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ORIGINAL ARTICLE

Distribution of intraocular pressure and central corneal thickness by age and gender: a population-based study

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Abstract

Purpose: The aim of the study was to examine the distribution of intraocular pressure (IOP) and central corneal thickness (CCT) by age and gender in the Turkish population.

Methods: In this population-based cross-sectional study, 3556 patients aged 40 years and older in Eskişehir were examined. Demographic, systemic, and eye health questions were asked of all subjects. IOP was measured with a Tono-Pen and a CCT ultrasound pachymeter. Statistical significance was accepted as $P < 0.05$.

Results: The mean age of the study was 56.86 ± 10.19 and 70.6% were women. The mean IOP was 16.06 ± 3.11 mm Hg and CCT was 553.83 ± 34.34 µm. IOP correlated positively with CCT ($r = 0.137$; $P < 0.001$). Age negatively correlated with IOP and CCT ($r = –0.057$, $P < 0.001$; $r = 0.037$, $P = 0.05$). When evaluated by gender, the mean age of women was 55.99 ± 9.98 years, IOP was 16.21 ± 3.10 mm Hg, and CCT was 552.44 ± 33.90 µm, whereas these values were 58.98 ± 10.41 years, 15.68 ± 3.11 mm Hg, and 557.17 ± 35.17 µm in men ($P < 0.001$ for each parameter). Multiple regression analysis revealed a significant correlation between IOP and CCT (unstandardized regression coefficient B = 0.013/µm, $P < 0.001$), age (B = –0.013/year, $P < 0.05$), and gender (B = 0.551, $P < 0.001$). CCT proved to be the independent variable with the greatest influence on IOP (standardized regression coefficient beta: 0.141, R2 = 0.028; F = 34.067; P = 0.000).

Conclusion: In our study, IOP and CCT decreased with age in both genders. IOP was found to be positively correlated with CCT and female gender and negatively correlated with age, and CCT was the key variable for IOP.

Keywords: Age; central corneal thickness; gender; intraocular pressure; population-based study.

Glaucoma, which ranks second among preventable causes of blindness worldwide, is a chronic progressive disease of the optic nerve that increases with age.[1] Intraocular pressure (IOP) is the only risk factor that can be controlled in the management of glaucoma.[2-6] Knowledge of IOP and the factors that influence it is important in planning the diagnosis and treatment of glaucoma. IOP has been reported to be related to age, gender, central corneal thickness (CCT), body mass index, diabetes, systemic blood pressure, iris color, and alcohol and cigarette use, but this relationship varies in different populations.[2,7-9] The distribution of IOP in the West and its related factors has been investigated in many population-based studies from Europe, America, East Asia, and Southeast Asia.[2-9,10-18] The mean IOP was

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approximately 2–5 mmHg higher in European and North American Caucasians than in East Asian populations.[2,4,6]

Knowing the distribution of IOP by age in a population is important in defining "normal IOP." Studies on this topic in Western societies[2,6,7,9] generally show an increase in IOP with age, whereas a negative correlation between age and IOP has been found in Japan and Eastern populations.[3,10-13] The reason for these conflicting results is unclear, and genetic (ethnic/racial) factors may be responsible for the differences.[3,8-13]

CCT, which is significantly associated with IOP, varies between societies and races.[17] The ocular hypertension treatment study underscored the association between IOP and CCT and reported that a thinner cornea is a strong risk indicator for developing glaucoma in people with ocular hypertension.[18] Therefore, the relationship between IOP and CCT is essential for accurate and reliable measurement and assessment in population screening and/or glaucoma diagnosis and follow-up.

There are few population-based studies to determine the factors associated with the distribution of IOP and CCT in the Turkish population. The aim of our study was to investigate the IOP and CCT values and their distribution by age and gender in the population over 40 years of age in Türkiye's Eskişehir region.

Materials and Methods

Individuals over 40 years of age living in four different regions of Eskişehir who agreed to participate in the study participated. After approval by the Ethics Committee of the Faculty of Medicine of Eskişehir Osmangazi University (Approval date and number: 2008/263), a questionnaire with questions on demographic characteristics and ocular and systemic factors was applied to individuals over 40 years of age who agreed to participate in the study. Patients whose examination could not be completed for any reason, who had difficulty cooperating, and who had ocular pathology that prevented IOP and CCT measurement were excluded from the study. Before measurement, a 0.5% proparacaine HCL local anesthetic was instilled, IOP (Tono-pen XL-Medtronic, Solan, Florida, USA), then CCT (Paclinepachymetry-optikon, Rome, Italy) was measured 3 times, first in the right eye and then in the left eye. The mean of the last three measurements was used for analysis. For the study, one eye from each participant was chosen at random.

The data of the participants who participated in the study were analyzed by gender and five age groups (40–49 years; 50–59 years; 60–69 years; 70–79 years; and over 80 years).

Statistical Analysis

For statistics, the SPSS 22.0 program (SPSS Inc., Chicago, IL, USA) was used to analyze the data. For normally distributed data, descriptive statistical tests, independent samples t-test, and analysis of variance were used to test the significant difference between groups. The relationship between the IOP and the independent CCT variables was assessed using the Pearson correlation test. The relationship between variables was determined by simple linear and multiple linear regressions analyzes. Statistical significance was achieved when $P \leq 0.05$.

Results

The study included 3556 individuals aged over 40 years registered in four different family medicine centers in Eskişehir province, Kaymaz Town, Esentepe, Şirintepe, and Osmangazi. The demographic characteristics of all cases are shown in Table 1. The mean age of the study participants was 56.86 ± 10.19 years, and 70.6% were women. Examination of the histograms of the IOP and CCT variables showed that the data associated with the variables conformed to the normal distribution (for IOP Fig. 1).

Table 1. Characteristics of the study population

Variable	Total number of participants=3556 (%)
Age	
Mean±SD	56.86±10.19
Median (range)	40–92
Age category	
40–49	995 (28)
50–59	1252 (35.2)
60–69	829 (23.3)
70–79	417 (11.7)
80+	63 (1.8)
Sex	
Female	2512 (70.6)
Male	1044 (29.4)
IOP (mmHg)	
Mean±SD	16.06±3.11
Median (range)	4–40
CCT (microns)	
Mean±SD	553.83±34.34
Median (range)	412–677

SD: Standard deviation, IOP: Intraocular pressure, CCT: Central corneal thickness.

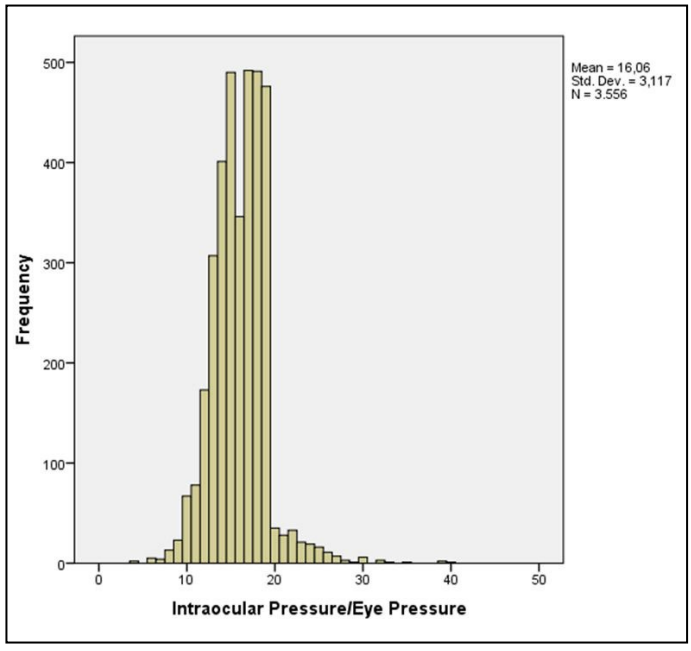

Fig. 1. Intraocular pressure distribution curve.

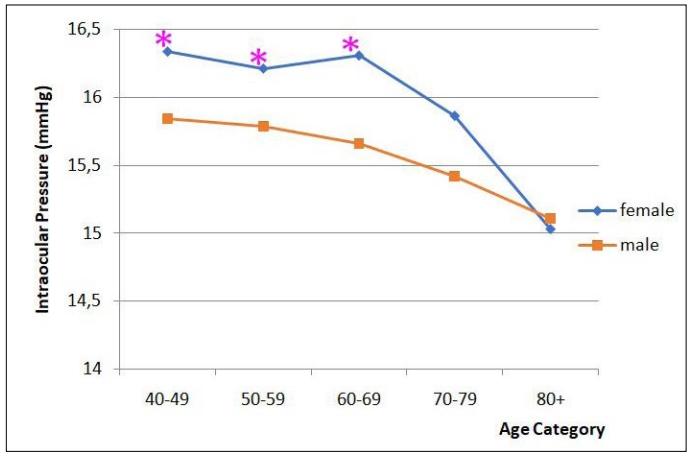

Fig. 2. Distribution of intraocular pressure by age groups in men and Women. *(P<0.05)

The change in IOP and CCT by age groups and gender is given in Table 2.

The mean IOP value of 3556 patients enrolled in the study was 16.06 ± 3.11 mm Hg, and 5% of them had an IOP value >20 mm Hg. The mean IOP value by gender was 16.21 ± 3.10 mm Hg in women and 15.68 ± 3.11 mm Hg in men, and there was a difference between them (P < 0.001).

When all cases were analyzed together, it was observed that IOP was negatively correlated with age (r = –0.057, P < 0.001), and the IOP value decreased with increasing age. Depending on the age group, the change in IOP was also statistically different (P = 0.004) (Table 2). The difference was significant between the age group of 40–49 years and the age group of 70–79 years (P = 0.023) and 80+ (P = 0.032).

The change in IOP with age was similar in men and women as in the general population, and there was a negative correlation (r = –0.045, P < 0.05; r = –0.055, P < 0.05, respectively). There was also a difference between age groups (P < 0.05 in both genders). When the changes in IOP between men and women were evaluated, it was found that IOP was higher in women aged 40–49, 50–59, and 60–69 years (P < 0.05 for each gender) (Fig. 2).

The simple linear regression model showed a negative change in IOP (IOP decreases with age) of 0.18 mm Hg every 10 years (P = 0.001). This change was 0.14 mm Hg in women and 0.16 mm Hg in men (P < 0.05 in both genders).

The mean CCT of all cases was 553.83 ± 34.34 µm, and it was 552.44 ± 33.9 µm in women and 557.17 ± 35.17 µm in men (P < 0.001) (Table 2).

There was a negative correlation between CCT value and age (r = –0.037, P < 0.05). There was a significant difference between age groups in CCT values (P = 0.023), and this difference persisted in women (P = 0.018) but was not statistically significant, although it decreased in men (P = 0.298) (Table 2).

Mean CCT values between genders were statistically different in the 50–59 and 70–79 age groups (P < 0.05 for each parameter), and CCT was thicker in men.

In a simple linear regression analysis, a negative change in CCT of 1.24 µm per decade was observed (P < 0.05). This change was 1.8 µm in women and 1.0 µm in men (P < 0.001, P < 0.05, respectively).

When the relationship between the CCT and the IOP variables was examined using simple and partial correlation analysis, a positive relationship was found between the variables (r = 0.137; r = 0.141, P < 0.001) (Table 3). It was observed that the relationship between CCT and IOP was similar in men and women as in the general population (r = 0.134; r = 0.167, P < 0.001, respectively).

Multiple regression analysis was used to analyze the change in IOP versus the change in CCT with the variables of age and gender. The results showed that IOP was positively correlated with CCT and female gender and negatively correlated with age. This relationship persisted in both univariate and multiple linear regression analyses. When other variables were held constant, IOP decreased by a mean of 0.13 mm Hg per decade (P < 0.05).

In the general population, each 100 µm increase in CCT was associated with a 1.3 mmHg increase in IOP (P < 0.001). A 100 µm increase in CCT was associated with a 1.2 mm Hg

Table 2. Mean values for IOP and CCT by category and sex in the study population

Age category	Sex	IOP (mm Hg)						CCT (µm)				
		n	mean	SD	P-value	95% CI ınterval for mean		mean	SD	P-value	95% CI ınterval for mean	
						Lower bound	Upper bound				Lower bound	Upper bound
40–49	F	785	16.33	2.76	0.023*	16.14	16.52	554.7	34.19	0.089	552.38	557.15
	M	210	15.84	2.88		15.44	16.22	559.29	34.80		554.19	563.71
	T	995	16.23	2.79		16.05	16.40	555.71	34.36		553.57	557.85
50–59	F	886	16.20	3.03	0.028*	16.00	16.41	551.38	33.17	0.002**	549.19	553.57
	M	366	15.78	3.17		15.46	16.11	557.88	34.94		554.25	561.41
	T	1252	16.08	3.08		15.91	16.25	553.28	33.81		551.40	555.15
60–69	F	552	16.30	3.35	0.007**	16.02	16.58	553.21	33.18	0.173	550.58	556.12
	M	277	15.66	3.08		15.29	16.02	556.62	35.28		552.53	560.86
	T	829	16.09	3.27		15.86	16.31	554.35	33.92		552.04	556.66
70–79	F	254	15.86	3.68	0.212	15.39	16.30	548.67	35.59	0.040*	543.76	552.60
	M	163	15.41	3.32		14.92	15.94	556.03	35.39		550.58	561.35
	T	417	15.68	3.55		15.34	16.03	551.54	35.65		548.11	554.98
80+	F	35	15.02	3.19	0.921	13.93	16.12	542.68	40.31	0.895	528.83	556.53
	M	28	15.10	3.02		13.93	16.27	544.00	37.75		529.35	558.64
	T	63	15.06	3.09		14.28	15.84	543.26	38.88		533.47	553.06
Total	F	2512	16.21	3.10	0.000**	16.09	16.33	552.44	33.90	0.000**	551.10	553.75
	M	1044	15.68	3.11		15.50	15.87	557.17	35.17		554.96	559.22
	T	3556	16.06	3.11		15.96	16.16	553.83	34.34		552.70	554.96

SD: Standard deviation; IOP: Intraocular pressure; CCT: Central corneal thickness; F: Female; M: Male; CI: Confidence interva; T: Total. *P<0.05; **P<0.01.

increase in IOP in women and a 1.5 mm Hg increase in men (P < 0.001 for both genders). CCT was negatively correlated with age and female gender and positively correlated with IOP as an independent variable, which was statistically significant (Table 3).

When we evaluated the power of our study using the results of regression analysis, we found α = 0.050: 1.000 and the power was 100%. Age, gender, and CCT associated with IOP were directly effective independent variables. CCT contributed the most to the change in IOP with the highest

Table 3. Multiple linear regression coefficients and correlation ratios for intraocular pressure and central corneal thickness

Response (dependent variable)		B	Beta	% 95 CI		P-value	Correlation	
				Lower	Upper		Simple	Partial
IOP	Age	–0.013	–0.041	–0.023	–0.003	0.013*	–0.057	–0.042
R2=0.028; F=34.067; P=0.000	Sex	0.551	0.081	0.327	0.776	0.000**	0.077	0.081
	CCT	0.013	0.141	0.010	0.016	0.000**	0.137	0.141
CCT	Age	–0.132	–0.039	–0.243	–0.022	0.019*	–0.037	–0.039
R2=0.026; F=31.352; P=0.000	Sex	–5.943	–0.079	–8.420	–3.467	0.000**	–0.063	–0.079
	IOP	1.556	0.141	1.197	1.915	0.000**	0.137	0.141

IOP: Intraocular pressure; CCT: Central corneal thickness; B: Non-standardized regression coefficient; Beta: Standardized regression coefficient; CI: Confidence interval.*P<0.05; **P<0.001.

Table 4. Characteristics of population-based population studies

Study	Ethnicity-year	Age	Method	Total number	Sex-race	Female ratio	Mean IOP	Mean CCT
Barbados	ABD. 1988–92	40–84	GAT	3752	F-B	58%	18.0±3.6	
					M-B		17.6±3.4	
					T-B		17.8±3.5	
Baltimore	ABD. 1985–88	≥40	GAT–UP	5308	W		17.17±3.35	558±34.5
					B		16±4.18	
Beaver dam	ABD.	43–84	GAT	4926	F	55%	15.5±3.3	
					M		15.3±3.4	
					T		15.3±3.2	
Rotterdam	Netherlands 1991–93	≥55	GAT	4187	T		14.7±3.2	537.4
Rejkavik	İceland	≥50	NCT	925	F	55%	15.8±3.1	527±39
					M		15.1±3.3	
Egna-neumarkt	İtaly	>40	GAT	4297	F	56%	14.94±2.6	
					M		15.14±2.8	
Blue mountains	Australia 1992–94	49–97	GAT	3260	T	57%	16.0±2.62	
Melbourne project	Australia. 1992–96	≥40	Tono-Pen	4576	T	53%	14.2±1.2	
Tehran study	İranian. 2002	≥10	GAT	3834	F	59%	14.5±2.5	
					M		14.4±2.7	
					T		14.5±2.6	
Lee et al.	Korea. 1997–2000	20–84	NCT	13212	F	49.40%	15.1±2.9	
					M		16.1±3.2	
					T		15.51±3.1	
Lingtou eye study	Chinese 2010–2012		NCT	3372	F	39,8%	15,4±2,3	
					M		15,2±2,3	
Tajimi study	Japanese 2008	>40	GAT-specular microscope	7313	T	61%	14.1±2.3	517.5±29.8
Shiose	Japanese 1984	≥40	NCT	8126	F	63%	13.4±3.0.	
					M		13.1±3.0	
Mori et al.	Japanese 2000	14–94	NCT	70139	F	37%	11.4±2.5	
					M		11.7±2.6	
Bhaktapur glaucoma study	Nepalese 2010	≥40	GAT-UP	2330	F	%51.8	13.3±2.2	539.1±33.7
					M		13.36±2.27	
					T		13.34±2.26	
Nomura	Japanese 2002	40–80	NCT-specular microscope	1317	F	%48.3	13.3±2.6	511.1±33.0
					M		13.6±2.6	518.3±33.2
Namil study	Southern Koreans 2012	40+	GAT–UP		T	%60.2	14.1±2.7	530.9±31.5
Yazd study	İranian 2017	40–80	GAT–UP	1159	T	%54.2	14.2±2.5	543±37
Liwan study	Chinese 2011		Tono-Pen UP	1348	T	58%	15.2±3.1	542±31.4
Our study	Eskişehir Türkiye 2002	40–90	Tono-Pen UP	3556	T	%70.6	16.06±3.11	553.83±34.34
					F		16.21±3.10	552.44±33.9
					M		15.68±3.11	557.17±35.17

IOP: Intraocular pressure; CCT: Central corneal thickness; GAT: Goldmann applanation tonometer; UP: Ultrasonic pachymeter; NCT: Non-contact pneumotonometer; T: Total, F: Female; M: Male; W: White patients; B: Black patients.

absolute standardized regression coefficient (standardized regression coefficient beta: 0.141, R2 = 0.028; F = 34.067; P = 0.000).

Analysis of the study results showed that IOP and CCT decreased with age, and this decrease continued in both CCT and IOP. Regardless of gender, there was a positive correlation between CCT and IOP. IOP was higher in women and CCT was thicker in men. This gender difference was greatest in the 60–69 age groups for IOP and in the 50–59 age group for CCT. IOP was negatively correlated with age and positively correlated with CCT and female gender.

Discussion

IOP is a significant risk factor for the development of glaucoma and is the only parameter considered in treatment.[2-6] Therefore, accurate measurement of IOP and knowledge of the factors affecting it is crucial. In glaucoma, the incidence of which increases with age, many countries have conducted their population studies to determine the normal values of IOP.[2-18]

In our study, in which we reported the normal distribution of IOP and CCT measurements in the Turkish population, IOP and CCT decreased with age in both sexes. According to the findings of our research, a mean decrease in IOP of 0.18 mm Hg per 10 years of age increase was observed in the population over 40 years of age in the Eskişehir region. Similarly, in the Namil study in South Korea, IOP decreased by approximately 0.2 mm Hg with each 10-year increase in age.[19] In studies from different countries investigating the relationship between age and IOP, Shiose from Japan,[3] Nomura et al.,[10] Tajimi Eye Study,[20] the study by Lee et al.,[11] the Lingtou study,[12] the Melbourne Project,[8] and the Liwan study[13] also found a negative correlation between IOP and age. In contrast to this finding, the Barbados Study,[2] the Beaver Dam Study,[7] the Egna-Neumarkt Study,[9] and the Tehran Study,[14] reported a positive correlation between age and IOP. In the Iran-Yazd study, IOP was found to increase by 0.2 mm Hg per decade.[21] In the Tehran study, the increase from the fourth to the sixth decade was 0.3 mm Hg.[14]

Some studies found no association between age and IOP. The Blue Mountains study,[6] and the Reykjavik study,[15] indicated no association between age years and IOP. When the results were evaluated according to different countries and ethnic characteristics, a positive association between age and IOP was found in Western societies, whereas it was negative in Eastern societies.

Shiose[3] suggested that the ocular hypotensive effect that develops with age is more pronounced in Asians than the ocular hypertensive effects of hypertension and obesity. According to this hypothesis, the fact that in Europe and America, where hypertension and obesity increase with age, the ocular hypertensive effect is more dominant than the ocular hypotensive effect of age may be the reason for the increase in IOP after middle age.[3,20] Apart from this, Shiose[3] again suggested that the number of obese and hypertensive individuals is decreasing because of cardiovascular accidents and deaths and that IOP does not increase with age in Eastern population studies because healthy individuals survive. However, studies of similar ethnic populations do not support this idea. A cross-sectional and long follow-up study by Nomura et al.,[10] in a Japanese population found that estimated IOP at age 50 years increased progressively in later birth cohorts, suggesting that IOP is higher in the younger generation than in the older generation of the same age. It has been suggested that the higher IOP in the younger generation may be related to Western lifestyle, diet, and environment.[10] Most studies that examined the association between age and IOP had a cross-sectional design. Future large-scale studies with longer follow-up periods are needed to determine the association between IOP and age. Therefore, the association between IOP and age is controversial.

As shown in Table 4, the mean IOP values in survey studies ranged from 11.4 to 18.0 mm Hg.[2-4,6-17,19-22] The mean IOP value obtained in our study was 16.06 ± 3.11 mm Hg and remained between Western and Eastern societies. This difference in population studies has been attributed to differences in measurement methods in addition to ethnicity, living conditions, dietary habits, educational level, environmental conditions, and differences in ocular anatomy, such as IOP-related CCT.[3,8,11-15]

In our study, the mean CCT of all cases was 553.83 ± 34.34 µm, and the mean CCT in women was 552.44 ± 33.90 and in men was 557.17 ± 35.17 µm ($P < 0.001$).

In our study, CCT showed a negative correlation with age. For every 10-year increase in age, a decrease in CCT of 1.24 µm was observed. In community studies, it has been revealed that CCT decreases with age in parallel with IOP.[13,16,23-27] A decrease in the density of keratocytes with age and degradation of collagen fibers of the cornea have been held responsible for this relationship.[16] It has been reported that prolonged exposure of the cornea to the environment with age may be the possible cause of its thinning.[16] However, some studies among Europeans have not shown a significant relationship between CCT and age.

[15,17] Possible explanations include chronic hyperglycemia negatively affecting corneal endothelial function, which is due to an osmotic gradient that draws fluid into the corneal stroma, and an increased DM rate in the elderly, including CCT.[13] This may reverse the trend of decreasing CCT with age in older Europeans.

As summarized in Table 4, mean CCT in population studies ranges from 511 to 558 µm.

African Americans and Japanese appear to have consistently thinner CCTs than other groups.[24] Hispanic, Latino, Chinese, Filipino, Korean, Malay, and Iranian populations have thicker CCTs than those listed above.[25] In general, given the differences, ethnicity should be considered when interpreting the CCT. In the study by Altınok et al.[27] in our country, the mean CCT was 552.2 ± 35.9, and our results were similar.

Considering the studies in general, they are population surveys over 40 years of age, in which women have a younger mean age and more than 50% of the study participants are women (Table 4). Our study has 70.6% women. Table 4 indicates 37–63% of women. In various studies, higher IOP was found in women (13.3–18.0 mm Hg),[2,3,7,15] and in some studies, higher IOP was found in men (11.7–15.8 mm Hg).[9-11,22] In various studies, no difference was found between genders.[6,8,13,14,16,20,24] In our study, we found higher IOP in women. The difference in the relationship between gender and IOP was explained by ethnicity, dietary habits, educational level, hormonal effects, environmental conditions, and structural characteristics.[3,9,12,20]

The role of gender on CCT is variable, as there are studies in which there is no difference between genders,[13,15-17,23,25] women have a thicker CCT than men,[18,25] or men have a thicker CCT than women.[20,24,25]

Although CCT was higher in men, IOP was higher in women in our study. Contrary to expectations, thinner CCT in women did not explain the increase in IOP. Although the reason for the difference in IOP and CCT between the genders is not clear, some studies suggest that hormonal balance changes and the effectiveness of estrogen decrease when women reach menopause.[28,29] If we look at the literature, estrogen is known to decrease IOP in women and increase corneal thickness.[30]

Based on these studies, and although there are no data on the age of menarche and menopause in our study, we assume that the difference in IOP and CCT between the two genders in the results of our study is due to the hormonal effect. Because of the total effect of estrogen deficiency on the dynamics of HA and the cornea in women, IOP may have been higher in women in the 40–49, 50–59, and 60–69 age groups in our study. It is noteworthy that gender is as important as age in screening for glaucoma and determining risk groups, and further research on this topic is needed. Mean IOP, the difference between the genders, and the relationship to age show up as different outcomes in different societies. In general, we see a decrease in mean IOP values from West to East countries and a trend from positive to negative in relation to age. Our results are consistent with those of many Asian studies and contrast with many other European and American population studies. Although the reason for this difference cannot be fully explained, we believe that ethnic and geographic factors may have an influence on IOP, as have been emphasized in studies.

Many studies have clearly shown that there is a positive correlation between IOP and CCT.[3,17,20,22,26] In our study, we found a positive correlation between corneal thickness and IOP when we evaluated the entire population ($P < 0.001$). We found that a 100 µm increase in CCT caused a 1.3 mm Hg increase in IOP. The literature reports that each 100 µm increase in corneal thickness causes an increase in IOP between 1.0 and 7.1 mm Hg.[16-18,20,22,23,25]

This suggests similar corneal biomechanics across ethnic groups.

The study's strengths are that it was conducted in a single community and included a wide range of cases. Its weaknesses are that it is a cross-sectional study in which IOP and CCT were measured in a single time period and it cannot be compared with a population younger than 40 years.

The menarche and menopause ages, sex hormone levels, and corneal endothelium count were not examined in our study, among other limitations. These flaws can serve as a roadmap for the research projects under the new title.

Therefore, epidemiological studies provide the necessary information for important concepts related to the diagnosis and treatment of diseases. Our study will help to determine the target IOP by determining the normal IOP, especially for the Turkish population.

Conclusion

This study reports the normal distribution of IOP and CCT measurements in the Turkish population. Moreover, IOP was negatively correlated with age and positively correlated with CCT and female gender. CCT made the biggest contribution to the IOP.

Ethics Committee Approval: This study was approved by Eskişehir Osmangazi University Faculty of Medicine Ethics Committee

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