Original Article

COMPARISON OF CENTRAL CORNEAL THICKNESS BETWEEN DIABETIC AND NON-DIABETIC POPULATION

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ABSTRACT

A case control study was conducted to compare the central corneal thickness between diabetic and non-diabetic population. The subjects were 185 Malaysian adults who came to the Universiti Kebangsaan Malaysia Medical Centre (UKMMC) Eye Clinic. The sample was divided into two groups in which there were 90 diabetic and 95 non-diabetic participants. All subjects who fulfilled the inclusion and exclusion criteria were recruited after obtaining informed consents. Central cornea thickness (CCT) measurement was carried out on right eye with a Topcon SP-2000P non-contact specular microscope. Readings would only be taken from the left eye if the right eye did not meet the inclusion criteria. Three measurements were taken and the mean was used as the final result. Over half were Malays (n=103, 55.7%) followed by Chinese (n=69, 37.3%) and Indians (n=13, 7.0%). The mean age for diabetic participants was 59.23±10.02 years, ranging from 38-74 years. Among the non-diabetic participants, the mean age was 57.07±13.68 years, ranging from 23-78 years. The difference between age of diabetics and non-diabetics was not statistically significant (p=0.22). CCT of all participants was normally distributed, with the mean of 526.55± 31.82 µm. The mean CCT in diabetic participants was 531.48± 32.88 µm whereas it was 521.88± 30.22 µm in non-diabetic participants. The increase in CCT found in diabetic participants was statistically significant (p=0.04). This study showed that diabetes is associated with thicker CCT which might contribute to overestimation of intraocular pressure in the management of suspected glaucoma patients.

INTRODUCTION

Diabetes mellitus is a common worldwide disease. It is a cause of major and growing concern due to its high prevalence, chronic complications and high mortality rate, affecting approximately 180 million people around the world [1]. The prevalence of diabetes in Malaysia has been increasing steadily over the years with an estimate of 0.65% in 1960, to 2% in 1982. In 1986, the prevalence was estimated to be 6.3% and is further increased to 8.3% in 1996 [2].

The measurement of central cornea thickness (CCT) helps in the clinical assessment of glaucoma [3]. Because diabetes mellitus is a common condition in most countries, the association between diabetes and CCT is important as it affects the measurement of true intraocular pressure (IOP). Ocular Hypertension Treatment Study has demonstrated that CCT was a predictor for the development of primary open angle glaucoma (POAG) [4]. The thickness of cornea has a significant effect on the measurement of intraocular pressure. A thicker cornea leads to an overestimation of IOP while a thinner cornea causes an underestimation of IOP.

There have been reports of increased central corneal thickness in patients in whom diagnosis of ocular hypertension was made. It had been found that CCT of eyes of patients with ocular hypertension was significantly greater (606±41µm) than that of eyes of patients with glaucoma (554±22µm) or of eyes of normal controls (561±26µm) [5]. These variations of CCT in eyes of different groups have also been shown in many other studies such as study by Patwardhan A et al in United Kingdom who found that the mean ± standard deviation of CCT was 561.5 ± 35.7 µm, 538.9 ± 41.4 µm, 538.3 ± 40.3 µm for ocular hypertension (OHT), primary open angle glaucoma (POAG) and normal pressure glaucoma (NPG) subjects respectively [6].

This overestimation or underestimation of IOP has important implications in diagnosis and management of patients. In term of diagnosis, a population may have higher prevalence of ocular hypertension if the population has a thicker CCT and vice versa. This would influence epidemiological study of the disease of that particular population.

On top of that, CCT must be considered when developing a treatment approach for a patient with ocular hypertension since the patient's ocular hypertension can be due thick CCT rather than other pathological changes. The same study by Patwardhan A et al demonstrated that CCT and adjusted IOP measurement can influence glaucoma management in a clinical context [6]. It helps attribute risk and hence aids patient management decisions. Their study revealed that the IOP adjustment was greater than ±2 mmHg in 33.9% (n=304) of eyes. This CCT and adjusted IOP information had led to different treatment option in 37% (n=152) of cases. Of the most important changes, 20.4% cases would have been commenced on additional IOP-lowering medication, 2.0% would have been counseled for trabeculectomy surgery and 3.3% of the cohort would have been observed rather than treated [6]. This clearly shows the importance of central corneal thickness in clinical decision making.

As diabetes is common in Malaysia, it is justified to study the effect of the disease on the CCT. To our best knowledge, there is little known about the CCT among diabetic and non-diabetic persons in Malaysia. Therefore, this study is designed to compare the CCT between those with and without diabetes, since CCT has been shown to influence diagnosis and management of the patients.

MATERIALS AND METHODS

This is a case-control study which was carried out in April 2009 among 90 diabetic and 95 non-diabetic participants who came to Ophthalmology Clinic, Universiti Kebangsaan Malaysia Medical Centre (UKMMC). The sampling frame consisted of all main races in Malaysia which are Malay (n=103, 55.7%), Chinese (n=69, 37.3%) and Indian (n=13, 7.0%); ages from 23 to 78 years old. Approval for the study protocol was granted by UKMMC Research Secretariat. Written informed consent was obtained from all the participants before enrollment.

All participants had gone through a standardized interview to determine if they were eligible to participate in the research based on the inclusion and exclusion criteria. Diabetes mellitus was defined in this study as those who have been diagnosed by a physician to have Diabetes Mellitus previously, and on diabetic medication or having non-fasting blood glucose of ≥11.1mmol/l. Non-diabetic participants were those who denied of having diabetes mellitus and having non-fasting blood glucose of <11.1mmol/l. Those with history of corneal disease, glaucoma, previous eye surgery including laser refractive eye surgery and usage of contact lens at the time of participation were excluded from the study. The subjects' non-fasting blood glucose was tested using OneTouch R Horizon glucometer with OneTouch R Horizon test strips. Three measurements of the CCT were obtained from the right eye with a Topcon SP-2000P non contact specular microscope (Topcon Corp., Tokyo, Japan). If the participant's right eye did not meet the inclusion criteria, measurements from the left eye were taken provided the left eye fulfilled the criteria. The mean CCT based on 3 measurements was used as the final result.

Statistical analysis was performed using SPSS for Window (version 13.0, SPSS Inc. Chicago. IL). The correlation of central corneal thickness between diabetic and non diabetic subjects was analyzed using the Student t-test.

RESULTS

A total of 185 subjects were recruited in this study and CCT measurements were taken. Over half were Malays (n=103, 55.7%) followed by Chinese (n=69, 37.3%) and Indians (n=13, 7.0%). The sample was divided into two groups in which there were 90 diabetic and 95 non-diabetic subjects. The mean age for diabetic subjects was 59.23 ± 10.02 years, ranging from 38-74 years. Among the non-diabetic subjects, we found that the mean age was 57.07 ± 13.68 years, ranging from 23-78 years old. The age difference between diabetic and non-diabetic subjects was statistically not significant. (p=0.22, Student t-test) (Table 1). The number of left eye measured is 9 (4.9%), while the remaining CCT were measured using right eye, 176 (95.1%).

CCT was normally distributed with a mean of 526.55± 31.82 µm. The mean CCT in diabetic subjects was 531.48± 32.88 µm whereas it was 521.88± 30.22 µm in non-diabetic subjects. The increase in CCT found in diabetic subjects was statistically significant (p=0.04, Student t-test). (Table 2 and Figure 1).

DISCUSSIONS

Since diabetes mellitus is a very common disease in Malaysia with increasing prevalence over the years, it is potentially important to associate diabetes and CCT. CCT must be considered when developing a treatment approach for a patient with glaucoma or ocular hypertension, since a thicker central cornea causes overestimation of IOP rather than presence of pathological changes. In addition, persons with diabetes are thought to be at higher risk of glaucoma, possibly due to the influence of chronic hyperglycaemia on corneal thickness and IOP measurement. The Blue Mountains Eye Study

Table 1: Demographic Data

Characteristic	Diabetic	Non-diabetic	Total	P value
Age				
Mean ±SD	59.23±10.02	57.07±13.68		0.22
Range	38-74	23-78		
Gender				
Male, n = (%)	44(51.8%)	41(48.2%)	85	0.09
Female, n = (%)	46(46.0%)	54(54.0%)	100	
Race				
Malay, n = (%)	48(46.6%)	55(53.4%)	103	0.26
Chinese, n = (%)	31(44.9%)	38(55.1%)	69	
Indian, n = (%)	11(84.6%)	2(15.4%)	13	

Table 2: Mean of Central Corneal Thickness

Characteristic	N	Mean ± SD (µm)	Student t-test P value
Diabetic	90	531.48±32.88	0.04
Non-diabetic	95	521.88±30.22	
Total	185	526.55± 31.82	

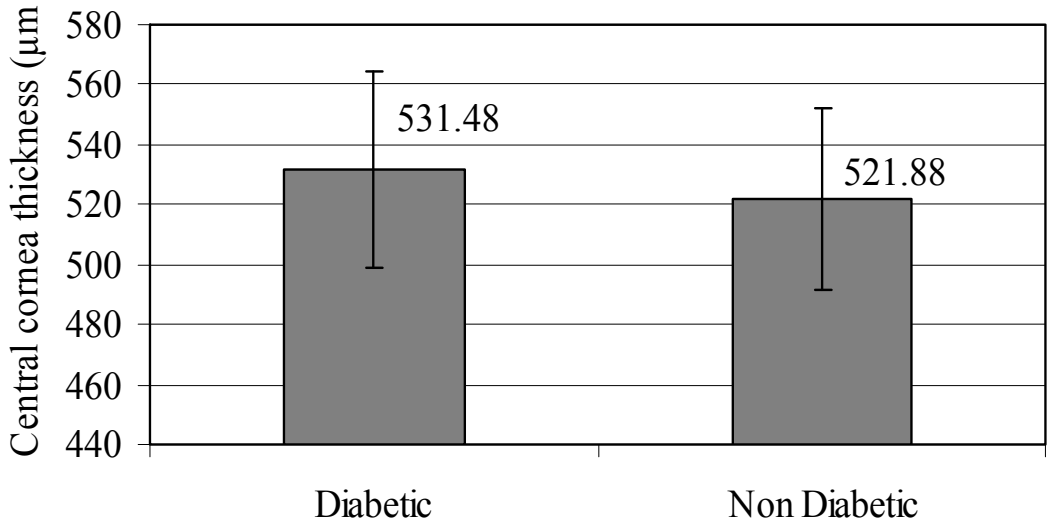

Figure 1: Mean (Standard Deviation) of Central Corneal Thickness (CCT)

and other studies showed that persons with diabetes are at increased risk of developing glaucoma [7]. Thus, the relation between diabetes, CCT, IOP and glaucoma plays an important aspect in our study.

This study demonstrates a relationship between CCT and diabetes. In our study, on average, the central cornea of a diabetic person is 9.6μm thicker than a person without diabetes mellitus (531.48μm vs 521.88μm). The difference between age of diabetics and non-diabetics was statistically insignificant (p=0.22), indicating that age is not a confounding factor in this study. The effect of diabetes on CCT is also seen in other races as shown by several studies done by other researches. A study by Brandt JD et al amongst Caucasians showed that mean CCT of subjects reporting a history of diabetes at the baseline was statistically significantly greater compared with subjects not reporting a history of diabetes (diabetics, n=128; 580.1±42.0 μm; non-diabetics, n=1101; 572.2±38.6 μm, p=0.02) [8]. The Singapore Malay Eye Study showed that the central corneas were significantly thicker in diabetic subjects as compared to non-diabetic subjects (diabetic, n=748, 547.2 μm vs non-diabetic, n=2491, 539.3 μm, p<0.001). The difference is comparable to our study. However, this study also demonstrated that thicker CCT was also associated with higher serum glucose (p=0.023) and higher HbA1c levels (p<0.001) [9]. A study by Claramonte PJ et al also showed that persons with diabetes had a thicker CCT than persons without diabetes (571.96±26.81μm vs 544.89±35.36μm) [10]. Data from a randomized clinical trial, the European Glaucoma Prevention Study, showed that participants with diabetes had thicker central corneas than persons without diabetes (588μm vs 571μm) [11]. As a result, our study implies that thicker central corneas have been associated with diabetes which may further influence the readings of IOP in the diagnosis of glaucoma in suspected patients.

Apart from that, our study also shows that the mean CCT in both diabetic and non-diabetic subjects are lower than the measurements found in the studies mentioned. This is possibly due to the usage of Topcon SP-2000P non-contact specular microscope as a tool to measure CCT in our study, as compared to the other studies which used ultrasonic pachymeter. According to a study by Shigenobu Suzuki et al, central corneal thickness measurements using noncontact specular microscope (Topcon SP-2000P) (525.3±31.4μm) gave significantly lower readings than scanning-slit topography (546.9±35.5μm) and ultrasonic pachymeter (548.1±33.0μm) [12]. Another study by Sallet G also showed that the mean CCT measured using non-contact specular microscope (Topcon SP-2000P) was significantly lower than mean CCT measured using ultrasonic pachymeter (535μm vs 540μm) [13]. K Kawana et al also demonstrated that the value obtained with SP-2000P non-contact specular microscope was significantly smaller than that taken with ultrasonic pachymetry (467.9±40.2μm vs 478.8±41.9μm, p<0.001) [14]. On top of that, the reason we use non-contact specular microscope to measure CCT is that we could eliminate the human error when using ultrasonic pachymetry. Because the latter is handheld, we may not be able to center the probe centrally. Even though ultrasonic pachymetry is a common approach and an efficient way to measure CCT, this probe must touch the corneal surface and topical anaesthesia is thus required. More over, its accuracy is dependent on the perpendicularity of the probe's application to the cornea and reproducibility relies on the precise probe placement on the corneal center [12]. Thus, due to the bias induced by ultrasonic pachymeter placement, the measurement of CCT is not consistent from one operator to another. Therefore, measurement of CCT using Topcon SP-2000P specular microscope is more consistent [15]. This is also the reason why we use the non-contact specular microscope to conduct this study as the CCT measurements could be taken by different operators in our study. Besides, the other advantages of using non-contact specular microscope are that it is easily mastered by a technician, there is no risk of transmitting infectious disease, the central alignment is easily achieved and there is no topical anaesthesia needed [13].

Several mechanisms can be speculated about the basis of association between diabetes and CCT. Hyperglycaemia may contribute to cornea endothelial dysfunction resulting in stromal hydration and cornea swelling. This was supported by McNamara NA et al who pointed that corneal structures are altered in diabetic patients, suggesting that hyperglycaemia affects control over corneal hydration, thus varying corneal thickness in diabetic patients [16]. In fact, abnormalities of cornea endothelial morphology such as polymorphism, polymegatheism, decrease in percentage of hexagonal cells, higher coefficient of variation, and increased CCT have been detected on specular microscope in persons with diabetes [17, 18].

On the other hand, we would like to make some recommendations after completing this study. We recommend that a study is done to show the relationship between duration of diabetes and CCT. A separate study to demonstrate relationship between CCT and adjusted IOP measurement amongst glaucoma patients could also be conducted. It is necessary to complement the findings in our study with the results of those recommended studies mentioned in an attempt to provide an appropriate management to suspected glaucoma patients.

CONCLUSION

In conclusion, our study showed that persons with diabetes have thicker central corneas than those without diabetes. These findings suggested that

CCT measurements were affected by the presence of diabetes. Thus, IOP must be adjusted when treating diabetic patients with suspected glaucoma or ocular hypertension.

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