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Distribution of intraocular pressure, central corneal thickness and vertical cup-to-disc ratio in a healthy Iranian population: the Yazd Eye Study

Mohammad Pakravan,[1] Mohammad Ali Javadi,[1] Shahin Yazdani,[1] Elham Ghahari,[1] Zohreh Behroozi,[1] Reza Soleimanizad,[2] Sasan Moghimi,[3] Naveed Nilforoushan,[3] Reza Zarei,[3] Yadollah Eslami,[3] Mahmood Ghassami,[1] Hossein Ziaei,[1] Marzieh Katibeh,[1] Hanif Tabesh[1] and Mehdi Yaseri[4]

[1]Ophthalmic Epidemiology and Prevention of Blindness Center, Shahid Beheshti University of Medical Science, Tehran, Iran
[2]Shahid Sadooghi University of Medical Sciences, Yazd, Iran
[3]Department of Ophthalmology and Eye Research Center, Tehran University of Medical Sciences, Tehran, Iran
[4]Department of Epidemiology and Biostatistics, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran

ABSTRACT.

Purpose: **To determine the distribution of intraocular pressure (IOP), central corneal thickness (CCT) and vertical cup-to-disc ratio (VCDR) in the healthy Iranian population.**

Methods: **This population-based, epidemiologic study evaluated Iranian aged 40–80 years, residing in Yazd, Iran, in 2010–2011. Eligible subjects were selected by cluster random sampling. Each participant underwent an interview and ophthalmologic examination including slit lamp examination, Goldmann applanation tonometry, binocular optic disc evaluation, stereoscopic fundus photography, ultrasonic pachymetry and visual field testing.**

Results: **Of 2320 eligible individuals, 2098 subjects (response rate of 90.4%) participated in the study. One eye from 1159 subjects (total of 2262 normal eyes) were randomly selected for the purpose of the study. Mean age was 53.1 ± 9.6 years. Mean IOP, CCT and VCDR were 14.2 ± 2.5 mmHg, 543 ± 37 μm and 0.32 ± 0.14, respectively. Multiple regression analysis showed a significant correlation between IOP and age (regression coefficient = 0.02 per year, p = 0.015), CCT (regression coefficient = 0.02 per micron, p < 0.001), Spherical equivalent (regression coefficient = −0.15 per dioptre, p = 0.0.024) and smoking (regression coefficient = 0.89 higher for smokers, p = 0.009); it also showed a significant correlation between CCT with spherical equivalent (regression coefficient = 3.6 per dioptre, p = 0.002) and IOP (regression coefficient = 3.6 per mmHG, p < 0.001). There was no significant correlation with VCDR.**

Conclusions: **Mean IOP, CCT and VCDR were 14.2 ± 2.5 mmHg, 543 ± 35 μm and 0.32 ± 0.14, respectively, in healthy Iranians that is different from other ethnicities. It seems advisable to pay attention to ethnicity for interpretation of each person's variables.**

Key words: central corneal thickness – healthy normal – intraocular pressure – vertical cup-to-disc ratio

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Introduction

Intraocular pressure (IOP) is the major risk factor for glaucoma. Americans and Europeans were found to have lower mean IOP than subjects of African and Asian descent (David et al. 1987). Also, reported IOP in Japanese (Fukuoka et al. 2008; Kawase et al. 2008; Tomoyose et al. 2010; Tsutsumi et al. 2012; 14.5, 15.1, 14.1, 15.1 mmHg) is lower than studies from China (Xu et al. 2005; 16.11 ± 3.39 mmHg) and India (Vijaya et al. 2008; 16.2 ± 3.7 mmHg).

It is now widely accepted that IOP alone is not an accurate diagnostic criterion for glaucoma.

Central corneal thickness (CCT) has been identified as an important factor to consider when measuring IOP (Hashemi et al. 2005; Kawase et al. 2008). CCT varies from one population or race to another. African Americans who are at higher risk of developing glaucoma were found to have a significantly lower mean CCT as compared to Caucasian subjects (Sommer et al. 1991; Nemesure et al. 2003).

The optic disc exhibits a wide range of variability in terms of shape and size, and studies have demonstrated that this variability depends on different factors such as race and refractive error (David et al. 1987). However, it is sometimes difficult to differentiate normal discs from glaucomatous ones

based on appearance and vertical cup–disc ratios (VCDR), but these parameters are still important clinical tools in evaluating the optic disc. However, clinical examination is not flawless and has been shown to exhibit a fairly wide range of variations even among normal persons.

We previously reported the prevalence and types of glaucoma in Yazd, central Iran (Pakravan et al. 2013). This study presents the normative data for IOP, CCT and VCDR within the healthy subjects of the same study population and also explores associations between these parameters and ocular or systemic variables.

Materials and Methods

This population-based cross-sectional study targeted residents of Yazd Province who were 40–80 years of age. Yazd Province is located in central Iran and has an estimated number of 526,000 residents in 2010–2011 based on the 2006 National Census. The study adhered to the Declaration of Helsinki and was approved by the Ethics Committee at Shahid Beheshti University of Medical Sciences. The sampling and study protocol have been published in depth in a separate article (Katibeh et al. 2013). As a brief, 58 clusters, each including 40 subjects, were selected from different urban and rural areas. Of 2320 eligible subjects, 2098 individuals (response rate, 90.4%) underwent a screening examination, which included an interview followed by ophthalmic examinations. After obtaining informed written consent from all eligible participants, a trained health worker administered a standard questionnaire to collect details on demographics, including age, sex and past ocular and medical history. All subjects were then referred to an equipped ophthalmic clinic within 1 week on a regular schedule for further examinations.

Visual acuity (VA) was measured from a 4-metre distance, using a NIDEK chart projector (CP670; Nidek Co., Gamagori, Japan) by an optometrist. Uncorrected and best corrected VA was evaluated separately for each eye. Refraction was performed using a Topcon automated refractometer (Topcon KR 8000; Topcon Co., Tokyo, Japan). The results were used as a starting point for a full subjective and manifest refraction. If auto refraction was not possible, manual retinoscopic manifest and subjective refraction was tried. Visual field was evaluated in all patients except persons with visual acuity of less than 1/10. First, the screening programme on frequency doubled technology (FDT) Matrix perimetry (Carl Zeiss Meditec, Dublin, CA, USA), was performed.

Then, one ophthalmologist undertook other ophthalmologic examinations. The anterior segment was examined using slit lamp biomicroscopy (Haag-Streit, Bern, Switzerland). Intraocular pressure (IOP) was measured by Goldmann applanation tonometry (Haag-Streit). Intraocular pressure (IOP) was measured three times in each eye, and the mean value was recorded. Gonioscopy was performed in all subjects with a Goldmann type four-mirror goniolens (Ocular Instruments Inc., Bellevue, WA, USA), in primary position and dark room illumination using a thin slit beam <2 mm in height. Indentation gonioscopy was performed when contact between the peripheral iris and posterior trabecular meshwork was visible, to differentiate appositional closure from peripheral anterior synechiae (PAS).

Occludable angles were diagnosed when the posterior pigmented trabecular meshwork was not visible in at least three quarters of the angle circumference without indentation; these cases were referred for neodymium-doped yttrium aluminium garnet (Nd:YAG) laser peripheral iridotomy (LPI).

In all eyes with non-occludable angles, or after LPI, the pupil was dilated with 1% tropicamide twice within a 5-min interval. After achieving maximum pupil dilation, the lens and optic disc were examined at the slit lamp and a 78 dioptre wide field lens (Volk Inc., St Louis, MO, USA). Vertical cup-to-disc ratio (VCDR) was determined with a 0.05 unit intervals. In the next stage, all subjects underwent stereoscopic fundus photography using Nidek stereo fundus camera (AFC-230/210; Nidek Co., Ltd.) by an optometrist. CCT was measured in all participants using the NIDEK UP-1000 Ultrasonic Pachymeter (Nidek Technologies, Gamagori, Japan). Standard visual field (VF) testing with the Humphrey Visual Field Analyzer (Carl Zeiss Meditec Inc., Dublin, CA, USA) using the Swedish Interactive Threshold Algorithm Standard 24-2 (SITA Standard 24-2) strategy was performed another day if any of the following conditions existed: history of taking glaucoma medications or glaucoma surgery; abnormal FDT (Matrix) visual field, defined as two abnormal points confirmed on repeat testing; IOP $\geq$ 22 mmHg; occludable or closed angles; and VCDR $\geq$ 0.6, VCDR asymmetry $\geq$ 0.2, presence of optic disc haemorrhage or notching, or obvious defects in the retinal nerve fibre layers. The VF was repeated 2 weeks later if test reliability was not satisfactory (fixation loss >20%, false positive >33%, and false negative >33%). Glaucomatous VF defects were defined if two of the three following criteria were met: (1) Glaucoma Hemifield Test (GHT) outside normal limits, (2) a cluster of 3 or more adjacent points in a location typical for glaucoma, all depressed on the pattern deviation plot at $p < 5\%$ level and one depressed at $p < 1\%$ level, and (3) pattern standard deviation (PSD) with p-value <5%.

Fundus images and all clinical and paraclinical records of participants were archived at Ophthalmic Research Center and separately evaluated and interpreted by another team. The reading group consisted of three glaucoma subspecialists. At the beginning, all three specialists evaluated the photographs and data for 150 cases independently and made a final diagnosis. We obtain the inter-rater agreement using the Fliess's Kappa method thorough the package of raters in R. The agreement was 0.73 (95% CI: 0.67–0.80).

For the remaining files, two of the three specialists assessed the records independently and classified the diagnosis. If their diagnoses were different, the third one would re-evaluate the records to reach to a consensus.

For determining normal subjects, eyes with missing values in CCT, VCDR and IOP as well as participants with history of intraocular surgery, diabetic retinopathy, primary angle closure suspect (PACS), primary angle closure (PAC), primary open-angle glaucoma (POAG), normal tension glaucoma (NTG), primary angle closure glaucoma (PACG), secondary and pseudoexfoliative glaucoma (PXG) were excluded. Eventually, 2262 eyes from 1159 normal persons were

included in this study. Statistical analysis was performed Using STATA 12.0 software package (Stata Corp LP, College Station, TX, USA). In describing the data, we used mean, standard deviation, median, range and percentiles and 95% confidence interval (95% CI). The linear association of different variables was assessed based on Pearson or Spearman correlation coefficient, whenever appropriate. In the total study population, associations between IOP, CCT and VCDR with various factors including age, family history of glaucoma, hypertension, diabetes mellitus and spherical equivalent were analysed using multiple linear regression analysis. In calculations of confidence intervals and p-values, design effect was considered. p-values <0.05 were considered as statistically significant.

Results

Overall 2262 normal eyes from 1159 persons were included, and one eye from each person was selected randomly for the purpose of the study.

Mean age was 53.1 ± 9.6 years, and 628 subjects (54.2%) were female. Diabetes mellitus and systemic hypertension were present in 949 (81.9%) and 737 (63.6%) individuals, respectively, and 174 participants (15.0%) smoked cigarettes. Other characteristics of the participants are presented in Table 1.

Mean IOP in this normal population was 14.2 ± 2.5 mmHg (Table 2).

The distribution of IOP in the study participants is depicted in Fig. 1.

As demonstrated in Fig. 1, there was no considerable difference between the smooth kernel of data and the normal curve. This shows an approximately normal distribution for IOP in this study (Skewness = +0.613).

Mean values for CCT and VCDR were 543 ± 37 μm and 0.32 ± 0.14, respectively (Table 2).

Simultaneous correlations between various factors and IOP, CCT and VCDR were investigated utilizing multiple regression analysis (Table 3).

Table 1. Characteristics of the study population.

Variable		Total number of participants = 1159
Age	Mean ± SD	53.1 ± 9.6
	Median (range)	51 (40 to 80)
Age category	40–49	480 (41.4%)
	50–59	406 (35.0%)
	60–69	164 (14.2%)
	70–80	109 (9.4%)
Area	Urban	1024 (88.4%)
	Rural	135 (11.6%)
Sex	Male	531 (45.8%)
	Female	628 (54.2%)
Selected random eye laterality	OS	564 (48.7%)
	OD	595 (51.3%)
BMI	Mean ± SD	27.5 ± 4.6
	Median (range)	27.2 (15.1 to 48.4)
Height	Mean ± SD	163 ± 10
	Median (range)	162 (135 to 196)
IOP (mmHg)	Mean ± SD	14.2 ± 2.5
	Median (range)	14 (9 to 25)
CCT (microns)	Mean ± SD	543 ± 37
	Median (range)	543 (165 to 682)
Spherical equivalent (dioptres)	Mean ± SD	−0.42 ± 1.73
	Median (range)	0 (−17.75 to 6.25)
VCDR	Mean ± SD	0.32 ± 0.14
	Median (range)	0.3 (0.1 to 0.85)
Family history of glaucoma	Yes	39 (3.4%)
	No	1120 (96.6%)
Diabetes Mellitus	Yes	949 (81.9%)
	No	210 (17.1%)
Systemic hypertension	Yes	737 (63.6%)
	No	422 (36.4%)
Smoking	Yes	174 (15.0%)
	No	985 (85.0%)

SD = standard deviation; IOP = Intraocular pressure; CCT = Central corneal thickness; VCDR = Vertical cup-to-disc ratio.

The results demonstrated that age, CCT, area of residence and smoking were positively, while spherical equivalent refractive error was negatively correlated with IOP. There is no correlation between IOP and gender, diabetes mellitus, hypertension, hyperlipidaemia and VCDR.

When keep the other variables constant, for each decade of increase in age, IOP increased by a mean of 0.2 mmHg (95% CI: 0.00–0.04, p = 0.015). Furthermore, each 100 μm of increase in CCT was associated with 2 mmHg (95% CI: 0.01–0.02, p < 0.001) increase in IOP.

There was a statistically significant relation between IOP and area of residency. On average, IOP of rural resident was 0.63 mmHg more than urban resident (p = 0.051). Being diabetic increased the mean of IOP by 0.44 mmHg (95% CI: −0.03 to 0.91, p = 0.068). Also, smoking increased the IOP 0.89 mmHg (95% CI: 0.22–1.56, p = 0.009).

A one-unit increase in spherical equivalent (equal to one dioptre towards increasing hyperopia or one dioptre decrease in myopia) would cause a change of −0.15 in IOP (95% CI: −0.27 to −0.02, p = 0.024). On the other hand, this change in spherical equivalent would result to 3.6 (95% CI: 1.4–5.8, p = 0.002) increase in CCT when the effect of other variables were adjusted.

It is revealed that a decade increase in age would increase 0.02 unit increase in VCDR; however, this change was not statistically significant (p > 0.01). Also, rural resident had 0.039 (95% CI: 0.007–0.07, p = 0.016) higher VCDR on average.

There was a statistically significant relation between CCT with SE and IOP. Central corneal thickness (CCT) was positively correlated with refraction (r = 0.062, p = 0.002), but there was no significant correlation with VCDR. Multiple linear regression analysis demonstrated a CCT increase of 3.6 μm per 1.0 dioptre increase in spherical equivalent (r = 0.062, 95% CI: 1.4–5.8, p = 0.002).

Discussion

In the current population-based study on healthy Iranians, mean IOP was 14.2 ± 2.5 mmHg which is lower in comparison to normal IOP values in

Table 2. Mean values and percentiles for IOP, CCT and VCDR by age and sex in the study population.

Parameter	Category		*n*	Mean	SD	95% Plausible value	95% CI	Min	2.50%	5%	25%	50%	75%	95%	97.50%	Max
IOP	Total		1159	14	3	9.2–19.1	14–14.3	9	10	10	12	14	16	19	20	25
	Sex	Male	480	14	2	9.2–18.5	13.6–14	9	10	10	12	14	15	18	20	23
		Female	406	14	3	9.4–19.5	14.2–14.7	9	10	10	12	14	16	20	20	22
	Age	40–49	164	14	2	9.5–19.3	14–14.7	9	10	10	13	14	16	19	19	21
		50–59	109	14	3	8.9–19.8	13.8–14.9	10	10	10	12	14	16	20	20	25
		60–69	531	14	2	9.2–18.8	13.8–14.2	9	10	10	12	14	16	18	20	25
		70–80	628	14	3	9.3–19.3	14.1–14.5	9	10	10	12	14	16	19	21	23
CCT	Total		1157	543	37	470–615	540.5–544.8	165	476	486	519	543	566	600	612	682
	Sex	Male	479	543	39	465–620	539.3–546.4	165	475	488	519	543	568	600	611	668
		Female	406	543	36	474–613	540–546.9	416	477	486	520	543	566	603	613	656
	Age	40–49	163	543	35	474–612	537.5–548.3	457	477	490	520	542	565	599	568	682
		50–59	109	538	34	472–605	531.9–544.7	460	475	485	516	537	561	597	566	652
		60–69	530	542	39	465–619	538.8–545.4	165	472	485	519	542	565	602	565	682
		70–80	627	543	35	474–612	540.3–545.8	371	472	490	520	543	567	599	561	668
VCDR	Total		1159	0.32	0.14	0.04–0.6	0.31–0.33	0.10	0.10	0.10	0.20	0.30	0.40	0.60	0.60	0.85
	Sex	Male	480	0.31	0.13	0.05–0.57	0.3–0.32	0.10	0.10	0.10	0.20	0.30	0.40	0.55	0.60	0.70
		Female	406	0.32	0.15	0.03–0.62	0.31–0.34	0.10	0.10	0.10	0.20	0.30	0.40	0.60	0.60	0.80
	Age	40–49	164	0.33	0.14	0.05–0.6	0.31–0.35	0.10	0.10	0.10	0.20	0.30	0.45	0.60	0.60	0.70
		50–59	109	0.38	0.14	0.09–0.66	0.35–0.4	0.10	0.10	0.10	0.30	0.40	0.45	0.60	0.65	0.85
		60–69	531	0.33	0.14	0.05–0.61	0.32–0.34	0.10	0.10	0.10	0.20	0.30	0.45	0.60	0.60	0.80
		70–80	628	0.32	0.14	0.04–0.6	0.31–0.33	0.10	0.10	0.10	0.20	0.30	0.40	0.55	0.66	0.85

IOP = Intraocular pressure; CCT = Central corneal thickness; VCDR = Vertical cup-to-disc ratio.

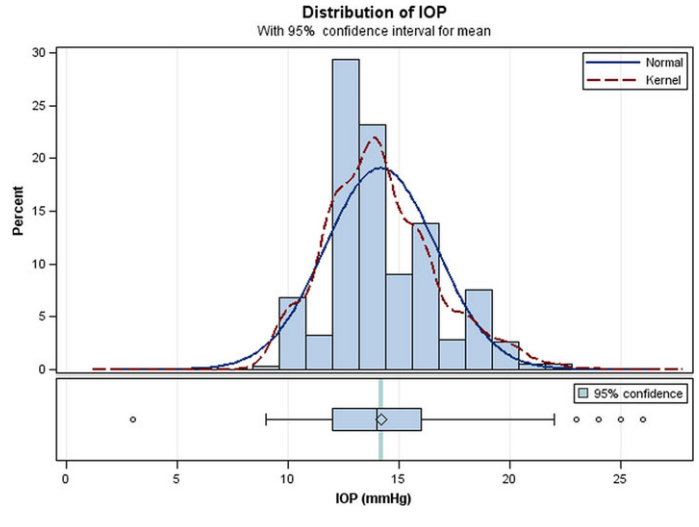

Fig. 1. Distribution of IOP in normal participants of the Yazd Eye Study.

some countries, but similar to that reported in Latino, South Korea, Japan, Singapore and previous report from Iran (David et al. 1987; Hashemi et al. 2005; Tomidokoro et al. 2007; Fukuoka et al. 2008; Kawase et al. 2008; Memarzadeh et al. 2008; Suh & Kee 2012; Chua et al. 2014; Table 4).

There is substantial discrepancy between different studies even when they are performed on populations within similar geographic locations or racial groups. According to 4th Consensus Meeting Book series on Intraocular pressure (ISBN-10: 90 6299 213, ISBN-13: 978-90-6299-213 3, Published by Kugler Publications), evidence for differences in IOP between blacks and white, relationship between IOP and age, and relationship between IOP and gender, is contradictory from available population-based studies.

Our results do not concur with other studies reporting higher mean IOP in Asian countries compared to European or American populations (David et al. 1987).

The normal IOP upper limit or its 97.5 percentile was 20 mmHg for the current study population. The prevalence of ocular hypertension (i.e. IOP 20 mmHg or more) was 1.2%, which is lower than the 3% to 10% rate previously reported (Stamper et al. 2009).

Intraocular pressure (IOP) was noted to follow a Gaussian-like distribution. Some researchers have proposed that IOP has a normal distribution up to the age of 20–30 years; thereafter, because of the small number of people who develop high IOP, it becomes skewed to the right (Armaly 1965). According to our study, the standard deviation for normal IOP increases slightly from 40 to 49 years up to 70 to 80 years (Table 2).

Several studies have reported different correlations between IOP and other factors. For example, IOP has been reported to increase with age in white, black and Latino populations (Klein et al. 1992; Nemesure et al. 2003; Memarzadeh et al. 2008) whereas it decreases with age in Singaporean, Chinese, Japanese and Taiwanese subjects (Klein et al. 1992; Tomidokoro et al. 2007; Fukuoka et al. 2008; Kawase et al. 2008; Tomoyose et al. 2010; Wang et al. 2011; Zhou et al. 2012; Chua et al. 2014).

In current study, increasing age was associated with increasing IOP. When

Table 3. Association between IOP, CCT and VCDR with various factors by multiple linear regressions.

Response			*r*	B	95% CI Lower	95% CI Upper	p-Value
IOP	Age		0.110**	0.02	0.00	0.04	0.015
	Sex (M)	M	0.060*	−0.38	−1.22	0.46	0.378
		F		–			
	Area (rural)		0.069*	0.63	0.00	1.25	0.051
	Spherical equivalent		−0.071*	−0.15	−0.27	−0.02	0.024
	Diabetes Mellitus	Yes	0.127**	0.44	−0.03	0.91	0.068
		No		–			
	BMI		0.133**	0.04	−0.01	0.08	0.089
	Height		−0.054	−0.03	−0.06	0.01	0.149
	Hypertension		0.125**	−0.04	−0.51	0.43	0.874
	Smoking		0.091**	0.89	0.22	1.56	0.009
	Hyperlipidaemia		0.019	0.10	−0.53	0.73	0.760
	CCT		0.188**	0.02	0.01	0.02	<0.001
	VCDR		0.097**	0.07	−1.40	1.53	0.927
CCT	Age		−0.053	−0.3	−0.6	0.1	0.134
	Sex (M)	M	0.011	−3.9	−14.9	7.0	0.478
		F		–			
	Area (rural)		0.037	8.1	−1.0	17.2	0.080
	Spherical equivalent		0.062*	3.6	1.4	5.8	0.002
	Diabetes Mellitus	Yes	0.028	−1.8	−9.9	6.3	0.666
		No		–			
	BMI		0.049	0.1	−0.9	1.1	0.868
	Height		0.034	0.3	−0.2	0.8	0.190
	Hypertension		0.000	3.9	−3.7	11.5	0.320
	Smoking		0.031	7.3	−0.3	14.9	0.059
	Hyperlipidaemia		0.038	−1.0	−11.1	9.1	0.851
	IOP		0.188**	3.6	2.1	5.2	<0.001
	VCDR		0.034	3.8	−24.0	31.6	0.789
VCDR	Age		0.091**	0.002	0.000	0.004	0.049
	Sex (M)	M	−0.047	−0.015	−0.063	0.033	0.532
		F		–			
	Area (rural)		0.133**	0.039	0.007	0.070	0.016
	Spherical equivalent		0.049	0.001	−0.007	0.010	0.761
	Diabetes Mellitus	Yes	0.040	−0.005	−0.033	0.023	0.738
		No		–			
	BMI		0.004	0.000	−0.004	0.004	0.940
	Height		0.007	0.000	−0.003	0.002	0.828
	Hypertension		0.041	−0.006	−0.040	0.028	0.731
	Smoking		0.020	0.026	−0.025	0.077	0.314
	Hyperlipidaemia		0.067	0.031	0.006	0.055	0.016
	IOP		0.097**	0.000	−0.005	0.005	0.899
	CCT		0.034	0.000	0.000	0.000	0.877

IOP = Intraocular pressure; CCT = Central corneal thickness; VCDR = Vertical cup-to-disc ratio; *r* = correlation.
*p < 0.05; **p < 0.01.

keeping other variables constant, each decade of increase in age was associated with an increase of 0.2 mmHg in mean IOP. In the Tehran Eye Study, mean increase in IOP from the second to the fourth decades of life was 0.8 mmHg, while the increase from the fourth to sixth decades was only 0.3 mmHg (Hashemi et al. 2005). In the Namil Study in South Korea, IOP decreased by approximately 0.2 mmHg for each decade of increase in age (Suh & Kee 2012). Most European and American studies have also reported a positive association between age and IOP (Kahn et al. 1977; Klein et al. 1992), but they followed a cross-sectional design. A longitudinal study by Hennis et al. (1997) reported a 2.5 mmHg increase in mean IOP during 4 years of follow-up, which favours the theory of IOP increase with age.

No significant association was observed between IOP and sex in the current study. The association of IOP with sex is inconsistent in the literature. Similarly, some studies using a multivariate model to evaluate simultaneous relations of risk factors with adjustment for confounders have reported no significant correlation between gender and IOP (Klein & Klein 1981; Xu et al. 2005), but some like the Namil Study (Suh & Kee 2012) and the Handan Eye Study (Zhou et al. 2012) have reported a correlation between female sex and higher IOP.

Other population-based studies including Latinos and whites also reported lower IOP among men (Klein et al. 1992; Memarzadeh et al. 2008). While the exact mechanisms are not known, one possible explanation for sex differences could be variations in

aqueous production related to hormonal factors.

There was a significant negative correlation between spherical equivalent refractive error and IOP. Other studies have also reported that spherical equivalent refractive error has a significant negative correlation with IOP (Klein et al. 1992; Weih et al. 2001; Hashemi et al. 2005; Xu et al. 2005; Kawase et al. 2008; Zhou et al. 2012). In Liwan Eye study (Wang et al. 2011), after excluding subjects with spherical equivalent refractive error less than -6 dioptres, the association between myopia and higher IOP becomes significant.

It is not clear why eyes with lower spherical equivalent refractive error or greater myopia have higher IOP. Its effect on the shape of the eye and subjecting it to greater stress might be most possible explanation.

The correlation between IOP and VCDR was positive but not significant in our study. There are conflicting reports on the correlation between VCDR and IOP. Many authors have reported a positive correlation (David et al. 1987; Hashemi et al. 2005), but others found no association (Klein et al. 1989).

Debate continues over the impact of tobacco use and smoking on IOP; however, several studies, like current study, have suggested that smokers have higher mean IOP as compared to non-smokers (Lee et al. 2003; Suh & Kee 2012; Zhou et al. 2012). There was a statistically significant relation between IOP and BP and BMI in our univariate correlation analysis. However, in contrast to other previous studies (Bengtsson 1972), it was diminished after adjusting for the effect of other variables in the model. It might be because of the effect of age. The age is related to BP and BMI, and this could prevent the effect of these variables become statistically significant.

Unlike other studies, we did not find a significant correlation between diabetes mellitus and IOP (Xu et al. 2005; Memarzadeh et al. 2008; Zhou et al. 2012). Diabetes mellitus may be associated with higher IOP and a greater risk for glaucoma, the reason for that remains undefined. Higher IOP measurements using the Goldmann applanation tonometer were found in diabetic subjects in a number of studies. In the Blue Mountains study, IOP more than 22 mmHg was reported in 6.7% of diabetic subjects as compared to 3.5% of those without diabetes. This finding could be related to a direct physiologic effect of diabetes on IOP or secondary to an increase in corneal rigidity due to collage (Ni et al. 2011).

Race has been reported to influence CCT in many population-based studies designed and conducted in different populations around the world (Sommer et al. 1991; Nemesure et al. 2003; Chua et al. 2014). Central corneal thickness (CCT) values are lower in Africans and possibly Mongolian descent (Foster et al. 1998) as compared to other ethnicities. Mean CCT values have been reported 531 in Pakistan (Channa et al. 2009) and 552 in Turkey (Altinok et al. 2007). Average CCT in our population (543 ± 37 μm) is higher than that of African Americans (529.8 ± 37.7 in pure black subjects of Barbados Eye Study by Nemesure et al. 2003; 531;.0 $\pm$ 36.3 in Baltimore Eye Survey by Sommer et al. 1991) and lower than some Caucasian population (Xu et al. 2005; Altinok et al. 2007; Zheng et al. 2008). The ultrasonic CCT in the present study is comparable to that of previous report of Iranians (Hashemi et al. 2009), Singaporean Malays (Chua et al. 2014), Latinos (Memarzadeh et al. 2008) and the white persons in the Barbados (Nemesure et al. 2003) and Baltimore (Sommer et al. 1991) studies. The mechanism underlying ethnic differences in CCT is unknown. Thus, genetic variation may well account for a significant portion of interethnic variability. Thinner central corneal thickness is known to be associated with lower measured IOP and may also be an independent risk factor for open-angle glaucoma.

Population surveys performed on Caucasians have been the basis for the definition of 'normal' IOP. The clinical implications of differences in mean CCT readings are significant in terms of determining high IOP in every population. We can further imply that glaucoma patients in every population may need to maintain a certain level of IOP based on having thinner or thicker corneas.

Several factors including age, gender, VCDR, diabetes mellitus, systemic hypertension, and smoking had no significant correlation with CCT however CCT was related to IOP and spherical equivalent refractive error.

Racial differences in optic disc morphology are well recognized. Vertical cup-to-disc ratio (VCDR) has long been used as a measure for assessing glaucomatous loss. In recognition of racial variations in optic disc morphology, International Society for Geographic and Epidemiologic Ophthalmology (ISGEO) classification of glaucoma (Foster et al. 2002) which attempted to provide a standardized definition of glaucoma for epidemiological surveys suggested that the statistical limits of normal VCDRs be derived from normal subjects within each population. The 97.5th percentile of the VCDR is 0.70 based on population-based studies in Asia, Africa and Caucasians (Foster et al. 2002; Tsutsumi et al. 2012). The 97.5th percentile of the VCDR in our study population was 0.6 using stereo photography-based planimetry. Such information in each ethnic group is considered essential to facilitate screening, diagnosis, and management of glaucoma in each region.

Mean VCDR estimated by the current study, 0.32 ± 0.14, is close to the estimation by the Andhra Pradesh Eye Disease Survey (APEDS; Sekhar et al. 2001), Jonas et al. (1988), and the Handan Eye Study (Zhang et al. 2014) but smaller than those reported by the Rotterdam (Ramrattan et al. 1999), Baltimore Eye studies (Varma et al. 1994), Tanjong Pagar Study (Foster et al. 2003; Bourne et al. 2008), and Japanese (Tsutsumi et al. 2012).

These discrepancies may be related to actual differences arising from racial variations in the number or arrangement of retinal nerve fibres at the optic disc.

As discussed in our previous report, the advantages of this study are its large sample size and population-based design. To the best of our knowledge, the current report is the first to report statistical normal limits (97.5th percentiles) for important parameters related to glaucoma diagnosis in an Iranian population.

From the standpoint of public health, severe visual impairment associated with glaucoma remains a challenge and a top priority in blindness prevention strategies. Epidemiologic studies provide the essential information for concepts of disease treatment and prevention. The current study can be helpful to set target IOP in Iranian patients and perhaps other subjects of Caucasian descent.

Table 4. Summary of results in various population-based studies of intraocular pressure, central corneal thickness and vertical cup-to-disc ratio.

Study	Ethnicity	Age	No of eyes or subjects	CCT	IOP	VCDR
Los Angeles Memarzadeh et al. (2008); Hahn et al. (2003)	Latino	40+	One eye of each 1699 participants for CCT	546.9 (33.5) Ultrasound	14.5(3.2) GAT	
Beaver Dam Klein et al. (1992)	White	43+			15.4 GAT	
Barbados Nemesure et al. (2003)	White	50+	50 eyes	545.2 ± 45.0 Ultrasound	14.6 ± 3.0 GAT	
	Black		2120 eyes	529.8 ± 37.7 Ultrasound	16.7 ± 4.0 GAT	
	Mixed (Black and White)		96 eyes	537.8 ± 34.0 Ultrasound	16.1 ± 3.9 GAT	
Blue Mountains Rochtchina et al. (2002)	White	49+	3260 subjects		16 GAT	
Baltimore Sommer et al. (1991)	White	40+	5308 black and white subjects	558.0 ± 34.5 Ultrasound	17.2 ± 3.4 GAT	
	Black			531.0 ± 36.3 Ultrasound	16.0 ± 4.2 GAT	
Rotterdam Wolfs et al. (1997)	White	55+	352 subjects	537.4 Ultrasound	14.6 GAT	
Tanjong Pagar Foster et al. (2003); Bourne et al. (2008)	Singaporean Chinese	40+	1232 subjects	539.6 Optical	15.6 ± 3.8 GAT	0.55 ± 0.10 Eyepiece graticule and Sequential Stereo photography
Malay Su et al. (2008)	Singaporean Malay	40+	3239 right eyes	541.2 ± 38.1 Ultrasound		
Mongolian Foster et al. (1998)	Mongolian	50+	1242 subjects	485.7 Optical	12.5 GAT	
Tajimi Kawase et al. (2008); Tomidokoro et al. (2007)	Japanese	40+	2868 CCT 2759 IOP	521.0 ± 32.0 Specular microscopy	14.5 ± 2.6 GAT	
Beijing Xu et al. (2005); Xu et al. (2008)	Northern Chinese	40+	3022 Eyes	556.2 ± 33.1 ASOCT	16.1 ± 3.4 Non-contact pneumotonometer	
Liwan Wang et al. (2011)	Southern Chinese	50+	1348 subject	511.6 ± 29.0 Optical 541.5 ± 31.4 Ultrasound	15.2 ± 3.1 Tonopen	
Kumejima study Tomoyose et al. (2010)	Japanese	40+	2641 subjects		15.1 ± 3.1 GAT	
Namil Study Suh & Kee (2012)	Koreans	40+		530.9 ± 31.5 on 1259 subject Ultrasound	14.1 ± 2.7 GAT on 3191 subject	
Handan Eye Study Zhou et al. (2012); Zhang et al. (2014)	Northern Chinese	30+	2 633 eyes	535.6 ± 32.5 Ultrasound	15.0 ± 2.8 Perkins (Haag-Streit)	0.27 ± 0.19 Heidelberg Retina Tomograph II (HRT II)
Singapore Epidemiology of Eye Diseases Study Chua et al. (2014)	Singaporean Chinese Singaporean Indian Singaporean Malay	40+	3251 3317 3232	552.3 ± 33.4 540.4 ± 33.6 540.9 ± 33.6 Ultrasound	14.3 ± 3.1 15.8 ± 2.9 15.3 ± 3.7 GAT	
Vijaya et al. (2008, 2010)	Southern Indian	40+	2532	520.7 ± 33.4 Ultrasound	16.2 ± 3.7 GAT	
Fukuoka et al. (2008)	Japanese	40+	7313 subjects		14.1 ± 2.3 GAT	
Tsutsumi et al. (2012)	Japanese eyepiece graticule, stereoscopic disc photographs		2507 Subjects	514 ± 33 Specular microscopy	15.1 ± 3.1 GAT	0.56 ± 0.08 Eyepiece graticule, Stereoscopic disc photography

IOP = Intraocular Pressure; CCT = Central Corneal Thickness; VCDR = Vertical Cup-to-Disc Ratio; ASOCT = Anterior segment optical coherence tomography; GAT = Goldmann applanation tonometer.

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Correspondence:
Elham Ghahari, MD
Ophthalmology Department
Labbafinejad Medical Center
Boostan 9 St., Pasdaran Ave.
Tehran 16666
Iran
Tel: +98 912 338 9763
Fax: +98 21 22590607
Email: elhamghahhari@gmail.com