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EC OPHTHALMOLOGY
Research Article

Central Corneal Thickness in Diabetic and Non-Diabetic Patients Attending B. P. Koirala Lions Centre for Ophthalmic Studies

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Received: August 19, 2021; **Published:** October 28, 2021

Introduction

The term Diabetes is a disease in which the body cannot produce sufficient insulin to adequately control the level of glucose in their blood [1]. IOP is a routine examination in all the subjects. The measurement of IOP is usually done in both diabetics and glaucoma [2]. The commonly accepted range for normal in the general population is 10 to 21 mm of Hg [2].

It has been traditional to classify Diabetes as being type I or type II. Type I is also called insulin dependent, where the body's immune system destroys the insulin producing beta cells in pancreas. Type II is characterized by insulin resistance and relative insulin deficiency. Any changes in retina due to diabetes are called Diabetic Retinopathy. Diabetic Retinopathy is again divided as Non-Proliferative and Proliferative type [3].

The prevalence of diabetes mellitus is increasing, with an estimated 366 million people affected worldwide by 2030 according to the WHO, among which more than half will be presumed to be in Asian countries.

The centre for eye research Australia, university of Melbourne underwent extensive research for the global prevalence of Diabetic Retinopathy. Based on that it was estimated there are around 93 million people with Diabetic Retinopathy, 17 million with Proliferative Diabetic Retinopathy (PDR), 21 million with Diabetic Macular Edema and 28 million with Vision Threatening Diabetic Retinopathy. Longer duration and uncontrolled blood sugar level leads to Diabetic Retinopathy [4].

Diabetes is the fourth leading cause of death in industrialized countries. Diabetes is a disease area of considerable concern because of its severe long- term complications. These include cardiovascular disturbances, retinopathy, neuropathy and nephropathy. Diabetic retinopathy is the most important cause of blindness, and is a growing concern in the developing world [5].

Intra Ocular Pressure (IOP) is an important parameter in the detection and monitoring of Glaucoma. The Goldmann applanation tonometer has become the international "gold standard" for IOP measurement. It is based on the Imbert-Fick's principle, which asserts that the pressure inside a liquid filled sphere can be determined by measuring the force required to flatten the surface of the sphere. External force (*W*) against a sphere equals the pressure in the sphere (*P*) times the area flattened or applanated (*A*) by the external force [6]: *W = Pt X A.*

The source of error with Goldmann Tonometry can be the corneal variables itself [7]. The thickness of the cornea has been shown to influence the pressure estimate, with thin corneas producing falsely low readings. A thick cornea causes a falsely high measurement if the

thickness is due to increased collagen fibrils [8], whereas low readings occur if the thickness is due to edema [9]. Patients with Diabetes may have thicker cornea than normal resulting in over estimation of their IOP and patients with thinner cornea have their IOP underestimated [7,8].

The effect of CCT as a confounding factor affecting the accuracy of the IOP as measured by Goldmann Applanation Tonometry (GAT) appears to be small and usually not clinically relevant. However, when CCT is markedly different from the normal, this factor should be taken into account. It is for this reason that during screening of Glaucoma, CCT, should be considered in trying to decide which of these individuals require closer observation or the initiation of therapy before definite damage occurs. Corneal pachymetry to measure CCT is clinically helpful in estimating the actual IOP and establishing a target pressure.

Methodology

A cross-sectional, case control hospital-based study was carried out in B. P. Koirala Lions Center for Ophthalmic Studies, Institute of Medicine 1st November 2018 to 30th October 2019). Random sampling was done. Diagnosed cases of Diabetes Mellitus and Control Group with age and gender matched non-Diabetic individuals were included in the study. Diabetes Insipidus, Ocular disorders altering central corneal thickness, history of any ocular surgery, Patients with corneal astigmatism > 4 D, contact lens wearers were excluded in the study.

Materials and Methods

All cases were taken from Retina clinic and general outpatient department of BPKLCOS, Institute of medicine, TUTH. A Performa was designed to record the relevant history and clinical findings. A detailed history and clinical evaluation were done. From the Retina clinic, diagnosed cases of Diabetic Retinopathy satisfying the inclusion criteria were included. Age and gender matched normal individual were selected from the general OPD.

For diagnosis of Diabetic Retinopathy, a set criterion developed by the Department of Ophthalmology was followed in consultation with the unit in charge of the Retina clinic. Detail history was taken with detailed slit lamp evaluation was done for every case under Haag Streit 900 Slit Lamp. Any relevant points regarding the status of the cornea, its clarity, thickness, opacities, keratic precipitates and pigmentary dusting on the endothelium were noted. Similarly, the depth of anterior chamber was assessed by Van Herick's method and activities of the anterior chamber or any abnormalities in anterior chamber were recorded. The texture and pattern of iris, its pigmentation and any abnormalities during slit lamp biomicroscopy were noted. The status of lens and anterior surface of the vitreous was also assessed under mydriasis. Intraocular pressure was recorded in all cases with Applanation tonometer. Applanation was done using Air-Puff applanation tonometer. Fundoscopy was done in the slit lamp with Volk + 90D lens. Mydriatic (Tropicamide 1%) solution was used for every patient and was not contraindicated for better viewing of optic disc and posterior pole. While doing fundoscopy, the size, and shape of the optic disc were evaluated. Similarly, the status of the central and peripheral blood vessels was assessed. Other vascular signs such as microaneurysm, hemorrhages, exudates, if present, were also noted. USG Pachymetry (Axis II PR) was done in every subjects. It uses ultrasonic sound waves and analyzes the echo time delay and records the CCT in microns. It can measure CCT within range of 200 to 900 microns. It allows 4 measurement methods naming central measurement and the three cartographic maps; automatic, continuous and scanning mode. We used the central measurement systems for measuring CCT. After applying topical anesthetics, the probe of the device was carefully placed above the patient's cornea to obtain 5 consecutive readings with the standard deviation less than ± 5 microns. The mean of the 5 readings were taken as the CCT of the eye being examined. All data were entered in the statistical package for social service (SPSS) version 19.0 for evaluation. A verbal consent was taken from each patient for participation in the study after explaining the objectives of the study and assuring that information collected was for research purpose only and was not going to be disclosed.

Results

A total of 274 eyes of 274 individuals comprising 137 eyes with Diabetes (38 eyes with DR, 99 eyes with NR), 137 eyes of age and gender matched control individuals were examined in the Diabetes Clinic and general Out Patients Department of B.P. Koirala Lions Centre

for Ophthalmic Studies, Institute of Medicine, Tribhuvan University, Kathmandu, Nepal, during the study period 1st November 2018 to 30th October 2019.

Among the 274 eyes (137 cases, 137 controls) enrolled in the study, 136 (49%) patients were male and 138 (51%) patients were female. Out of 99 eyes of NR cases, 49.5% (n = 49) were of male and 50.5% (n = 50) were of female. Among the 38 eyes of DR cases, 42.10% (n = 16) were of male and 57.90% (n = 22) were of female. Similarly, of the 137 eyes of Controls, 51.8% (n = 71) were of male and 48.2% (n = 66) were of female as shown in table 1.

	Gender		Total number of eyes
	Male	Female	
Eyes of Control	71 (51.8%)	66 (48.2%)	137 (100.0%)
Eyes with Diabetes (NR)	49 (49.5%)	50 (50.5%)	99 (100.0%)
Eyes with Diabetes (DR)	16 (42.10%)	22 (57.90%)	38 (100%)
Total	136 (45.0%)	138 (55.0%)	274 (100.0%)

Table 1: *Gender distribution of the cases and controls.*

Age distribution

Diabetes was found most frequently in between fourth and sixth decade whereas DR had its peak at sixth decade. Similarly, Diabetes was found to have its highest incidence in the age group of 50 - 59 years and DR in the age group 60 - 69 as shown in table 2.

Age range	Control	Diabetics (NR)	Diabetics (DR)
30 - 39	17	14	3
40 - 49	18	33	6
50 - 59	43	33	10
60 - 69	28	14	14
70 - 79	10	5	5
%	50%	72.25%	27.75%
Total	137 (100.0%)	99 (100.0%)	38 (100.0%)

Table 2: *Age distribution among the cases and controls.*

The mean age of DR group was higher than the others as illustrated in table 3. There was no significant difference in mean age of controls, NR and DR (p = 0.028, p-value > 0.01).

Type	n	Minimum	Maximum	Mean age	Std. Deviation
Control	137	31.00	78.00	52.59	11.20
Diabetic (NR)	99	32.00	75.00	50.75	9.74
Diabetic (DR)	38	34.00	78.00	57.76	10.79

Table 3: *Mean and range of age (years) in each of the test groups.*

Age-gender distribution among cases

The highest number of males belonged to age group of 50 to 59 years and that of the female belonged to age group of 40 to 49 years among the cases taken as in figure 1.

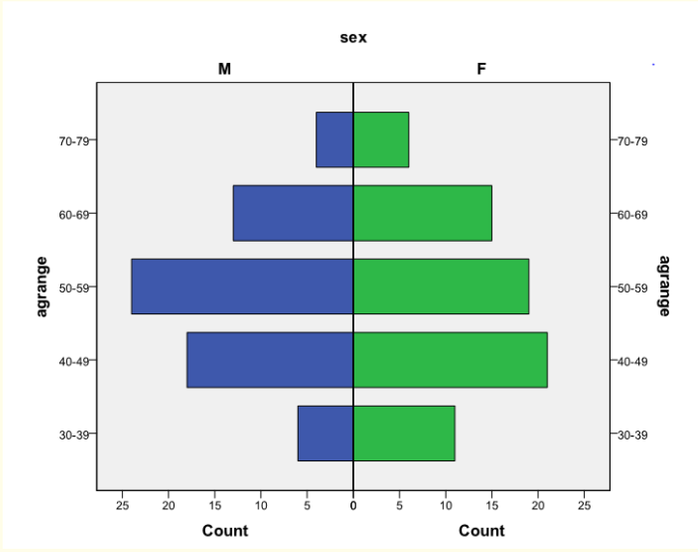

Figure 1: *Population pyramid of the total enrolled cases.*

Central corneal thickness

Of the total eyes studied, majority of control group (86.13%) had the central corneal thickness in the range of 500 to 550 µm. Majority of Diabetics (81.81% in Diabetics (NR) group and 97.36% in Diabetics (DR) had the central corneal thickness in the range of > 550 µm as shown in table 4.

CCT Range	Control	Diabetes (NR)	Diabetes (DR)
< 500	5	4	0
	3.64%	4.04%	0%
500 - 550	118	14	1
	86.13%	14.14%	2.63%
> 550	14	81	37
	10.21%	81.81%	97.36%
Total	137	99	38
	100.0%	100.0%	100%

Table 4: *Number of patients in each range of values of CCT.*

Mean central corneal thickness and gender

There was no significant difference found in the mean CCT of male and female individuals in control (p = 0.405), in Diabetics (p = 0.865) using ANOVA (p-value > 0.01), as in table 5.

Type	Gender	n	Minimum (µm)	Maximum (µm)	Mean (µm)	Std. Deviation
Control	M	71	490.00	563.00	530.9014	15.35313
	F	66	485.00	570.00	533.2121	16.99820
Diabetes	M	65	480.00	605.00	566.0615	20.88725
	F	72	498.00	594.00	565.5278	15.63580

Table 5: *Mean central corneal thickness in total of male and female patients.*

Mean central corneal thickness in each age group

The mean CCT was found to be highest in the age group of 30 to 39 years in control cases, 70 to 79 years in eyes with Diabetics (NR) and 30 to 39 years in eyes of Diabetics (DR). Lowest mean CCT was present in age group of 70 to 79 years in eyes of control cases, 40 to 49 years in Diabetics (NR) eyes and 70 to 79 years in eyes with Diabetics (DR) in table 6 but there was no significant difference in mean CCT of the age groups in controls (p = 0.349), Diabetics (NR) (p = 0.985) and Diabetics (DR) (p = 0.300, p-value > 0.01).

Age Range	Controls		Diabetes (NR)		Diabetes (DR)	
	N	Mean CCT (S. D.)	N	Mean CCT (S. D.)	N	Mean CCT (S. D.)
30 - 39	17	546.11 (19.88)	14	560.00 (19.95)	3	598.00 (7.54)
40 - 49	39	533.97 (14.74)	33	558.00 (21.42)	6	578.00 (13.81)
50 - 59	43	532.39 (13.96)	33	562.00 (17.43)	10	574.30 (9.09)
60 - 69	28	523.32 (14.33)	14	565.85 (10.77)	14	576.64 (11.37)
70 - 79	10	523.10 (8.74)	5	570.60 (3.13)	5	570.80 (16.84)

Table 6: *Mean central corneal thickness in each age group in cases and control.*

Mean central corneal thickness in different groups

The mean CCT was found to be lowest in the control group 532.01 ± 16.14 microns and the highest in the Diabetics (DR) being 577.15 ± 12.97 microns. The comparison of mean CCT in diabetic groups using Paired samples t-test shows no significant difference in the mean among the groups (p = 0.09, p-value > 0.01) but significant difference among controls (532.01 ± 16.14 μm) and diabetic individuals (565.78 ± 18.26 μm) (p = 0.001, p-value < 0.01).

Type	n	Mean CCT (microns)	Std. Deviation
Control	137	532.01	16.14
Diabetic (NR)	99	561.41	18.14
Diabetic (DR)	38	577.15	12.97
Total	274		

Table 7: *Mean central corneal thickness in each test groups.*

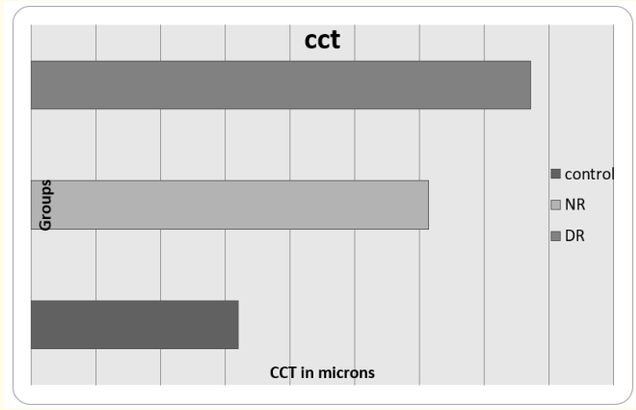

Figure 2: *Bar diagram showing mean CCT (microns) in each of the test groups.*

Blood sugar level and central corneal thickness

The mean CCT among diabetic individuals did not show significant relationship with blood sugar level using ANOVA test (p = 0.580 p-value > 0.01).

Blood sugar level (f)	Cases no	Mean CCT (µm)	Std.Deviation
81 - 150	57	564.54	15.08
151 - 220	51	565.33	20.37
221 - 290	21	570.85	15.32
> 290	8	564.12	18.24

Table 8: *Mean values of CCT for different blood sugar level groups.*

Classification on the basis of duration of diabetes

The total diabetic individuals were again distributed into further subgroups based on diabetic duration. The mean CCT was 558.58 ± 20.17 µm in duration 0-5 years while CCT was 590.66 ± 12.50 µm in duration > 20 years which was statistically significant using ANOVA test (p = 0.001, p < 0.01).

Diabetes duration (years)	No. of patients	Mean cct (µm)	Standard deviation
0 - 5	70	558.82	20.17
6 - 10	39	570.48	13.28
11 - 15	17	574.17	10.40
16 - 20	8	576.50	5.68
> 20	3	590.66	12.50
Total	137	565.782	18.24

Table 9: *Distribution of cases of diabetes on the basis of diabetes duration.*

Discussion

IOP is an important risk factor that has a significant influence in the diagnosis and follow-up of Glaucoma [10]. Goldmann Applanation Tonometry is used worldwide because it is recognized as an accurate measure of intraocular pressure, although it may be significantly influenced by the central corneal thickness. As the extremes of underestimation and overestimation span a range of almost 12 mm Hg, the CCT may affect IOP values [11].

A total of one hundred thirty-seven patients were included in this study to compare the central corneal thickness. One hundred thirty-seven eyes of age and sex matched control, ninety-nine eyes with Diabetes (NR), Thirty-eight eyes with Diabetes (DR).

In the NR group, 50.5% (n = 50) of eyes were of females and 49.5% (n = 49) of eyes were of males. In the DR group, 42.10% (n = 16) of eyes were of male and 57.90% (n = 22) of eyes were of female. In the study conducted by Claramonte PJ., *et al.* 55.3% of the diabetic patients were males (n = 26), while the remaining 44.7% were females (n = 21). Similarly, in a study done by Yashemen Ozdamar., *et al*. to compare the CCT between the diagnosed cases of Diabetic individuals, there were 51 men and 49 females out of 100 cases [12]. These studies show no sex preponderance in Diabetes affecting both male and female equally, which is similar as in our study.

In this study, Diabetes was most frequently diagnosed in the 5th decade. Comparing with the study done by Claramonte PJ., *et al.* having 34% of Diabetics at 5th decade and by Yashemen Ozdamar., *et al.* having 48% of Diabetics at 5th decade, this study shows accordance with

both the studies. 31.38% total Diabetic and 33.33% of NR were at 5th while 36.84% of DR were found to be at 6th decade. This gives the impression that diabetes is prevalent in an older age group in Nepalese population.

In this study, mean value of CCT in eyes of Diabetics was 565.78 ± 18.26 µm, NR was 561.41 ± 18.14 µm and DR was 577.15 ± 12.97 µm, while that of the normal was 532.01 ± 16.14 µm. The eyes with DR had thicker CCT than NR and controls. CCT found in diabetic patients compared to non-diabetic patients was statistically significant ($p < 0.001$, Student-t test) in comparison to control subjects.

Claramonte PJ., *et al*. did a study to assess CCT in patients with Diabetes compared it with normal subjects [12]. The average central corneal thickness in diabetic patients was 571.96 ± 26.81 microns with a range between 514 and 626. The average CCT found in non-diabetic patients was 544.89 ± 35.36 microns with range of 448 to 649. The increase in central corneal thickness found in diabetic patients compared to non-diabetic patients was statistically significant ($p < 0.001$, Student-t test) in comparison to control subjects.

Similarly, the mean CCT was significantly greater in study group (564 ± 30 mm) compared with control group (538 ± 35 mm) ($P = 0.001$). In addition, mean CCT was found to be greater in subgroup PDR (582 ± 23 mm) compared with NR (565 ± 32 mm) and NPDR (558 ± 31 mm); but the difference did not reach statistical significance ($P = 0.056$), which is similar to this study.

In the study conducted by Yasemin Ozdamar., *et al,* MM Choo., *et al.* and Pascual J. Claramonte Meseguer., *et al.* there was no significant correlation of blood sugar level and diabetes duration. Similarly, in our study blood sugar level was not statistically significant for CCT change, using ANOVA test ($p = 0.580$, p-value > 0.01). contrary to previous studies, present study shows statistically significant correlation of diabetes duration with CCT, using ANOVA test ($p = 0.001$, $p < 0.01$).

Conclusion

There was also significant correlation between Diabetes duration and CCT.CCT was found significantly thicker in groups with duration more than 20 years with mean CCT of 590.66 ± 12.50 whereas least in duration upto 5 years with mean CCT of 58.82 ± 20.17.

There was no significant difference in CCT in different blood sugar level groups. Conclusion can also be derived that CCT is not significantly associated with blood sugar level.

There was not significant correlation between age and central corneal thickness in Diabetes group only. Central corneal thickness was significantly correlated in normal and Diabetes patients. The mean central corneal thickness was not significantly different in male and female.

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Volume 12 Issue 11 November 2021