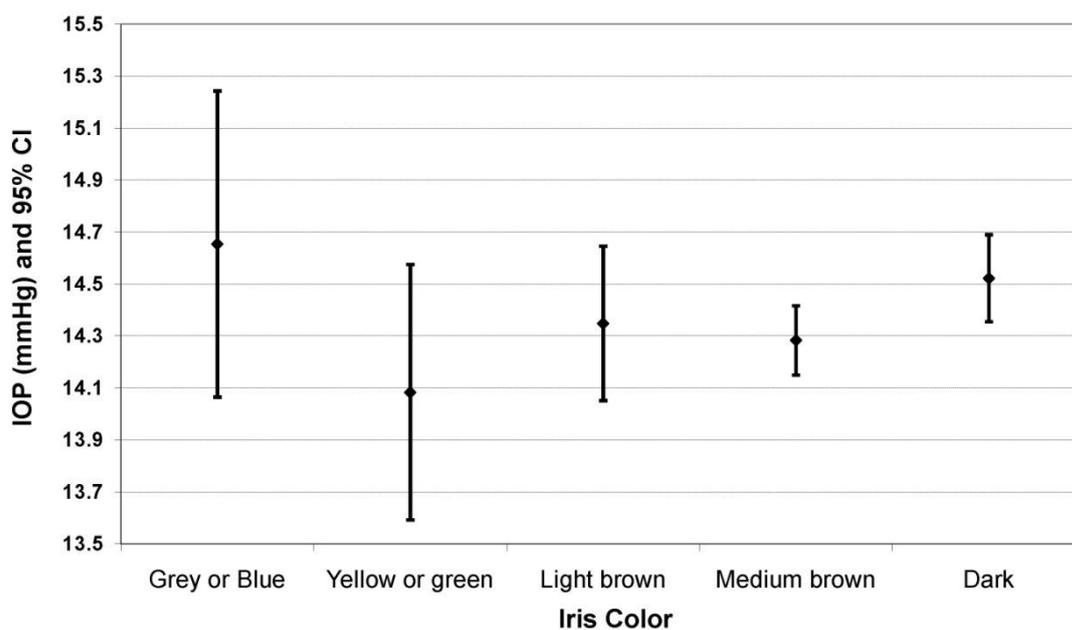**Figure 1.** Iris color definition patterns

Figure 2. Distribution of intraocular pressure by iris color

Table 1. Distribution of iris color by ethnicity

	Dark	Medium Brown	Light Brown	Yellow or Green	Grey or Blue
	% (95% CI)	% (95% CI)	% (95% CI)	% (95% CI)	% (95% CI)
Persian	32.90 (29.94-35.87)	53.98 (51.43-56.53)	8.83 (7.40-10.26)	2.31 (1.73-2.88)	1.91 (1.39-2.44)
Turk	27.62 (22.54-32.71)	53.08 (48.35-57.8)	13.12 (9.97-16.28)	3.96 (2.37-5.55)	2.22 (0.84-3.59)
Kurd	21.23 (7.11-35.35)	60.89 (42.96-78.82)	10.48 (1.72-19.24)	3.06 (0.39-7.42)*	4.34 (0.025-9.99)*
Arab	38.28 (21.77-54.8)	56.86 (41.67-72.04)	0	4.86 (0.08-16.31)*	0
Afghan	45.80 (44.89-46.72)	49.03 (44.08-53.98)	5.17 (1.13-9.20)	0	0
Other	17.27 (6.06-28.48)	61.86 (47.32-76.39)	18.97 (11.13-26.81)	1.91 (0.06-5.77)*	0
Total	31.74 (29.02-34.45)	54.09 (51.74-56.44)	9.60 (8.30-10.91)	2.56 (2.03-3.1)	1.96 (1.43-2.48)
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Persian ***	1	1	1	1	1
Turk	0.78 (0.6-1.02)	0.96 (0.79-1.18)	1.56 (1.14-2.13)**	1.74 (1.06-2.87)**	1.16 (0.61-2.19)
Kurd	0.55 (0.24-1.28)	1.33 (0.63-2.82)	1.21 (0.46-3.15)	1.34 (0.31-5.79)	2.33 (0.58-9.27)
Arab	1.26 (0.65-2.48)	1.12 (0.61-2.07)	-	2.16 (0.19-24.96)	-
Afghan	1.72 (1.5-1.99)	0.82 (0.65-1.03)	0.56 (0.24-1.31)	1.74 (1.06-2.87)	-
Other	0.43 (0.19-0.94)**	1.38 (0.74-2.57)	2.42 (1.39-4.21)**	0.82 (0.1-6.62)	-

CI: Confidence interval
OR: Odds ratio
*: The 95% CI was calculated using binomial distribution.
**: Statistically significant
***: Reference group

Table 2. Distribution of iris color by age-related macular degeneration

Iris color	Age-related macular degeneration		
	% (95% CI)	OR (95% CI)	P-value
Dark (reference group)	1.27 (0.68-1.85)	1	
Medium Brown	2.13 (1.51-2.75)	1.7 (0.96-2.99)	0.067
Light Brown	3.97 (2.13-5.8)	3.22 (1.68-6.17)**	<0.001
Yellow or Green	3.09 (0.08-6.1)	2.49 (0.8-7.71)	0.114
Grey or Blue	0.91 (0.2-2.73)*	0.72 (0.09-5.68)	0.752

CI: Confidence interval
OR: Odds ratio
*: The 95% CI was calculated using binomial distribution.
**: Statistically significant

Table 3. Distribution of iris color by cataract

Iris color	Cataract			
	Nuclear	**Cortical**	**Posterior subcapsular**	**Total**
	% (95% CI)	% (95% CI)	% (95% CI)	% (95% CI)
Dark	1.91 (1.17-2.65)	0.54 (0.18-0.91)	0.48 (0.07-0.90)	4.17 (2.95-5.40)
Medium Brown	4.79 (3.72-5.86)	0.78 (0.45-1.11)	0.65 (0.34-0.97)	6.16 (5.09-7.22)
Light Brown	4.59 (2.43-6.75)	0.45 (-0.18-1.07)	0.79 (0.07-1.69)*	6.26 (3.93-8.59)
Yellow or Green	5.11 (1.08-9.13)	1.95 (0.08-4.69)*	2.54 (0.05-5.39)*	9.40 (4.20-14.60)
Grey or Blue	2.41 (0.07-5.76)*	0	1.25 (0.28-3.69)*	3.34 (0.17-7.15)*
	OR (95% CI)	**OR(95% CI)**	**OR (95% CI)**	**OR (95% CI)**
Dark (reference group)	1	1	1	1
Medium Brown	2.58 (1.67-4.00)**	1.44 (0.65-3.17)	1.35 (0.50-3.65)	1.51 (1.06-2.14)**
Light Brown	2.47 (1.27-4.81)**	0.82 (0.17-3.9)	1.64 (0.39-6.89)	1.53 (0.91-2.58)
Yellow or Green	2.77 (1.13-6.79)**	3.65 (0.75-17.65)	5.35 (1.26-22.67)**	2.38 (1.22-4.65)**
Grey or Blue	1.27 (0.29-5.66)	-	2.60 (0.30-22.72)	0.79 (0.24-2.59)

CI: Confidence interval,
OR: Odds ratio
*: The 95% CI was calculated using binomial distribution.
**: Statistically significant

Discussion

The present report is part of the TES with the purpose to study the distribution of different iris colors and its association with other ocular variables and conditions. The color of the iris is affected by genetic and racial factors, and suggested as an independent factor in ocular conditions.[1,2] This report is one of the few reports in the world in which the distribution of iris color is studied in a population; nonetheless, use of different definitions and measurement techniques for iris colors makes comparisons with other reports difficult. Determining the association between iris color and different eye conditions can help us use iris color as a predictive factor in these conditions. For example, ocular melanoma, which is a life threatening disease, is more prevalent among blue and green eyes, and knowledge of this association can help in the diagnosis of ocular melanoma.[7,14,17] Furthermore, understanding the pathophysiology of such associations can be

of great importance in our understanding of disease processes.

Studies have used different definitions and grouping approaches for iris colors. Some have grouped them into 3 categories of "dark", "medium brown", and "light brown", which is quite similar to our approach, and others have grouped them in two categories of "tan/brown" and "dark brown". Here we found that more than 50% of Tehran's population has "medium brown" eyes, while "grey/blue" eyes were seen in only 1.96% of the population. This indicates a different distribution of iris colors in comparison to other studies which are mostly done in European countries.[18] In the Blue Mountains Eye Study, they found that about 47% of people had blue eyes, and only 10% of the population had dark brown iris colors.[11-13] Researchers in Beaver Dam Eye Study reported that iris colors were gray/blue in 51.6%, and tan/brown in 26.7%.[8] Differences in iris color prevalence and distribution in

different studies are attributable to genetics and races of studied populations.

AMD is one the most important eye conditions and its association with iris color has been reported by several studies.[4,8,9,13,19-21] Similarly, we found that light brown eyed people were at higher risk of AMD than people with dark eyes. In the Blue Mountains Eye Study,[13,20] people with lighter eye colors were at more risk for AMD, while in the Beaver Dam Eye Study, greater risk for AMD was found among those with brown eyes.[8] Overall, our results are different from those who found light eyes and blue eyes at higher risk for AMD such as that found in reports by Holz, Hyman, Weiter, Frank and Mitchell.[4,13,19,21,22] The main cause of this difference may be genetic and racial differences in the studied populations, as AMD, like iris color, is affected by racial factors. In people with bright eyes, the higher risk of AMD can be due to less pigments and more light transfer to the retina, which is again at greater risk of degeneration by light due to less pigmentation.

In terms of cataract, we found that people with medium brown and yellow or green eye were at greater risk than those with dark ones. Previous studies have found a higher risk of cataract among darker eye colors, and reported this to be a risk factor.[9,10,12,23] This contradicts our results in that we found greater odds for cataract among green yellow or green eyes as well. The association between nuclear cataract and dark eyes has been demonstrated by many studies, and our findings further confirm this.[9,12,23] On the other hand, findings on PSC are inconsistent. Some studies reported dark iris colors a risk factor for PSC, but Bochow et al[24] found an association between PSC and blue eyes while in our study, it was between PSC and yellow or green iris color.

Race has been suggested to affect IOP. In a study by Hiller,[5] the IOP was on average 2.0 mmHg lower in Caucasians compared to blacks, and IOP was found to have a linear correlation with iris pigmentation. Most reported a higher rate of glaucoma among people with darker eyes.[11,25]

In the Blue Mountain Eye Study, they found a significant correlation between iris color and IOP; the IOP was highest among people with darker eyes, and lowest in blue eyed people.[10] We found lowest IOP readings in our yellow/green group, and the IOP increased with iris pigmentation. However, highest IOP values were seen among people with blue eyes and this warrants more studies.

Iris pigmentation has been shown to reduce significantly from darker eyes to blue eyes, and should an eye condition be correlated with iris pigmentation, we would expect to see decreased or increased prevalence rates in the same order. However, the prevalence of some conditions such as AMD and cataracts increases in this range up to green, and then decreases. Similarly, we found the greatest IOP difference between green and blue. Therefore, it seems that there are other factors involved in addition to pigmentation, and further studies on the issues of iris color, pigmentation, and eye conditions are recommended.

Although the study had some strengths such as population-based sampling method and the sample size, a limitation of the study was the fact that the iris color was not digitally analyzed, which could led us to more precise results on iris color.

Conclusion

The most prevalent iris color in the people of Tehran was "dark brown". Some eye conditions such as AMD and cataracts are more prevalent among people with bright eyes, but the amount of pigmentation is not always a determinant. Further studies into the pathobiology of such associations are recommended.

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