



Association of Central Corneal Thickness with Age and Serum Electrolytes in Hypertensive and Non-Hypertensive Patients

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ABSTRACT

Background and Objectives: The normal Central corneal thickness (CCT) ranges about 510-520 microns. It is normally seen in clinical practice that corneas which are thicker are linked with greater intraocular pressures (IOPs). The purpose of the study was to determine the central corneal thickness and establish its relationship with age and serum electrolytes in hypertensive and non-hypertensive patients. **Methodology:** A total of 108 subjects were included in our cross-sectional comparative study (54 hypertensive and 54 non-hypertensive). Written informed consent was taken. We measured blood pressure with mercuric sphygmomanometer. Ultrasound pachymeter was used to measure central corneal thickness while we drew 5 ml of blood for estimation of the serum electrolytes. Data was entered and evaluated using IBM SPSS 17. Quantitative variables were presented as Mean \pm SD. Pearson correlation was used to find correlation of normally distributed variables p -value ≤ 0.05 was considered to be statistically significant. **Results:** Central corneal thickness was statistically same in hypertensive and non-hypertensive subjects. Serum Na⁺ was significantly increased in hypertensive subjects while serum K⁺ and Cl⁻ were significantly decreased in hypertensive subjects. No significant correlation was seen in hypertensive while weak negative correlation was observed between CCT and age in non-hypertensive patients. Weak positive correlation was observed between CCT and Na⁺ both in hypertensive and non-hypertensive. Significant correlation was observed in CCT and K⁺ in hypertensive while negative correlation was seen in non-hypertensive. Weak correlation was observed in CCT and Cl⁻ both in hypertensive and non-hypertensive. **Conclusion:** Mean CCT was significantly lower in hypertension. CCT and age showed weak and positive correlation in hypertensive while weak and negative correlation in non-hypertensive. Serum electrolytes and CCT showed no significant correlation.

Keywords: Hypertension, Central corneal thickness, Intra ocular pressure, Na⁺, K⁺

INTRODUCTION

Dehydrating function of the endothelium of cornea of the human eye is the main determinant of the thickness of the cornea [1]. Thickness of cornea can be measured secondarily by pachymetry [2]. The normal central corneal thickness (CCT) which is measured using optical or ultrasound methods is about 510-520 microns [3]. It is normally seen in clinical practice that corneas which are thicker are linked with greater Intraocular pressures (IOPs) [4-6] because of rise in resistance to indentation and vice versa in thin corneas. CCT is documented to play a significant role in surgeries of refraction [7,8]. Central corneal thickness (CCT) was supposed to be a persistent when Goldmann planned and designed his applanation tonometer. Awareness of the CCT is of significance in valuation of Intraocular pressures (IOPs) Though CCT was anticipated to remain constant but consequently great variations were found in it [9],

Therefore giving importance to this, we analyzed the association of CCT with ocular, demographic data and serum electrolytes.

Arterial hypertension is one of the common ailments. Middle aged and elderly persons have a strong tendency towards a rise in Blood pressure (BP) which often becomes sharper with age [10]. Hypertension leads to systemic mortality and morbidity than normotensives. Stroke, congestive cardiac failure, and peripheral arterial disease are likely to be common in hypertensive than normotensives. Arterial hypertension plays a significant role in the progress of hypertensive fundus changes which constitutes a key part of the pattern of malignant arterial hypertension [11].

The pressure build up inside the eye ball is the Intraocular pressure (IOP) which is due to equilibrium amongst production of aqueous humor and its drainage. It ranges from 11-21 mmHg with no absolute value [3]. It fluctuates with aging, central corneal thickness, blood pressure myopic refractive error, diabetes and vascular disease [12]. IOP shows 24-hour variation tending to be higher in morning and lower in evening. It shows diurnal variation of 5 mmHg [10]. Hyperopic eyes show a larger diurnal variation as compared to myopic eyes [13]. As measurement of IOP is directly related with flattening of cornea so, CCT is the vital determining factor of IOP and generally it is 490-560 μm thick centrally [14].

Higher blood pressure is the main independent determinant of higher IOP [15]. Increased salt intake is associated with hypertension due to increased serum sodium concentration and also increased sodium intake causes resistance to antihypertensive treatment [16,17]. Hypertension is associated with hypokalemia while low serum chloride is associated with higher mortality in hypertensive population [18,19]. So all these parameters suggest important correlation of serum electrolytes with hypertension and thus also correlate well with intraocular pressure.

Though correlation amongst aging and CCT had been explored but it is found to show contradictory results. Results of various researches conducted on Caucasians and black population have proposed that CCT is free of the influence of age. However it was found that CCT falls with age in Asian people [20-23]. Additionally, the eye study conducted in Beijing did not discover age to be meaningfully linked with CCT [24]. It was found CCT is a predictive aspect for glaucomatous advancement in patients of ocular hypertension by the study of ocular hypertension treatment and it was further found to be a great eventual effort [25]. It was concluded by the authors that persons with reduced CCT shows a greater progression to glaucoma. Moreover, CCT has been stated to show influence of various aspects such as age, gender, ethnicity, and various tonometry measurements. All of them have inspiration on the IOP [26,27].

According to literature, there exists a strong correlation between IOP, age, pressure of blood, and central corneal thickness [28]. However few studies reported that IOP increases with increased systolic blood pressure and with younger age [29]. While according to another study, IOP decreases with age [30]. It was also reported in a study that there is no noteworthy correlation of CCT with IOP, age, gender, and hypertension [31]. While another study proves that there is no significant association of IOP with age and index of body mass [32].

As IOP and CCT are determined in Pakistani population in previous studies but their important correlation with variables like age, gender, blood pressure, and serum electrolytes are not yet determined. There is no study done in local and international population in which correlation was done between CCT and serum electrolytes in hypertensive and non-hypertensive.

Therefore we conducted this study to measure and correlate all these factors in both hypertensive and non-hypertensive population and to generate new data for our population directly affecting the diagnosis and management of patients with glaucoma [33-35].

MATERIALS AND METHODS

We conducted this cross-sectional comparative study in ophthalmology OPD of Mayo Hospital, in collaboration of Physiology Department of KEMU, Lahore. Total 108 subjects were included in our research with the age ranges from 45 to 65 years. Out of 108 subjects, 54 were normotensive and 54 were hypertensive. Comprehensive ophthalmic assessment was done after taking written informed consent. Finest adjusted visual acuity was achieved followed by slit lamp examination to exclude anterior segment pathologies, pathologies of cornea, and different infections. Blood

pressure was measured in sitting position of the same person in all cases by means of same mercuric sphygmomanometer and an average of three readings was taken. CCT was measured with ultrasound pachymeter. Tropical proparacaine 0.5% was used to sedate the cornea and the subject was asked to look in primary gaze position. We then placed the pachymeter probe on the center of the cornea. We took 5 measurements from both eyes and then average was used for further evaluation. Blood sample was taken to determine serum electrolytes concentration. It was taken by means of a 5 cc sterile syringe under aseptic conditions from prominent arm veins and sent in a vial to main clinical laboratory of Mayo Hospital Lahore for estimation of electrolytes.

Data was entered and evaluated using IBM SPSS 17. Quantitative variables were presented as mean \pm SD. Pearson correlation was used to find correlation of normally distributed variables p-value \leq 0.05 was considered to be statistically significant.

RESULTS

Mean age of people with hypertension was 56.37 ± 6.71 and without hypertension were 52.35 ± 5.92 years. CCT in right and left eye was lower in hypertensive as compared to normotensives though not statistically significant. Serum sodium was significantly higher in hypertensive than normotensive patients ($p=0.019$). Serum potassium was significantly lower in hypertensive and normotensive patients ($p<0.001$). Serum chloride was lower in hypertensive than normotensive, but not significant ($p=0.05$) (Table 1).

Among hypertensive patients no statistically significant correlation was seen between CCT and age in right and left eye. Among non-hypertensive individuals weak negative correlation was seen between CCT and age in right and left eye. i.e. (R): r (HTN)=0.025, p -value=0.857 and (L): r (HTN)=0.087, p -value=0.533. (R): r (N-HTN)=-0.303, p -value=0.026 and (L): r (N-HTN)=-0.267, p -value=0.051 (Figure 1).

Correlation between Sodium (Na) and CCT in right and left eye was weak in hypertensive patients. Among non-hypertensive patients correlation between Sodium (Na) and CCT was very weak in right and left eye. i.e. (R): r (HTN)=-0.193, p -value=0.163, r (N-HTN)=-0.169, p -value=0.221 and (L): r (HTN)=-0.196, p -value=0.156, r (N-HTN)=-0.182, p -value=0.187 (Figure 2).

Among hypertensive patients in right eye potassium and CCT was weakly but significantly correlated with each other but in left eye correlation between K and CCT was weak but not statistically significant. Among non-hypertensive patients correlation between K and CCT was very weak in right and left side eye. i.e. (R): r (HTN)=0.204, p -value=0.140, r (N-HTN)=-0.137, p -value=0.324. (L): r (HTN)=0.280, p -value=0.041, r (N-HTN)=-0.179, p -value=0.196 (Figure 3).

In right and left eye among hypertensive and non-hypertensive individuals no statistically significant correlation was seen between Cl⁻ and CCT. i.e. (R): r (HTN)=0.068, p -value=0.623, r (N-HTN)=-0.015, p -value=0.915 and (L): r (HTN)=0.149, p -value=0.283, r (N-HTN)=-0.082, p -value=0.556 (Figure 4).

Table 1 Comparison of all parameters in hypertensive and non-hypertensive patients

Parameters	Hypertensive	Non-hypertensive	p-value
Age (n=54)	56.37 ± 6.71	52.35 ± 5.92	0.000
CCT (right eye)	525.90 ± 30.16	529.57 ± 42.51	0.606
CCT (left eye)	526.42 ± 28.84	533.38 ± 37.93	0.285
Na ⁺	140.07 ± 3.26	138.66 ± 2.88	0.019
K ⁺	3.44 ± 0.32	3.80 ± 0.23	0.000
Cl ⁻	102.64 ± 3.15	103.70 ± 2.31	0.050

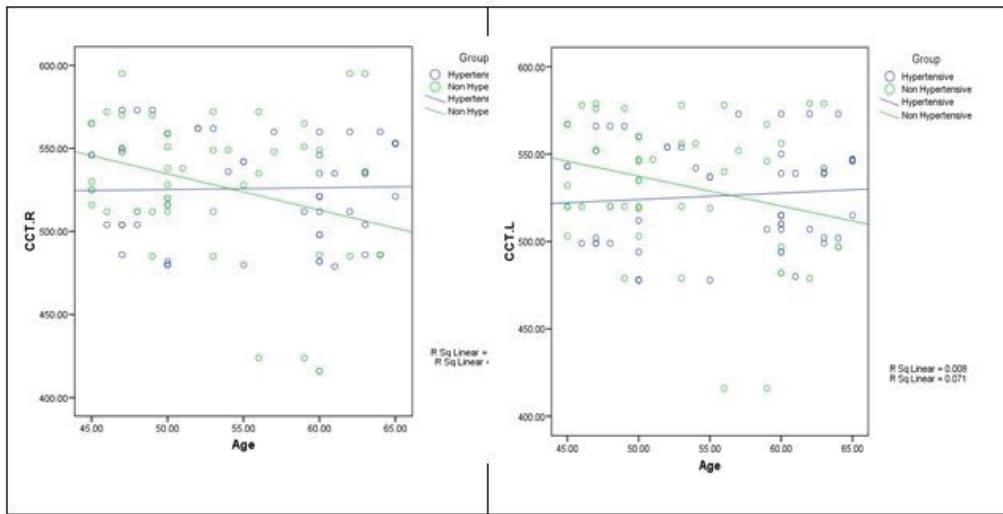


Figure 1 Correlation of CCT with age in hypertensive and normotensive

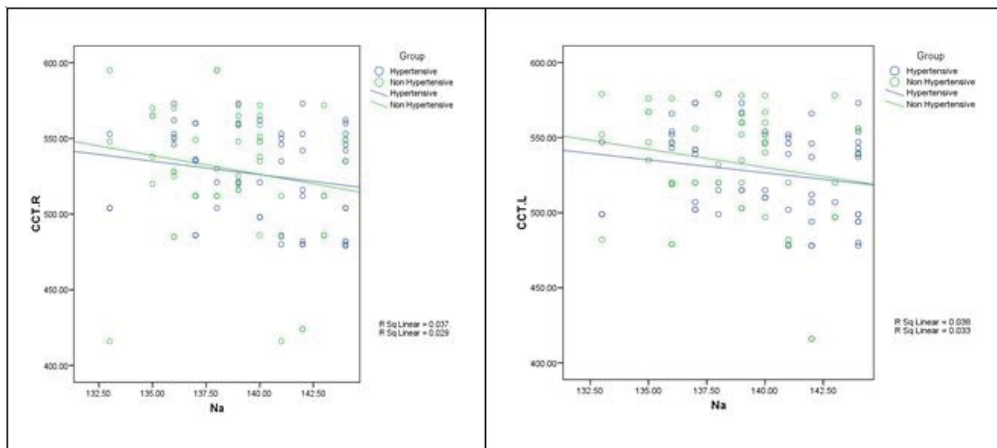


Figure 2 Correlation between CCT and Na in hypertensive and non-hypertensive

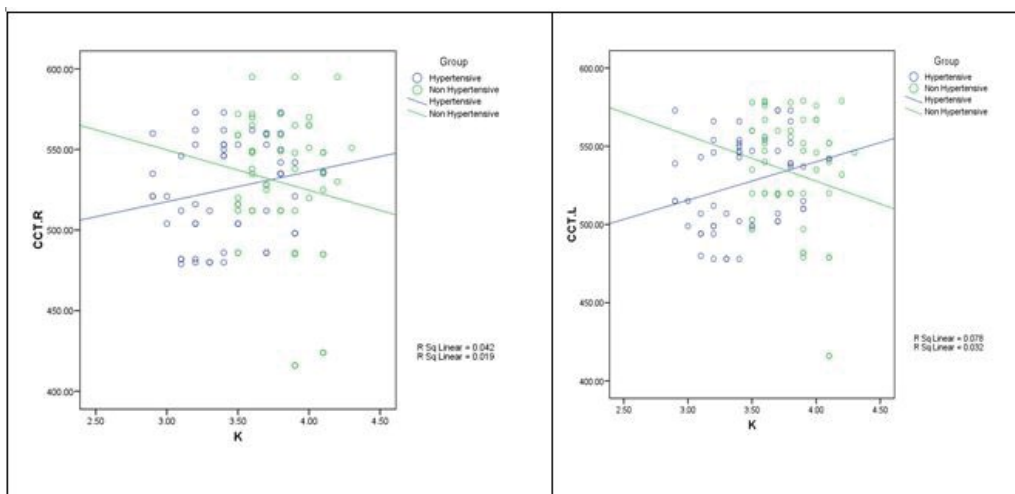


Figure 3 Correlation between CCT and K in hypertensive and non-hypertensive

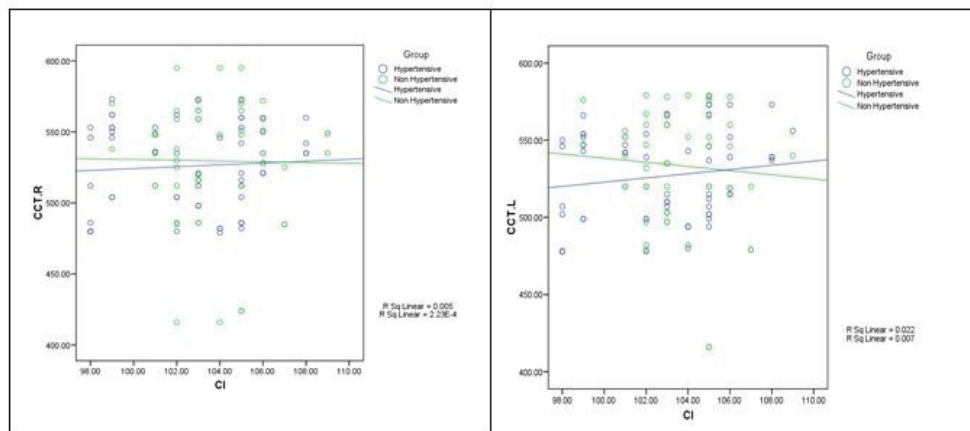


Figure 4 Correlation between CI and CCT in hypertensive and non-hypertensive

DISCUSSION

Intra ocular pressure is documented to be key reason that has noteworthy influence in the analysis and follow up of glaucoma. Diagnosis of glaucoma clinically relies heavily on the central corneal thickness. A number of evidence proposes that CCT has a strong influence on IOP and it also helps to forecast the risk of neuropathy of glaucoma. Our study showed significant decrease in CCT in hypertensive patients.

We could not find any noteworthy correlation of CCT with age in hypertensive patients however CCT was found to be inversely related to age in normotensive subjects. A number of studies have shown inverse relationship of age with CCT. European Glaucoma Prevention study group found significant negative correlation amongst age and CCT [36]. Likewise Brandt, et al. and Hahn, et al. also established a statistically significant inverse relationship between age and CCT [37,38]. Various researches stated CCT and age as opposing. Surprisingly certain studies witnessed no noteworthy linkage amongst those aspects [39].

In our study serum sodium was significantly raised while K^+ and Cl^- were significantly decreased in hypertensive patients. According to Nigerian study both serum and urinary Na^+ and Cl^- were elevated in hypertensive patients while K^+ was lowered significantly [40]. An Indian study also demonstrated high serum Na^+ and low K^+ and Cl^- in essential hypertension [41]. This might make ground for compromised vascular task and can turn to be a vital feature in the disease process and pathogenesis of HTN in this population of sub-urban locality. Many of the patients included in the study were poor, particularly patients with older age with lower potassium use, and so turn out to be vulnerable to hypokalemia and a small number of patients whose socioeconomic status is high the use is more of sodium and thus waste potassium. Management of various electrolytes is controlled by a range of stuffs like catecholamine, prostaglandins, aldosterone and angiotensin II. It is found that aldosterone is the chief factor balance of potassium [42]. The point that serum K^+ was considerably lesser in hypertensive patients proposes that the patients are suffering from primary aldosteronism as K^+ and Cl^- are controlled by the system of renin angiotensin aldosterone [43].

However weak correlation was found between these electrolytes and CCT. In literature no study has investigated the correlation between serum electrolytes CCT and IOP in hypertensive and normotensive. This is the first study of its kind in which this relation has been investigated. We conducted this study to measure and correlate all these factors in both hypertensive and non-hypertensive population and to generate new data for our population directly affecting the diagnosis and management of patients with glaucoma.

CONCLUSION

We concluded that mean CCT was significantly lower in hypertensive subjects. CCT and age showed weak and positive correlation in hypertensive while weak and negative correlation in non-hypertensive subjects. Serum electrolytes and CCT showed no significant correlation. There was no conflict of interest in our study. Large sample size study will

help to generate further better results so that monitoring and screening of IOP and CCT along with electrolytes may be planned well in advance to improve the quality of life.

DECLARATIONS

Conflicts of Interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

REFERENCES

- [1] Nemesure, Barbara, et al. "Corneal thickness and intraocular pressure in the Barbados eye studies." *Archives of Ophthalmology*, Vol. 121, No. 2, 2003, pp. 240-4.
- [2] Kremer, F. B., P. Walton, and G. Gensheimer. "Determination of corneal thickness using ultrasonic pachometry." *Annals of Ophthalmology*, Vol. 17, No. 8, 1985, pp. 506-7.
- [3] Mishima, Saiichi. "Corneal thickness." *Survey of Ophthalmology*, Vol. 13, 1968, pp. 57-96.
- [4] Doughty, Michael J., and Mohammed L. Zaman. "Human corneal thickness and its impact on intraocular pressure measures: A review and meta-analysis approach." *Survey of Ophthalmology*, Vol. 44, No. 5, 2000, pp. 367-408.
- [5] Brandt, James D. "Corneal thickness in glaucoma screening, diagnosis, and management." *Current Opinion in Ophthalmology*, Vol. 15, No. 2, 2004, pp. 85-9.
- [6] Shah, Sunil, et al. "Relationship between corneal thickness and measured intraocular pressure in a general ophthalmology clinic." *Ophthalmology*, Vol. 106, No. 11, 1999, pp. 2154-60.
- [7] Pallikaris, Ioannis G., George D. Kymionis, and Nikolaos I. Astyrakakis. "Corneal ectasia induced by laser in situ keratomileusis." *Journal of Cataract and Refractive Surgery*, Vol. 27, No. 11, 2001, pp. 1796-802.
- [8] Binder, Perry S. "Ectasia after laser *in situ* keratomileusis." *Journal of Cataract and Refractive Surgery*, Vol. 29, No. 12, 2003, pp. 2419-29.
- [9] Shimmyo, Mitsugu, et al. "Intraocular pressure, Goldmann applanation tension, corneal thickness, and corneal curvature in Caucasians, Asians, Hispanics, and African Americans." *American Journal of Ophthalmology*, Vol. 136, No. 4, 2003, pp. 603-13.
- [10] Page L. B. Epidemiology of hypertension. In: Genest J, Kuchel O, Hamet P, Cantin M, editors. *Hypertension: Physiopathology and treatment*. 2nd ed. New York: McGraw Hill, 1983, p. 683-99.
- [11] Kannel WB, Sorlie P. Hypertension in Framingham. In: Oglesby P, editor. *Epidemiology and control of hypertension: Papers and discussions from the second International Symposium on the Epidemiology of Hypertension*. The Chicago Heart Association. New York: Stratton Intercontinental Medical Book Corp, 1975, p. 553-92.
- [12] Kanski, Jack J., and Brad Bowling. *Clinical Ophthalmology: A systematic approach*. Elsevier Health Sciences, 2011.
- [13] Feltgen, Nicolas, Dorothee Leifert, and Jens Funk. "Correlation between central corneal thickness, applanation tonometry, and direct intracameral IOP readings." *British Journal of Ophthalmology*, Vol. 85, No. 1, 2001, pp. 85-7.
- [14] Loewen, Nils A., John HK Liu, and Robert N. Weinreb. "Increased 24-hour variation of human intraocular pressure with short axial length." *Investigative Ophthalmology and Visual Science*, Vol. 51, No. 2, 2010, pp. 933-7.
- [15] Foster, Paul J., et al. "Determinants of intraocular pressure and its association with glaucomatous optic neuropathy in Chinese Singaporeans: The Tanjong Pagar Study." *Investigative Ophthalmology and Visual Science*, Vol. 44, No. 9, 2003, pp. 3885-91.

- [16] Erdem, Yunus, et al. "The relationship between hypertension and salt intake in Turkish population: SALTURK study." *Blood Pressure*, Vol. 19, No. 5, 2010, pp. 313-8.
- [17] Pimenta, Eduardo, et al. "Effects of dietary sodium reduction on blood pressure in subjects with resistant hypertension: Results from a randomized trial." *Hypertension*, Vol. 54, No. 3, 2009, pp. 475-81.
- [18] Liamis, George, et al. "Electrolyte disorders in community subjects: Prevalence and risk factors." *The American Journal of Medicine*, Vol. 126, No. 3, 2013, pp. 256-63.
- [19] McCallum, Lindsay, et al. "Serum chloride is an independent predictor of mortality in hypertensive patients." *Hypertension*, Vol. 62, No. 5, 2013, pp. 836-43.
- [20] Wolfs, Roger CW, et al. "Distribution of central corneal thickness and its association with intraocular pressure: The Rotterdam Study." *American Journal of Ophthalmology*, Vol. 123, No. 6, 1997, pp. 767-72.
- [21] Cho, Pauline, and Carly Lam. "Factors affecting the central corneal thickness of Hong Kong-Chinese." *Current Eye Research*, Vol. 18, No. 5, 1999, pp. 368-74.
- [22] Foster, Paul J., et al. "Central corneal thickness and intraocular pressure in a Mongolian population." *Ophthalmology*, Vol. 105, No. 6, 1998, pp. 969-73.
- [23] Suzuki, Shigenobu, et al. "Corneal thickness in an ophthalmologically normal Japanese population." *Ophthalmology*, Vol. 112, No. 8, 2005, pp. 1327-36.
- [24] Zhang, Haitao, et al. "Central corneal thickness in adult Chinese. Association with ocular and general parameters. The Beijing eye study." *Graefe's Archive for Clinical and Experimental Ophthalmology*, Vol. 246, No. 4, 2008, pp. 587-92.
- [25] Gordon, Mae O., et al. "The ocular hypertension treatment study: Baseline factors that predict the onset of primary open-angle glaucoma." *Archives of Ophthalmology*, Vol. 120, No. 6, 2002, pp. 714-20.
- [26] Doughty, Michael J., et al. "Central corneal thickness in European (white) individuals, especially children and the elderly, and assessment of its possible importance in clinical measures of intraocular pressure." *Ophthalmic and Physiological Optics*, Vol. 22, No. 6, 2002, pp. 491-504.
- [27] Herndon, Leon W. "Measuring intraocular pressure-adjustments for corneal thickness and new technologies." *Current Opinion in Ophthalmology*, Vol. 17, No. 2, 2006, pp. 115-9.
- [28] Wong, Tina T., et al. "The relationship of intraocular pressure with age, systolic blood pressure, and central corneal thickness in an Asian population." *Investigative Ophthalmology and Visual Science*, Vol. 50, No. 9, 2009, pp. 4097-102.
- [29] Tomoyose, Eriko, et al. "Intraocular pressure and related systemic and ocular biometric factors in a population-based study in Japan: The Kumejima study." *American Journal of Ophthalmology*, Vol. 150, No. 2, 2010, pp. 279-86.
- [30] Nomura, Hideki, et al. "The relationship between age and intraocular pressure in a Japanese population: The influence of central corneal thickness." *Current Eye Research*, Vol. 24, No. 2, 2002, pp. 81-5.
- [31] Channa, Roomasa, et al. "Central corneal thickness of Pakistani adults." *Journal of the Pakistan Medical Association*, Vol. 59, No. 4, 2009, p. 225.
- [32] Xu, Liang, et al. "Intraocular pressure correlated with arterial blood pressure: The Beijing Eye Study." *American Journal of Ophthalmology*, Vol. 144, No. 3, 2007, pp. 461-2.
- [33] Ul Hassan, Mazhar, et al. "Relationship between central corneal thickness and intraocular pressure in selected Pakistani population." *Pakistan Journal of Ophthalmology*, Vol. 26, No. 2, 2010.
- [34] Onakoya, A. O., J. N. Ajuluchukwu, and H. L. Alimi. "Primary open angle glaucoma and intraocular pressure in patients with systemic hypertension." *East African Medical Journal*, Vol. 86, No. 2, 2009, pp. 74-8.

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- [35] Langman, M. J. S., et al. "Systemic hypertension and glaucoma: Mechanisms in common and co-occurrence." *British Journal of Ophthalmology*, Vol. 89, No. 8, 2005, pp. 960-3.
- [36] European Glaucoma Prevention Study Group. "Central corneal thickness in the European glaucoma prevention study." *Ophthalmology*, Vol. 114, No. 3, 2007, pp. 454-9.
- [37] Brandt, James D., et al. "Central corneal thickness in the ocular hypertension treatment study (OHTS)." *Ophthalmology*, Vol. 108, No. 10, 2001, pp. 1779-88.
- [38] Hahn, Sora, et al. "Central corneal thickness in Latinos." *Investigative Ophthalmology and Visual Science*, Vol. 44, No. 4, 2003, pp. 1508-12.
- [39] Shimmyo, Mitsugu, et al. "Intraocular pressure, Goldmann applanation tension, corneal thickness, and corneal curvature in Caucasians, Asians, Hispanics, and African Americans." *American Journal of Ophthalmology*, Vol. 136, No. 4, 2003, pp. 603-13.
- [40] Iyalomhe, Godfrey BS, et al. "Electrolyte profiles in Nigerian patients with essential hypertension." *African Journal of Biotechnology*, Vol. 7, No. 10, 2008, pp. 1404-8.
- [41] Gupta, Pawan Kumar. "Disorders of cholesterol and electrolytes metabolism in hypertension." *International Journal of Bioassay*, Vol. 2, No. 9, 2013, pp. 1207-9.
- [42] McCabe, Richard D., Manis J. Smith, and Terry M. Dwyer. "Aldosterone secretion and the mechanism of potassium adaptation in rats." *Steroids*, Vol. 58, No. 7, 1993, pp. 305-13.
- [43] Vikrant, Sanjay, and S. C. Tiwari. "Essential hypertension-pathogenesis and pathophysiology." *Journal, Indian Academy of Clinical Medicine*, Vol. 2, No. 3, 2001, pp. 140-61.