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Study to compare anterior chamber angle parameters between diabetics and non-diabetics using anterior segment optical coherence tomography

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ABSTRACT

Aim: To correlate anterior chamber angle parameters with severity and duration of diabetes in diabetic patients and compare with non-diabetics.

Materials and Methods: Prospective cross-sectional study with 200 subjects each in diabetic and non-diabetic group. Comprehensive ocular examination was done. RBS at the time of examination was noted and AS-OCT examination was performed for all. The parameters were central corneal thickness (CCT), angle opening distance at 500μ (AOD500), and750μ (AOD750), trabecular iris space area at 500μ(TISA500) and 750μ(TISA750), scleral spur area (SSA),lens vault (LV), angle (in °),anterior chamber depth (ACD) and angle to angle distance (mm). Data was recorded and appropriate analysis was done. p-value of <0.05 was considered significant.

Results: Males were more than females. Mean age for diabetic group was 49.07 years in diabetics and 37.34 years in non-diabetics. CCT values increased with increase in blood sugar and duration of diabetes. Except SSA continuous decrease in median values were seen for all angle parameters with an increase in blood sugar, duration and severity of diabetes. But overall change in the value of angle parameters was statistically significant between the groups. Gonioscopy findings confirmed that anterior chamber was shallower in patients with longer duration of diabetes and higher grades of retinopathy.

Conclusion: Diabetes mellitus and its association with glaucoma has been studied mostly for open angle glaucoma. The findings of the present study confirms that diabetics are at high risk of angle closure and it is associated with the duration, severity and control of diabetes Hence, early detection by gonioscopy and AS-OCT may aid in better management.

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1. Introduction

Sense of sight is one of the most important gifts humans have. Visual function is maintained by all ocular structures working in tandem with the systemic structures. Amongst ocular diseases, glaucoma is emerging as one of the leading causes of blindness worldwide.[1,2] Similarly, Diabetes mellitus (DM)is a global health issue nothing short of a pandemic.[3–5] Vision related changes in diabetes can be due to diabetic retinopathy, cataract or glaucoma.[6,7] Increased risk of glaucoma in diabetes has been described in several studies.[8–10] Though most studies have talked about association with open angle glaucoma, its association with angle closure is still elusive. Apart from retina, diabetes may affect anterior segment structures of the eye such as cornea, iris, ciliary processes, lens, anterior chamber and posterior chamber. The narrowest portion of the anterior chamber is at the angle and structural changes due to diabetes may affect these angle parameters. Gonioscopy is an effective method to evaluate the depth of the anterior chamber. But with the advent of Anterior Segment Optical Coherence Tomography (AS-OCT) which is a non-contact,

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rapid imaging device that takes cross sectional images of anterior segment, early and minute changes of the angle can be picked up.[11] The present study aims to find out how the duration and severity of diabetes affect the angle structures of the eye and then compare these parameters with people without diabetes. This can help in early diagnosis of vision related complications and plan the management better thus improving the prognosis.

2. Materials and Methods

This was a prospective cross-sectional study conducted from September 2020 to September 2022 in a tertiary eye care centre in eastern India. Institutional ethical clearance was obtained (KIIT/KIMS/IEC/433/2020) and the study complied to the principles of Declaration of Helsinki. 400 patients out of which 200 were diabetic patients and 200 were non diabetic patients were included in the study. Eligible patients were identified and informed consent was taken. The demographic profile of all eligible patients was recorded. Thorough clinical history was taken. The right eye of all patients was taken for consideration. Diabetic and non-diabetic patients of both genders within the age group of 35-70 years were included in the study. Patients with essential hypertension, dyslipidemia, a history of ocular inflammations, history of ocular surgeries and ocular trauma were excluded. Patients in whom the fundus could not be visualized, high refractive error (myopia > 6D/ hypermetropia >5D) and dense cataract were excluded from the study. Comprehensive ocular examination including visual acuity assessment with Snellen's vision chart, slit lamp (Zeiss Slit Lamp) examination, Intraocular Pressure (IOP)assessment with Goldmann Applanation Tonometer (AT), gonioscopy using Volk G-2 gonio lens, fundus examination with Indirect ophthalmoscope / 90D and AS-OCT by Zeiss Cirrus HD-OCT Module 500 was done on all patients. Angle was graded as per Shaffer's grading. Three AS-OCT readings were taken and average of the three readings was calculated. If the difference in readings were significant, then the procedure was repeated again. Two different assessors well trained in glaucoma procedures performed Gonioscopy AS-OCT in patients and findings of each test was masked to the other. The parameters recorded were central corneal thickness (CCT), angle opening distance at 500μ (AOD500), angle opening distance at 750μ (AOD750), trabecular iris space area at 500μ(TISA500), trabecular iris space area at 750μ(TISA750), scleral spur area (SSA), lens vault (LV), angle (in °), anterior chamber depth (ACD) and angle to angle distance (mm). Pupil was dilated using phenylephrine (5% w/v) and tropicamide (0.8% w/v) eye drops. Fundus was examined using indirect ophthalmoscope, 20D lens and 90D lens. Grading of diabetic retinopathy was done as per ETDRS classification of diabetic retinopathy as no retinopathy, mild non-proliferative diabetic retinopathy(NPDR), moderate NPDR, severe NPDR, and proliferative retinopathy. Random blood sugar was recorded for all diabetic patients. AC depth (ACD) was defined as distance from corneal endothelium to anterior surface of the lens. Angle to angle distance was considered to be a horizontal distance between two scleral spurs. Angle opening distance (AOD) was the distance in linear terms between the iris and the inner corneoscleral wall. Trabecular iris space area (TISA) was the measurement of the total filtering area which is trapezoid in shape bounded by: AOD anteriorly, a line drawn from the sclera spur perpendicular to the plane of the inner scleral wall to the opposing iris posteriorly, the inner corneoscleral wall superiorly, and, the iris surface inferiorly. Lens vault (LV) was defined as the distance between the crystalline lens's anterior pole and the horizontal line connecting the two scleral spurs

2.1. Statistical analysis

Data was collected and analysis done by IBM SPSS version 25 software. All the parameters underwent normality check by Shapiro Wilk Test. The variables not falling under normality assumptions are expressed in median and interquartile range(IQR). All the categorical variables are expressed in frequency and percentage. The comparison between groups are done by Mann Whitney U test. The measure of association between the categorical variables are done by Chi square test. Spearmann correlation coefficient was used for finding correlation between gonioscopy and duration and severity of diabetes. p –value of<0.05 was considered statistically significant.

3. Results

A total of 400 patients were included in the study where 200 were in the diabetic group and 200 in the non-diabetic/control group. The mean age of subjects in the non-diabetic group was lower (37.34 years) than that of subjects in the diabetic group(49.07 years).number of males were more than females in both the groups. Maximum number of subjects in the diabetic group had diabetes for less than 5 years and the grade of retinopathy was also mild as per ETDRS classification. With respect to control of blood sugar, all subjects in the non-diabetic group had Random blood sugar(RBS) levels of <110 mg% while in the diabetic group 145 had RBS values between 110-140 mg% and 45 had RBS >140 mg% at the time of examination. The baseline demographic values are described in Table 1.

Gonioscopy was done in all subjects as a part of routine ophthalmological examination and graded as per Shaffer's grading i.e higher grades meant open angles. Maximum number of subjects in both groups had open angles. Co-relation of the grades of gonioscopy with duration of diabetes and severity of retinopathy was found out using spearman correlation coefficient. Both severity

Table 1: Baseline demographic values

Parameters		Diabetics (n=200)	Non-Diabetics (n=200)
Mean Age(in years)		49.07	37.34
Gender	Male	107	103
	Female	93	97
Duration	<5 years	122	NA
	5-10 years	59	
	>10 years	19	
Grade of retinopathy	Mild NPDR	68	NA
	Moderate NPDR	9	
	Severe NPDR	11	
	PDR	3	
Blood sugar level (RBS)	<110mg%	-	200
	110-140mg%	145	NA
	>140mg%	55	NA

of retinopathy and duration of diabetes were negatively correlated with the grades of gonioscopy. This implied that wider angles or higher shaffer's grading were found in people who had diabetes of lesser duration than those suffering from diabetes over a longer period of time. Similarily, lower grades of retinopathy was seen in patients with open angles. The detailed values are described in Table 2.

AS-OCT was performed for all subjects and data was recorded. All the AS-OCT parameters recorded were then correlated with the level of blood sugar(RBS), severity of retinopathy and the duration of diabetes. In order to maintain normality of the data recorded, appropriate tests were used and data was interpreted in form of median and interquartile range.

Random blood sugar levels for all patients were recorded and on the basis of RBS, patients were divided into three groups. One group with RBS levels less than 110mg%, second group between 110-140 mg% and third group had patients with RBS more than 140 mg% at the time of examination. All AS-OCT parameters were then correlated with these three groups. It was found that median value of all parameters decreased with an increase in blood sugar levels. This difference in the parameters between the three groups was found to be statistically significant. The details are described in Table 3.

For duration of diabetes, again three groups were made. One with subjects suffering from diabetes for less than five years, second had subjects with duration of diabetes between five to ten years and third group with subjects suffering from diabetes for more than ten years. All anterior chamber parameters for these groups were compared with that of the non-diabetic group. It was found that the absolute median values for all parameters decreased with an increase in the duration of the disease except for the Scleral spur area and anterior chamber depth. But overall calculation showed that the changes in the values when compared between the groups were statistically significant for all parameters. This has been elaborated in Table 4.

As per the ETDRS classification, fundus findings were graded into four groups. Three groups as no retinopathy, mild NPDR, moderate NPDR as first three groups and severe NPDR and PDR were clubbed as the fourth group. The group having no retinopathy had 200 non diabetic patients and 109 diabetic patients. As seen with duration of diabetes and level of blood sugar, here too for all the parameters there was decrease in the absolute median value and ultimately the difference was statistically significant. This has been shown in Table 5.

In the present study all AS-OCT parameters measurement led to the conclusion that the anterior chamber indeed became narrower with increase in the blood sugar levels, duration of diabetes and severity of retinopathy. The only parameter which did not follow this trend was the central corneal thickness(CCT). Though the difference in CCT between all groups for all scenarios was statistically significant, the absolute median values gradually increased with increasing blood sugar levels, duration of diabetes and severity of retinopathy. This can be attributed to the basic pathologic process that occurs in diabetes along with glaucoma.

4. Discussion

The present study shows male predominance. Some studies have shown female predominance and some have shown no clear gender variation.[12,13] Though females may be more predisposed to develop angle closure by virtue of anatomy, the present study concentrates on the blood sugar levels and duration of diabetes. Hence, the variation in gender predisposition does not affect the study results ultimately. The mean age group in the present study was more for diabetic group indicating higher prevalence of retinopathy in older patients but it has to be correlated with the blood sugar control as well.[14]

Several studies have shown that diabetes not only affects the retina but the anterior segment structures of the eye as well.[15–17] In corroboration to the present study, several other studies have also found the CCT to be more in patients with diabetes and more so when the diabetes is uncontrolled.[18,19] This is probably because hyperglycaemic status results in corneal endothelial dysfunction resulting in stromal hydration and thus increased thickness.[20]

The present study showed that on gonioscopic grading angle became shallower as the duration and severity of diabetes increased. This is similar to the findings of study by Premnath G et al and Aung T et al.[21,22] Increase in lens thickness may be attributed to this finding.[23]

Table 2: Co-relation of gonioscopy with duration and severity of diabetes

Gonioscopy Grades		Grade 1	Grade 2	Grade 3	Grade 4	Statistics	
						Co-relation coefficient	p-value
Duration of diabetes	<5 years	-	20	24	78	-0.395	<0.001
	5-10 years	-	21	28	10		
	>10 years	5	7	7	-		
Grades of Retinopathy	No retinopathy	-	18	34	57	-0.200	0.004
	Mild NPDR	-	14	13	41		
	Moderate NPDR	2	6	1	-		
	Severe NPDR	1	-	10	-		
	PDR	2	-	1	-		

Table 3: Co-relation of blood sugar levels with AS-OCT parameters

Blood Sugar levels	Non-diabetics RBS<110mg%		Controlled diabetics RBS<140mg%		Uncontrolled Diabetics RBS>140mg%		p-value
AS-OCT Parameters	Median	Interquartile range	Median	Interquartile range	Median	Interquartile range	
AOD500 (AVG)(in μm)	0.40	0.34-0.47	0.37	0.34-0.41	0.35	0.32-0.37	<0.001
AOD 750 (AVG) (in μm)	0.69	0.56-0.83	0.58	0.53-0.65	0.58	0.48-0.64	<0.001
TISA500 (AVG) (in μm)	0.17	0.14-0.19	0.15	0.14-0.18	0.14	0.11-0.15	<0.001
TISA750 (AVG) (in μm)	0.29	0.20-0.31	0.28	0.25-0.31	0.26	0.24-0.30	<0.001
SSA (AVG) (in μm)	37	34.0-39.5	35.00	34.50-37.50	34.50	29.50-37.0	0.01
ACD (in mm)	2.5	2.43-2.70	2.21	1.76-2.55	1.96	1.78-2.43	0.04
Angle (AVG) (in degrees)	33.00	31.50-35.00	31.50	26.50-34.0	27.00	24.50-32.50	<0.001
Lens Vault (in μm)	1393.19	1279.73-1461.39	1311.16	1225.97-1419.42	1302.21	1219.82-1425.23	<0.001
ANG TO ANG Distance(in mm)	11.34	10.52-11.67	11.66	11.09-12.10	11.46	10.75-11.96	<0.001
CCT)(in μm)	513.00	497.00-532.0	524.00	504.00-548	552.00	524.00-578.0	<0.001

AS-OCT: Anterior segment optical coherence tomography; AOD500: Angle opening distance at 500μ; AOD750: Angle opening distance at 750μ; TISA500: Trabecular iris space area at 500μ(); TISA750: Trabecular iris space area at 750μ; SSA: Scleral spur area; ACD: Anterior chamber depth; CCT: Central corneal thickness

Studies have shown that duration of diabetes and severity of retinopathy do affect the anterior chamber depth. Though acute hyperglycaemic status may not affect the anterior chamber angle structures but still parameters like anterior chamber depth and lens thickness are narrower when compared to normal population as found in the present study.[24,25] While other studies have compared the angle parameters with respect to HbA1c status and did not find significant association between HbA1c and angle parameters, the present study has taken into account the RBS on the day of examination and the difference in angle parameters between diabetics and non-diabetics has been found to be statistically significant.[26,27]

The present study has used AS-OCT to calculate the angle parameters which gives a detailed account of angle parameters and has good reproducibility.[28,29] Suraida et al and Bayat et al have also used AS-OCT in their study to assess angle parameters. The findings of both studies corroborate to the present study with respect to the fact that the overall anterior chamber parameters indicate a shallower anterior chamber in diabetics than non-diabetics.[26,30] TISA 500 values in study by Bayat et al showed no significant difference between diabetics and non-diabetics as against the present study where the difference was significant. This was probably because they had not taken the duration and severity of the disease into consideration. Several other studies have found the AOD, ACD, angle of the anterior chamber to be shallower in diabetics though the effect of short stature, and female gender cannot be ruled out in these studies.[31,32] The present study on the other hand had more male patients.

The present study found that CCT was more in patients with increased duration and severity of diabetes which is corroborated by a meta-analysis with similar findings.[33]

Table 4: Co-relation of duration of diabetes with AS-OCT parameters

Duration	**Non-diabetics**		**<5 years**		**5-10 years**		**>10 years**		**p-value**
AS-OCT Parameters	Median	Interquartile range	Median	Interquartile range	Median	Interquartile range	Median	Interquartile range	
AOD500 (AVG) (in μm)	0.40	0.34-0.47	0.36	0.33-0.40	0.37	0.34-0.42	0.34	0.24-0.37	<0.001
AOD 750 (AVG) (in μm)	0.69	0.56-0.83	0.62	0.53-0.67	0.58	0.55-0.61	0.58	0.47-0.62	<0.001
TISA500 (AVG) (in μm)	0.17	0.14-0.19	0.14	0.13-0.15	0.16	0.16-0.21	0.14	0.09-0.15.	<0.001
TISA750 (AVG) (in μm)	0.29	0.20-0.31	0.29	0.26-0.31	0.26	0.24-0.29	0.27	0.23-0.29	<0.001
SSA (AVG) (in μm)	37	34.0-39.5	34.50	32.75-37.50	36.00	35.00-37.0	37.00	29.00-38.50	0.05
ACD (in mm)	2.5	2.43-2.70	2.14	1.76-2.55	2.11	1.98-2.45	2.20	1.96-2.45	<0.001
Angle (AVG) (in degrees)	33.00	31.50-35.00	30.50	26.38-33.00	32.00	27.50-35.00	26.25	23.50-31.50	<0.001
Lens Vault (in μm)	1393.19	1279.73-1461.39	1296.02	1221.76-1386.4	1342.72	1219.33-1485.24	1396.31	1302.21-1439.91	<0.001
ANG to ANG Distance (in mm)	11.34	10.52-11.67	11.45	10.98-11.99	11.72	11.49-11.96	11.45	10.75-12	<0.001
CCT) (in μm)	513.00	497.00-532.0	530.00	504.00-552.75	544.00	520.00-552.0	547.00	520.00-571	0.03

AS-OCT: Anterior segment optical coherence tomography; AOD500: Angle opening distance at 500μ; AOD750: aAngle opening distance at 750μ; TISA500: Trabecular iris space area at 500μ(); TISA750: Trabecular iris space area at 750μ; SSA: Scleral spur area; ACD: Anterior chamber depth; CCT: Central corneal thickness

Table 5: Co-relation of severity of retinopathy with AS-OCT parameters

Severity	**No retinopathy (n=309)**		**Mild NPDR (n=68)**		**Moderate NPDR (n=9)**		**Severe NPDR and PDR (n=14)**		**p-value**
AS-OCT Parameters	Median	Interquartile range	Median	Interquartile range	Median	Interquartile range	Median	Interquartile range	
AOD500 (AVG) (in μm)	0.32	0.30-0.35	0.36	0.33-0.37	0.38	0.25-0.38	0.32	0.30-0.33	<0.001
AOD 750 (AVG) (in μm)	0.65	0.55-0.85	0.56	0.52-0.61	0.58	0.47-0.58	0.64	0.54-0.64	<0.001
TISA500 (AVG) (in μm)	0.17	0.15-0.19	0.15	0.14-0.16	0.15	0.10-0.16	0.22	0.10-0.22	<0.001
TISA750 (AVG) (in μm)	0.25	0.19-0.32	0.25	0.24-0.28	0.29	0.26-0.31	0.32	0.25-0.32	<0.001
SSA (AVG) (in μm)	31.03	27.00-34.0	35.00	34.00-36.38	37.00	32.00-39.25	41.50	34.63-41.50	<0.001
ACD (in mm)	2.43	2.38-2.7	2.11	1.76-2.45	2.15	1.78-2.27	1.91	1.55-2.21	<0.001
Angle (AVG) (in degrees)	30.5	26.5-33	30.75	26.50-34.0	32.50	27.50-35.0	28.50	22.50-35.0	<0.001
Lens Vault (in μm)	1262.95	1225.97-1414.77	1336.62	1263.24-1427.62	1399.84	1209.45-1454.33	1351.93	1211.25-1421.40	<0.001
ANG to ANG Distance (in degrees)	11.49	10.71-11.67	11.68	10.79-11.99	11.96	11.48-11.96	11.41	11.12-11.66	<0.001
(CCT) (in μm)	518.0	497-530	521.00	498.75-544.0	578.00	559.00-581.5	580.00	556.75-595.0	<0.001

AS-OCT: Anterior segment optical coherence tomography; AOD500: Angle opening distance at 500μ; AOD750: Angle opening distance at 750μ; TISA500: Trabecular iris space area at 500μ(); TISA750: Trabecular iris space area at 750μ; SSA: Scleral spur area; ACD: Anterior chamber depth; CCT: Central corneal thickness

This might be because excess glucose in the corneas of patients with diabetes leads to intracellular accumulation of sorbitol, which acts as an osmotic agent and results in the swelling of endothelial cells.

According to Ellis et al, in 2.5% to 15.6%. of diabetic patients, glaucoma can be detected.[34] Diabetes compromises glial and neuronal functions in retina and therefore acts a predisposing factor for glaucomatous optic neuropathy. There occurs increased glycation of lipids and abnormal lipid metabolism in diabetes which increases oxidative stress and promotes apoptosis. Similar mechanism causes damage to retinal ganglion cells and results in glaucoma. Vascular dysregulation occurs in diabetes and in glaucoma as well. Alexander et al proved the importance of protein kinase C in the pathophysiology of diabetes. Protein kinase C has been linked to alterations of the matrix metalloprotease in the trabecular meshwork, which impairs aqueous outflow and raises IOP. This role of protein kinase C in the pathophysiology of diabetes has also been proven.[35] In diabetes and glaucoma, the delivery of neurotrophic factors is reduced in the optic nerve due to aberrant axonal transport, and expression of neurotrophic factors like insulin-like growth factor along with neurotrophin-3 is altered.[36] The evidence presented above may explain the likelihood of POAG in diabetic patients. Open angle glaucoma and diabetes have been definitively linked in most of the research, although angle closure glaucoma and diabetes have received less attention. Diabetics are at an increased risk of angle closure as seen by the findings of the present study.

While other studies have compared between various groups of diabetic patients or between diabetics and non-diabetics, the present study has made comparisons of angle structures between both diabetics and non-diabetics as well as between the different grades of diabetes based on duration and severity. It is one of the few studies comparing the angle parameters via AS-OCT in eastern Indian population.

5. Conclusion

Diabetes and glaucoma are both turning into a global problem affecting the quality of life of patients. Patients having both diabetes are at increased risk of not only open angle but also angle closure glaucoma as well. The need of repeated fundoscopy for detecting retinopathy changes further increases the risk of angle closure. With modern tools like AS-OCT at our disposal and keeping in mind the serious consequences of the disease, early and timely examination of angle parameters can help strategize our treatment for each individual and prevent the bigger problem at bay.

6. Source of Funding

None.

7. Conflict of Interest

The authors declare that there is no conflict of interest.

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