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# VARIATION OF CENTRAL CORNEAL THICKNESS IN PATIENTS WITH DIABETIC RETINOPATHY AS DETECTED BY ULTRASONIC PACHYMETRY IN PATIENTS PRESENTING TO A TERTIARY CARE HOSPITAL

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### ABSTRACT

*Objective:* To compare the central corneal thickness between patients with diabetic retinopathy and non diabetics. *Study Design:* A cross sectional study.

Place and Duration of Study: Lahore General Hospital Lahore, from 1st Dec 2015 to 31st May 2016.

*Material and Methods:* A cross-sectional study was conducted in the ophthalmology outpatient department of Lahore General Hospital. A total of one hundred and fifty subjects from different age groups were selected for the study. An ultrasound pachymeter was used to measure CCT. There were two groups for sample, 75 were patients with diabetic retinopathy and 75 of them were non-diabetic subjects.

*Results:* The diabetic patients had average central corneal thickness of value  $554.93 \pm 33.73$  microns. The average central corneal thickness found in non-diabetic patients was  $520.41 \pm 26.06$  microns. The diabetic patients showed an increased central corneal thickness as compared to non-diabetics. The result of this study was statistically significant (*p*=0.001).

*Conclusion:* The diabetic patients showed an increased central corneal thickness as compared to non-diabetic patients.

Keywords: Central corneal thickness, Diabetes mellitus, Diabetic retinopathy.

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#### INTRODUCTION

Diabetes mellitus (DM) is a major health problem worldwide. It is associated with significant morbidity due to its microvascular complications like neuropathy, nephropathy Significant macrovascualr and retinopathy. complications such as ischemic heart disease and peripheral vasculopathy are also associated with it. It can affect all ages including children, young people and adults. In diabetes mellitus ocular complications are usually significant and progressive. They are now becoming world's most significant cause of morbidity. Many of these complications can be prevented with early detection and timely treatment<sup>1</sup>. Diabetes mellitus is a severe metabolic disease and its prevalence is on the rise due to increase in the population size, aging, urbanization, increased incidence of obesity and also due to physical

inactivity<sup>2</sup>. Patients with diabetes develop complications in all parts of the eye but mostly present with diabetic retinopathy along with keratoepitheliopathy and corneal endothelial damage such as persistent epithelial defects, recurrent corneal erosions and superficial punctate keratitis<sup>3,4</sup>. Diabetes mellitus invariably impairs the corneal sensitivity in diabetic patients and approximately 20% of patients suffer to some degree of decreased corneal sensations<sup>5</sup>. In addition to increase in the thickness of the corneal epithelial basement membrane, corneal morphological changes include polymorphism, polymegethism, irregular cellular distribution and stunting of surface cell microvilli<sup>6,7</sup>. All these changes result in loss of epithelial barrier function leading to a fivefold increase in corneal epithelial permeability and loss of function of corneal endothelium8-10. Various changes have been observed in corneal endothelial cell morphology in patients with diabetic retinopathy. It is thought to be associated with chronic metabolic changes at the cellular level

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which leads to abnormalities in endothelial cell layer. Loss of endothelial cells results in increased stromal hydration leading to increased central corneal thickness<sup>11</sup>. Massive thickening of basement membranes has been associated with long term diabetic retinopathy and as a result of these morphological changes, the success rate of corneal transplant in diabetic patients is greatly affected12. Similarly refractive surgery is of a great concern in diabetic patients as they have poor corneal healing<sup>13</sup>. Refractive surgery including LASIK is currently a relative contraindication in patients suffering from diabetes mellitus. Weakened immune response and delay in wound healing along with the various pathologic changes in cornea in the diabetic population has led to reservations about performing refractive surgery in these patients<sup>14</sup>. Current trends in glaucoma management requires measurement of central corneal thickness (CCT). There is increasing evidence that the risk of glaucomatous optic neuropathy and intraocular pressure (IOP) levels is influenced by CCT<sup>15</sup>. This survey aimed towards increasing awareness among eye care professionals about strong association between diabetic retinopathy and increased corneal thickness that can adversely result in inaccurate estimation of intraocular pressure (IOP). This ultimately leads to wrong interpretation of patient having glaucoma, thereby putting the patient through unnecessary investigations and treatment. The objective of this study was to compare the central corneal thickness between patients with diabetic retinopathy and non diabetics and to determine if it is increased in the former and thus a correction factor may be applied in cases of thicker corneas for correct estimation of IOP.

# MATERIAL AND METHODS

This population based cross sectional study was done in Lahore general hospital from 1<sup>st</sup> Dec 2015 to 31<sup>st</sup> May 2016. Non probability consecutive sampling technique was used. One hundred and fifty patients, both male and female, between the ages of 20 to 80 years were part of the study (using WHO sample size calculator (7.4a), level of significance 5%, power of the test 95%, population SD 28.505, test value of population mean 541.61, anticipated population mean 518.41<sup>16</sup>. A sample size of 75 was taken in each group). Patients with history of recent eye surgery, ocular trauma, corneal or media opacity or history of contact lens use were excluded. Selected patients included both with diabetic retinopathy and non-diabetics, having reliable visual fields and intra ocular pressure.

As a protocol all patients were subjected to auto-refraction and measurement of both eyes along with visual acuity by a random masked examiner were taken. After an informed consent, the subjects underwent history, anterior segment and fund us examination. On the basis of this information the patients were selected for the study and divided in two groups. Group-1 consisted of the control group without diabetes and normal healthy eyes and group-2 consisted of eyes of subjects with diabetic retinopathy which included both proliferative diabetic retinopathy (PDR) and non- proliferative diabetic retinopathy (NPDR). They were then subjected to the Quantal Ultrasonic pachymetery (model class-II; type BF; made in France). The probe was disinfected with alcohol swab for every patient to prevent transmission of infectious diseases. For standardization, convenience of analysis and to decrease the chances of bias the measurement of CCT was measured in right eye only. CCT value were taken by trainee researcher and a mean of ten readings were calculated for each patient.

Data were analyzed using SPSS version 20. Mean  $\pm$  standard deviation was calculated for age of patient, CCT. Difference of mean CCT between diabetic patients and controls were assessed using two samples t-test. A *p*-value less than 0.05 was considered significant.

## RESULTS

The study showed that the mean age of the patients in the control group was 34.07 years and that in the diabetic retinopathy group its 57.21

years (table-I). Similarly there were 41 males and 34 females in the control group and 50 males and 25 females in the diabetic retinopathy group (table-II). The mean and standard deviation for CCT in micrometer in group-1 was calculated to 520.41  $\pm$  26.06  $\mu$ m and also the mean and standard deviation for CCT in micrometer in group-2 (Diabetic retinopathy group) was 554.93  $\pm$  33.73  $\mu$ m (table-III). The increase in central corneal thickness found in patients with diabetic retinopathy compared to non-diabetic patients was statistically significant.

the early changes in ocular tissue for their proper management. This study investigates the effect of diabetic retinopathy on the thickness of the cornea and its possible implications. According to this study there is an increase in corneal thickness in patients with diabetic retinopathy. This population-based study shows a comparison between CCT of patient with diabetic retinopathy, to those without diabetes and is independent of age, IOP, and other factors. On average, patients with diabetic retinopathy had central corneas, 34.52 micron, thicker than those

		Mean (years) ± SD	
Control (non diabetic)		$34.07 \pm 10.94$	
Cases (diabetic)		57.21 ± 8.53	
Table-II: Gender distribution in control and study group.			
	Gender		Total
1	Male (%)	Female (%)	IUIdl
Control 4	1 (54.7%)	34 (45.3%)	75
Study 5	0 (66.7%)	25 (33.3%)	75
Total 9	1 (60.7%)	59 (39.3%)	150
Table-III: Mean status of central corneal thickness in both groups.			
Groups	Mea	an CCT (µm) ± SD	<i>p</i> -value
Group-1 (n=75)		520.41 ± 26.06	n = 0.001
Group-2 (n=75)		554.93 ± 33.73	<i>p</i> =0.001

## DISCUSSION

The prevalence of diabetes mellitus is on the rise worldwide causing a huge burden on the health system. Currently the prevalence has been reported up to 56.9%<sup>17</sup>. This study of diabetic retinopathy (DR) does not identify the reason for this sharp rise but one can speculate the reason for this which are mainly due to lack of patient education, poor diabetic control, poor compliance to treatment, lack of regular screening of diabetic retinopathy, increase in duration of diabetes, hyperlipidemia, smoking and obesity.

A well-known cause of visual impairment in diabetic population is diabetic retinopathy and is one of the leading causes of blindness in adults<sup>18</sup>. Uncontrolled diabetes affecting all body organs also has an adverse effect on all tissues of eye. It is therefore imperative for all clinicians to detect of persons without diabetes mellitus, and mean CCT was positively increased with diabetic retinopathy. This association was essentially similar in men and women.

McNamara et al<sup>19</sup> showed that the diabetics have altered corneal structure and that corneal hydration is affected by hyperglycemia leading to changes in corneal thickness. Another study by Sonmez et al<sup>20</sup> showed that hyperglycemia causes refractive change in cornea of diabetic patients and was detected by corneal topography. Lee et al<sup>21</sup> showed that patients who had diabetes for more than or equal to 10 years duration had advanced corneal morphological abnormalities. He also demonstrated that duration of diabetes had a strong correlation with central corneal thickness. Busted et al<sup>10</sup> showed that the diabetics had increased thickness of corneas than normal population but there was no significant correlation between duration of disease and central corneal thickness. Abdul Ghani and coworkers established a significant correlation between central corneal thickness and duration of diabetic retinopathy. They suggested that the CCT increased as the diabetic retinopathy progressed<sup>16</sup>. Another significant finding showed by Zaidi et al<sup>22</sup> that it took much longer for damaged corneal tissue to recover than normal population.

Since there is already structural damage in corneal endothelium in diabetic patients, a further functional disorder can be induced by lack of oxygen supply or harmful stimulus like stress and trauma. Skarbez et al<sup>23</sup> suggested that increase in central corneal thickness may be one of the first detectable corneal change in patients with diabetic eye disease. Diabetic patients showed significant increase in central corneal thickness when compared to normal population according to result of this study. These results are consistent with the previous studies done worldwide<sup>16</sup>. The relationship between central corneal thickness and glaucoma has already been established. Day et al<sup>24</sup> showed that age and IOP are significantly associated with CCT and that central corneal thickness should be taken into account as a separate risk factor in the diagnosis of glaucoma. Sng et al<sup>25</sup> suggested that the central corneal thickness may affect the accuracy of IOP measurements so it must be taken into consideration in diagnosis and management of glaucoma. It is suggested that thicker corneas in diabetic patients is one of unnoticed signs of diabetic retinopathy. Therefore, thicker corneas having increased thickness in diabetes should be taken into consideration while measuring IOP in diabetic patients. This study had limited number of patients belonging to an urban population. Studies on a larger scale including rural population are required for optimizing awareness among masses regarding diabetic retinopathy and its adverse effects on ocular tissues along with potential benefits of its successful management.

### CONCLUSION

The diabetic patients showed an increased central corneal thickness as compared to nondiabetic patients.

### **CONFLICT OF INTEREST**

This study has no conflict of interest to declare by any author.

#### **REFERENCES**

- 1. Sayin N, Kara N, Pekel G. Ocular complications of diabetes mellitus. World J Diabetes 2015; 6(1): 92-108.
- Cai D, Zhu M, Petroll WM, Koppaka V, Robertson DM. The impact of type-1 diabetes mellitus on corneal epithelial nerve morphology and the corneal epithelium. Am J Pathol 2014; 184(10): 2662-70.
- 3. Pai SG, Vasuraj Correlation between central corneal thickness in diabetics and non diabetics when measured with spectral domain optical coherence tomography. IJSR 2016; 5(4): 670-72.
- 4. Ozdamar Y, Cankaya B, Ozalp S, Acaroglu G, Karakaya J, Ozkan SS. Is there a correlation between diabetes mellitus and central corneal thickness? J Glaucoma 2010; 19(9): 613-6.
- Neira-Zalentein W, Holopainen JM, Tervo TM, Borrás F, Acosta MC, Belmonte C, et al. Corneal sensitivity in diabetic patients subjected to retinal laser photocoagulation. Invest Ophthalmol Vis Sci 2011; 52(8): 6043-9.
- 6. Tsubota K, Chiba K, Shimazaki J. Corneal epithelium in diabetic patients. Cornea 1991; 10(2): 156-60.
- Taylor HR, Kimsey RA. Corneal epithelial basement membrane changes in diabetes. Invest Ophthalmol Vis Sci 1981; 20(4): 548-53.
- Parrish CM: The cornea in diabetes mellitus. Feman SS (ed): Ocular problems and diabetes mellitus, p 179. Boston, Blackwell Scientific, 1992.
- 9. Göbbels M, Spitznas M, Oldendoerp J. Impairment of corneal epithelial barrier function in diabetics. Graefes Arch Clin Exp Ophthalmol 1989; 227(2): 142-4.
- Busted N, Olsen T, Schmitz O. Clinical observations on the corneal thickness and the corneal endothelium in diabetes mellitus. Br J Ophthalmol 1981; 65(10): 687-90.
- Storr-Paulsen A, Singh A, Jeppesen H, Norregaard JC, Thulesen J. Corneal endothelial morphology and central thickness in patients with type II diabetes mellitus. Acta Ophthalmol 2014; 92(2): 158-60.
- 12. To M, Goz A, Camenzind L, Oertle P, Candiello J, Sullivan M, et al. Diabetes induced morphological, biomechanical and compositional changes in ocular basementmembranes. Exp Eye Res 2013; 116: 298-307.
- 13. Waring GO III: Examination and selection of patients for refractive keratotomy. In Waring GO III (ed): Refractive Keratotomy for Myopia and Astigmatism, p 309. St Louis, Mosby Year Book 1992.
- 14. Simpson RG, Moshirfar M, Edmonds JN, Christiansen SM. Laser in-situ keratomileusis in patients with diabetes mellitus: a review of the literature. Clin Ophthalmol 2012; 6: 1665-74.
- Su DH, Wong TY, Wong WL, Saw SM, Tan DT, Shen SY, et al. Diabetes, hyperglycemia, and central corneal thickness: the Singapore Malay Eye Study. Ophthalmology 2008; 115(6): 964-68.

- Abdulghani YS, Ali TO. Correlation between central corneal thickness and diabetes in sudanese patients. Natl J Med Res 2013; 3(4): 309-11
- 17. Sohail M, Prevalence of diabetic retinopathy among type-2 diabetes patients in Pakistan Vision Registry Pak J Ophthalmol 2014: 30; 204-12.
- Threatt J, Williamson JF, Kyle Huynh K, Davis RM. Ocular Disease, Knowledge, and Technology Applications in Patients with Diabetes. Am J Med Sci 2013; 345(4): 266–70.
- McNamara NA, Brand RJ, Polse KA, Bourne WM. Corneal function during normal and high serum glucose levels in diabetes. Invest Ophthalmol Vis Sci 1998; 39(1): 3-17.
- 20. Sonmez B, Bozkurt B, Atmaca A, Irkec M, Orhan M, Aslan U. Effect of glycemic control on refractive changes in diabetic patients with hyperglycemia. Cornea 2005; 24(5): 531-7.

- Lee JS, Oum BS, Choi HY, Lee JE, Cho BM. Differences in corneal thickness and corneal endothelium related to duration in diabetes. Eye (Lond) 2006; 20(3): 315-8.
- Ziadi M, Moiroux P, d'Athis P, Bron A, Brun JM, Creuzot-Garcher C. Assessment of induced corneal hypoxia in diabetic patients. Cornea 2002; 21(5): 453-7.
- Skarbez K, Priestley Y, Hoepf M, Koevary SB, Comprehensive review of the effects of diabetes on ocular health. Expert Rev Ophthalmol 2010; 5(4): 557–77.
- 24. Day AC, Machin D, Aung T, Gazzard G, Husain R, Chew PT et al. Central corneal thickness and glaucoma in East Asian people. Invest Ophthalmol Vis Sci 2011; 52(11): 8407-12.
- Sng C, Barton K, Kim H, Yuan S, Budenz DL. Central corneal thickness and its associations with ocular and systemic factors in an urban west african population. AJO 2016; 169: 268-75.