

**Original article:**

## **Comparison of Optic nerve head parameters in patients of Primary Open Angle Glaucoma with and without Diabetes Mellitus**

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### **ABSTRACT:**

**Background:** Glaucoma is a complex and genetically heterogenous disease characterised by structural damage to optic nerve head and visual field loss, eventually producing blindness if left untreated<sup>1</sup>, with diabetes posing a major risk factor.

**Aims and Objectives:** 1) To study the optic nerve head parameters in patients with primary open angle glaucoma. 2) To study optic nerve head parameters in patients of POAG with diabetes mellitus. 3) Comparison of optic nerve head parameters in patients with POAG with and without diabetes mellitus

**Methodology:** Patients attending Ophthalmology outpatient department in our institute diagnosed with POAG were enrolled. Patients of POAG with DM were allotted into Group- 1 and POAG without DM Group-2. Optic nerve head parameters were compared on OCT.

**Result:** Out of 166 enrolled, 83 patients were grouped as cases and control. Mean IOP levels were higher in cases (19.28 mmHg) than control group (15.3 mm Hg), difference was significant ( $p=0.000$ ). Average RNFL thickness was thinner in cases (85.27  $\mu\text{m}$ ) as compared to control group (90.69  $\mu\text{m}$ ), difference was significant ( $p=0.000$ ). Average Rim-area was less in cases (1.27  $\text{mm}^2$ ) compared to control group (1.39  $\text{mm}^2$ ), difference in rim area was significant ( $p=0.049$ ). Rest parameters were not statistically significant.

**Conclusion:** We got statistically significant difference between average retinal nerve fibre layer thickness and rim area in POAG patients with diabetes mellitus against POAG without diabetes mellitus.

**Key words:** POAG, DM, Optic nerve head parameters, Average RNFL thickness

### **BACKGROUND:**

Glaucoma is a complex and genetically heterogenous disease characterised by progressive apoptotic death of retinal ganglion cells that leads to structural damage to optic nerve head and visual field loss, eventually producing blindness if left untreated. <sup>1</sup>It is the second leading cause of blindness worldwide. Twelve million people worldwide are estimated to be blind because of the disease. It is estimated that 70- 80 million people will have glaucoma by year 2020 worldwide.<sup>2</sup> Primary open angle glaucoma (POAG) is the most common type of glaucoma.<sup>3</sup> It is a multifactorial optic neuropathy characterized by chronic progressive retinal ganglion cell death and tissue remodeling of the optic nerve head (ONH). It is followed by visual field defects corresponding to the neuroretinal rim (NRR) damage occurred as a result of disease.<sup>4</sup> Individuals with diabetes mellitus pose a risk of developing glaucoma and elevated intraocular pressure.<sup>5</sup> Several epidemiological studies with larger populations have reported

positive associations between diabetes with primary open angle glaucoma (POAG)<sup>6-11</sup>. Our aim of the study is to compare the optic nerve head parameters in diabetic and non-diabetic patients of POAG using OCT.

**AIMS AND OBJECTIVES:** 1) To study the optic nerve head parameters in patients with primary open angle glaucoma. 2) To study optic nerve head parameters in patients of POAG with diabetes mellitus. 3) Comparison of optic nerve head parameters in patients with POAG with and without diabetes mellitus.

#### **MATERIALS AND METHODS**

Study site : Medical college ; study population: Patients attending ophthalmology OPD ; study design: Comparative study; sample size : 83 eyes of 83 patients of both study and control group ; Time frame to address study: November 2016 to November 2018

#### **INCLUSION CRITERIA**

##### **Eyes of patient with POAG without Diabetes mellitus**

1. Patients older than 30 years
2. Patients diagnosed with POAG
3. No history of diabetes mellitus
4. No history of laser treatment or any ocular surgery

##### **Eyes of patient with POAG with Diabetes mellitus**

1. Patients older than 30 years
2. Patients diagnosed with POAG
3. Patients with diabetes mellitus
4. POAG patients having non proliferative diabetic retinopathy on fundus examination or on OCT scan.

#### **EXCLUSION CRITERIA**

1. Patient refusal to participate in study.
2. Poor media clarity affecting vision of patient (Corneal opacity, mature cataract, vitreous opacity)
3. Presence of Proliferative Diabetic retinopathy
4. Presence of previous intraocular surgeries (including trabeculectomy)
5. Presence of other macular pathology.
6. Any other retinal pathologies.
7. Any other ocular pathologies affecting vision (Inflammatory eye disease, pituitary lesion, demyelinating lesions, AIDS)
8. Secondary causes of glaucoma ( pseudoexfoliation, pigment dispersion glaucoma, iridocyclitis and trauma)

#### **MATERIALS REQUIRED**

1. Applanation Tonometry
2. 3 Mirror Gonioscope
3. Fundus Examination (by 90 D lens)
4. Slit Lamp microscope

5. Humphrey's Field Analyser Perimeter
6. SLO-OCT

## **METHODOLOGY**

- Subjects were selected among patients attending eye OPD of medical college.
- Ethical approval was taken from the ethical committee of the institute.
- A valid and informed consent was obtained from the patients willing to participate in the study once they received a detailed explanation of the evaluation procedure.
- All patients underwent complete ophthalmic examination, including visual acuity, refraction, slit-lamp examination, and fundus examination.
- IOP was measured by Applanation Tonometer.
- Gonioscopy was performed using a 3-mirror lens. Topical 0.5% proparacaine was used to anaesthetize cornea.
- Visual field changes were diagnosed using 24-2 SITA standard test strategy on Humphrey field analyser perimeter. A reliable VF defect was defined as one with less than 33% fixation loss and less than 20% false positives and false negatives.
- POAG diagnosis was done with following factors –(1) an optic disc or nerve fiber layer suspicious for glaucomatous damage, (inter-eye cup asymmetry  $> 0.2$ ; or neuroretinal rim notching, focal thinning, disc haemorrhage , or vertical elongation of the optic cup). (2) a visual field suspicious for glaucomatous damage, (3) consistently elevated IOP associated with normal appearance of the optic disc and retinal nerve fiber layer and with normal visual field test results. The anterior chamber angles must be open by gonioscopy, and there is no known secondary cause for suspicion of glaucoma.
- Patients with a known history of Diabetes Mellitus were enrolled
- Optic nerve heads were analyzed with the Spectral OCT SLO.
- Statistical analysis of the readings was done.

## **STATISTICAL METHODS**

Analyses were performed using Statistical Package for Social Sciences version 25. Normality of the groups was evaluated. The student t test was used for parametric data. Pearson's correlation coefficient was used when both the variables were parametric. Results were reported as mean $\pm$ SD with 95% confidence intervals and P=0.05 was considered as statistically significant.

**OBSERVATIONS & RESULTS**

Total 166 patients were enrolled in this study of which 83 patients were enrolled as cases and control groups for each category and equal distribution was obtained.

<b>TABLE 1. AGE DISTRIBUTION OF CASES AND CONTROL GROUPS</b>					
			<b>Cases</b>	<b>Control</b>	<b>Total</b>
<b>Age Groups</b>	<b>&lt; 40</b>	<b>Count</b>	2	1	3
		<b>% within Group</b>	2.4%	1.2%	1.8%
	<b>40-49</b>	<b>Count</b>	18	15	33
		<b>% within Group</b>	21.7%	18.1%	19.9%
	<b>50-59</b>	<b>Count</b>	31	26	57
		<b>% within Group</b>	37.3%	31.3%	34.3%
	<b>60-69</b>	<b>Count</b>	25	27	52
		<b>% within Group</b>	30.1%	32.5%	31.3%
	<b>70-79</b>	<b>Count</b>	7	14	21
		<b>% within Group</b>	8.4%	16.9%	12.7%
	<b>Total</b>	<b>Count</b>	83	83	166
		<b>% within Group</b>	100.0%	100.0%	100.0%

Table 1 shows age distribution of study and control population. In cases, 31 (37.3 %) patients were between 50- 59 years of age and 25 (30.1%) patients were between 60-69years of age. In the control group, 27 patients (32.5%) were between 60-69 years of age and 26(31.3%) patients were between 50-59 years of age.

The difference in age distribution in POAG in DM and without DM was not statistically significant.

There were 48.2%(40 out of 83) male cases and 51.8%(43 out of 83) male control respectively, Similarly 51.8% (43 out of 83) were female cases and 48.2% (40 out of 83) females in control which showed slight gender wise difference i.e. females slightly more than males amongst cases but statistically showed no significant difference.

. The mean IOP levels were higher in cases that is 19.28 mmHg as compared to control group which is 15.3 mm Hg respectively, and the difference of IOP levels of PAOG with and without DM was significant.(p=0.000).

The average RNFL thickness were thinner in cases that is, 85.27 um as compare to control group which is 90.69 um respectively, and the difference was significant.(p=0.000).

The average **Rim-area** was less in cases that is 1.27 mm<sup>2</sup> as compare to control group which is 1.39 mm<sup>2</sup> respectively, and the difference in rim area was significant in study group.(p=0.049).

The average disc area was nearly same in cases that is, 2.1282 mm<sup>2</sup> and control group which is 2.0130 mm<sup>2</sup> respectively, and the difference in disc area between cases and control was not found to be significant.(p=0.141)

The average Cup disc ratio was nearly same in cases that is, **0.6898** and control group which is **0.7028** respectively, and the difference in average Cup disc ratio was found to be insignificant(p=0.410).

The vertical Cup disc ratio was nearly same in cases that is, **.6578** and control group which is **.6810** respectively, and the difference in vertical Cup disc ratio was found to be insignificant (p=0.150).

. The **Cup-volume** was nearly same in cases that is **0.41821** and control group which is **0.42314** respectively, and the difference in cup volumes was found to be non significant (p=0.870).

## DISCUSSION

In this study, we attempted to make a comparison of Optic nerve head parameters using Optical Coherence Tomography in patients of Primary Open Angle Glaucoma with and without Diabetes Mellitus. **Females** were slightly more common in cases 43 out of 83 cases i.e 51.8 % ,than males 40 out of 83 cases i.e 48.2% but the difference was not statistically significant (p=0.641). **S. Akkaya**<sup>12</sup> noted higher prevalence in women though the difference was insignificant. **Vajaranant et al**<sup>13</sup> suggest female are at higher risk of developing POAG than male. Our study is in keeping with Vajaranant et al and S. Akkaya whereas not correlating with Bayesian meta-regression model. We got IOP levels 19.28 mmHg in cases and 15.13 mm Hg in cases and control and the difference was statistically significant(p=0.000)

Studies by **Guo L et al**<sup>14</sup> and **Soto I et al**<sup>15</sup> indicate that increased IOP in diabetes is associated with the death of retinal ganglion cells which progressively damages optic nerve head due to mechanical compression. IOP levels appeared low with tight glycemic control.

**Maggie B et al**<sup>16</sup> indicated that long-term diabetic patients with elevated HbA1c levels exhibit significantly higher IOPs compared to those with lower HbA1c levels. In particular, findings indicate a statistically significant difference in HbA1c levels between diabetic subjects with low IOP and those with high IOP. Our findings are in keeping with above authors with statistically significant difference in IOP levels in POAG with diabetes and without diabetes.

We got **average RNFL thinning** in study group 85.27 microns while in control it was 90.69 microns. In our study ,the difference in average RNFL thickness between case control was statistically significant. **Sari MD et al.** <sup>17</sup> demonstrated that there was a statistically significant reduction in superior RNFL thickness in open angle glaucoma with DM Type . Sari et al noted average RNFL thickness 60.43 which is in keeping with our study while differs from study Budde et al<sup>18</sup> and Jeong et al.<sup>19</sup>

We got **rim area** in case 1.27 mm<sup>2</sup> and 1.39 mm<sup>2</sup> in control the difference was significant (p=0.049) In study by S. Akkaya, mean rim area was 1.63 and 1.42 in cases and control respectively (p = 0.04) <sup>27</sup> difference was statistically significant.

Table 2 :

Study	Rim area(mm <sup>2</sup> )		P value
	Cases	Controls	
S. Akkaya	1.63	1.42	0.04
Our study	1.27	1.39	0.049

**Rim-area** was less in diabetic POAG patients as compared to non-diabetic POAG patients. Decreased Rim area may be due to the possibility of decreased number of optic nerve fibers in diabetic with POAG, so our results are not in favor of above study so there is need for further studies to establish the correlation between rim area in Diabetic POAG patient.

Our study demonstrated mean disc area in cases of 2.12 mm<sup>2</sup> while in control we got 2.0130 mm<sup>2</sup>. But the difference was not statistically significant.(p=0.141)

Budde et al<sup>18</sup> concluded that diabetes does not have a marked effect on ONH damage in POAG patients including disc area , rim area.Thus , our results are in keeping with the above study.

We got average cup disc ratio of 0.6898 in cases while 0.7028 in control suggesting the protective effect of diabetes in POAG.

S. Akkaya et al <sup>12</sup> did not find significant differences in cup area and cup volume between diabetic and nondiabetic POAG patients. In diabetic POAG patients, greater measurements of rim area and rim volume together with the absence of any increase in the optic cup depth lead to consideration that diabetes may cause protective effect on optic nerve and retinal nerve fibers in POAG.

The findings are in keeping with the study but the difference of average cup disc ratio was not statistically significant (p=0.410).

Similarly, Vertical CDR and Cup volume showed no statistically significant difference in our study (p=0.150) and (p=0.870) respectively which is again correlating with study by S. Akkaya as discussed above.

Jeong et al <sup>19</sup> found no statistically significant difference in ONH parameters of POAG with and without DM including cup related parameters average CDR, vertical CDR, and cup volume.

Thus it can be argued that our study showed protective effect of diabetes in POAG but the effect was not statistically significant.

## CONCLUSION

In our study, there existed a statistically significant difference between average retinal nerve fibre layer thickness and rim area in POAG patients with diabetes mellitus against POAG without diabetes on basis of optic nerve head parameters evaluated on optical coherence tomography. Also, there was significant difference between intraocular pressure levels in patients of POAG with DM and without DM.

We need further similar studies to establish a better understanding of effect of diabetes mellitus on optic nerve head parameters in patients primary open angle glaucoma in support of our study.

## ABBREVIATIONS:

OCT – Optical coherence tomography

CDR- Cup to Disc Ratio

DM-Diabetes Mellitus

IOP-Intraocular Pressure

MD-Mean Deviation

OAG-Open Angle Glaucoma

POAG-Primary Open Angle Glaucoma

PSD-Pattern Standard Deviation

RNFL-Retinal Nerve Fibre Layer

VF-Visual Fields

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