



## COMPARISON OF CHANGE IN CENTRAL CORNEAL THICKNESS IN PATIENTS OF PRIMARY OPEN ANGLE GLAUCOMA ON PROSTAGLANDINS MONOTHERAPY, BETA BLOCKERS MONOTHERAPY AND CARBONIC ANHYDRASE INHIBITOR-BETA BLOCKER COMBINATION THERAPY

Sara Ashraf<sup>1\*</sup>, Ramsha Jehangir<sup>2</sup>, Faraz Munir<sup>3</sup>, Abeer Fatima<sup>4</sup>, Hira Shuja Khokhar<sup>5</sup>, Syed Muhammad Jahangir<sup>6</sup>, Ayesha Naeem<sup>7</sup>

<sup>1\*</sup>Senior Registrar, Al-Aleem Medical College, Lahore, Pakistan, saraashraf91@gmail.com

<sup>2</sup>Consultant Ophthalmologist, VR Fellow, Lahore General Hospital, Lahore, Pakistan.  
ophthalmologist.rj@gmail.com

<sup>3</sup>Senior Registrar, Department of Ophthalmology, Akhter Saeed Teaching Hospital, Lahore, Pakistan.  
drfarazmunir@gmail.com,

<sup>4</sup>Consultant ophthalmologist Khizar Eye Center, abeer.jalil92@gmail.com

<sup>5</sup>Senior Registrar, Department of Ophthalmology, Gujranwala Medical College Teaching Hospital, Gujranwala, Pakistan. hirashuja@gmail.com

<sup>6</sup>Consultant Ophthalmologist, Eye Site Clinic, Lahore, Pakistan, dr-jahangir@hotmail.com

<sup>7</sup>Doctor of Pharmacy, Forman Christian College, University, Lahore ayeshanaeem5855@gmail.com

**\*Corresponding author:** Sara Ashraf

\*Senior Registrar, Al-Aleem Medical College, Lahore, Pakistan, saraashraf91@gmail.com

### ABSTRACT

**BACKGROUND:** The most prevalent type of glaucoma worldwide is the primary open angle glaucoma (POAG). It features progressive retinal ganglionic cell axons' loss causing peripheral visual field loss initially and ultimately leading to irreversible blindness if left unmanaged. IOP is the only modifiable factor with proven effect in stopping glaucomatous damage.

**OBJECTIVE:** To compare the change in central corneal thickness (CCT) in patients of primary open angle glaucoma (POAG) on Prostaglandins monotherapy, beta blockers monotherapy and Carbonic Anhydrase Inhibitor (CAI) - Beta Blocker combination therapy.

### MATERIALS AND METHODS

This quasi-experimental study was carried out at Institute of Ophthalmology Unit III, KEMU/Mayo Hospital, Lahore. The study was completed in 1 year after the approval of synopsis. Patients were started on prostaglandins monotherapy (latanoprost), beta blockers monotherapy (betagan) or CAI-beta blockers combination therapy (Co-dorzal) as per the need; placed in groups A, B and C respectively. CCT was measured before the start of therapy with the use of pachymeter.

**RESULTS:** The results showed the mean age of all patients to be  $51.65 \pm 9.62$  years with minimum and maximum age as 40 and 85 years. In this study there were 65(45.1%) male and 79(54.9%) female cases. At baseline, the mean CCT of the right side was  $540.12 \pm 4.10$ ,  $539.25 \pm 3.35$  and  $538.98 \pm 3.17$  in the groups A, B and C respectively with no significant difference. On the left side, the mean

CCT was  $539.75 \pm 3.43$ ,  $538.71 \pm 2.47$  and  $538.98 \pm 3.09$  for groups A, B and C respectively with no significant difference.

**CONCLUSION:** It is concluded that the mean change in central corneal thickness and IOP was statistically higher in group A (prostaglandins monotherapy) patients as compared to group-B (beta-blockers) and group-C (beta-blockers and carbonic anhydrase inhibitors combination therapy) in primary open angle glaucoma patients. Hence in future the effect of drugs must be borne in mind when measuring IOP and the measurement be adjusted with repeated central corneal thickness measurements.

**Keywords:** Primary open angle glaucoma, Central corneal thickness, prostaglandins monotherapy, beta blockers monotherapy, carbonic anhydrase inhibitor.

## INTRODUCTION

Glaucoma is a term used for multi-factorial ocular disorders combined by specific features of optic nerve head changes and visual field defects; one cause of which is raised intraocular pressure.<sup>1</sup> According to WHO, it stands second as the commonest cause of blindness globally.<sup>2</sup> It accounts for 6.6% of the worldwide blindness.<sup>3</sup> Asia accounts alone for 60% of world's cases.<sup>4</sup> Glaucoma patients have risen from 64 million to 76 million by 2020 with maximum load in Africa and Asia.<sup>5</sup> Glaucoma prevention and treatment was a major focus of WHO VISION 2020 Campaign.<sup>6</sup> POAG is the most common form characterised by progressive loss of retinal ganglionic cell axons causing peripheral visual field loss initially and ultimately leading to irreversible blindness if left unmanaged.<sup>7</sup> Intraocular pressure (IOP) lowering is the primary goal of therapy as it reduces the risk of progression of loss of visual field and damage to optic disc.<sup>1, 8</sup> It can be achieved by medical, laser or surgical intervention with no evidence supporting as to which of these modalities is superior to be opted first. CIGTS (Collaborative Initial Glaucoma Treatment Study) has shown no significant difference in outcome of the patients opting either medical or surgical therapy. Commonly we start with medical therapy.<sup>9</sup> Surgery is opted in case of worsening of optic neuropathy at any given level of IOP. Topical drug classes commonly used include beta blockers, alpha agonists, prostaglandin analogues, miotic agents, carbonic anhydrase inhibitors.<sup>10</sup> Management and long term follow up depends upon IOP. However, these topical medications cause changes in corneal thickness confounding the IOP readings as the conventional tonometers like Goldmann, Perkins and tonopen used for IOP recording are dependent on CCT.

Studies show that topical prostaglandins lower CCT by upregulating MMPs.<sup>11, 12</sup> Study by Grub showed that CCT is increased by topical beta blockers.<sup>13</sup> CAI are also known to have similar effect.<sup>12</sup> James in his study documented that topical prostaglandins led to more decrease of CCT per year as compared to treatment with beta blockers alone.<sup>14</sup> Seibel and others had similar results with prostaglandins causing decreased CCT and keratocyte density.<sup>15-18</sup> Viswancithan had comparable outcome while comparing prostaglandins and beta blockers.<sup>19</sup> A study on north Indian population showed decreased CCT with prostaglandins.<sup>20</sup> However, few studies show CCT is increased by prostaglandins.<sup>21, 22</sup> Some studies show that this change in CCT is likely to influence IOP reading.<sup>12, 21, 22</sup> while others show it to be insignificant clinically.<sup>14, 17, 20</sup>

## MATERIALS AND METHODS

It was a quasi-experimental study. The study was carried out at Institute of Ophthalmology Unit III, KEMU/Mayo Hospital, and Lahore. Duration of study is One Year after the approval of synopsis. Hypothesis for two population mean (one-sided test). Sample size is 144 patients (48 in each group). Sampling technique was a non-probability, convenient sampling technique.

◆ **Inclusion criteria:**

- i. Patients above 40 years of age of both genders.
- ii. Patients diagnosed with primary open angle glaucoma with grade 4 on gonioscopy.
- iii. Patients with corneal thickness above 535µm.

◆ **Exclusion criteria:**

- i. Patients having corneal opacity, corneal dystrophies and degenerations.
- ii. Patients having keratitis, corneal ulcers and corneal perforation.
- iii. Patients having metabolic, exposure and neurotrophic keratopathy.
- iv. Patients having undergone refractive surgery and keratoplasty.
- v. Prolonged contact lens wearers.
- vi. Raised IOP not diagnosed as POAG.

Patients were recruited from the outpatient department of Ophthalmology Unit 3 of Mayo Hospital Lahore. An informed and written consent was taken from the participants of this study. Associated risk factors were documented in specially designed Performa. Patients were started on prostaglandins monotherapy (latanoprost), beta blockers monotherapy (betagan) or CAI-beta blockers combination therapy (Co-dorzal) as per the need and placed in groups A, B and C respectively. CCT was measured before initiation of therapy with the use of pachymeter. Patients were followed at monthly intervals to ensure compliance with topical medications. CCT was measured at 1, 3 months and 6 months after initiation of therapy. Patients not responding to topical medication in either group were excluded out of the study and managed appropriately for their disease control. SPSS version 26 was used to analyse the data. Quantitative variables like IOP and CCT were presented as mean ±SD. Qualitative variables like gender were presented as frequency and percentages. Comparison of the change in CCT of three groups topical prostaglandins monotherapy (group A), beta blockers monotherapy ( group B) and beta-blockers CAI combination therapy ( group C) was done using repeated measures of ANOVA test. One way ANOVA was also applied. Where ANOVA results were significant, LSD test for multiple comparison tests was applied. P value ≤ 0.05 was taken as being significant.

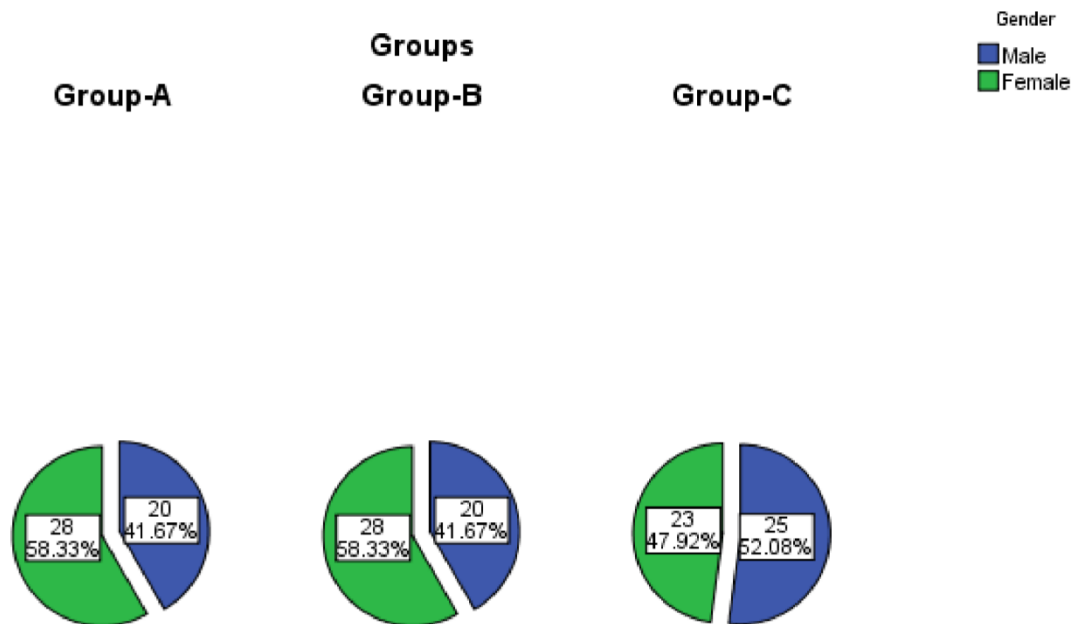
**RESULTS**

**Table-2: Descriptive statistics of age (years) in study groups**

Study groups	Age (years)				p-value
	Mean	S.D	Minimum	Maximum	
<i>Group-A</i>	53.46	11.38	40	85	0.272
<i>Group-B</i>	50.48	9.17	40	85	
<i>Group-C</i>	51.02	7.92	41	73	
<i>Total</i>	51.65	9.62	40	85	

The mean age of all patients was 51.65 ± 9.62 years with minimum and maximum age as 40 and 85 years respectively. The mean age in group-A was 53.46 ± 11.38 years , for group-B 50.48 ± 9.17 years and group-C 51.02 ± 7.92 years. The mean age was statistically same in groups, p-value > 0.05.

**Fig-4: Descriptive statistics of gender in study groups**



In this study there were 65(45.1%) male and 79(54.9%) female cases. In group-A there were 20(41.67%) male and 28(58.33%) female cases, while in group-B there 20(41.67%) male and 28(58.33%) female cases and in group-C there were 25(52.08%) male and 23(47.92%) female cases.

**Table-3: Comparison of visual acuity in RIGHT eye in all study groups**

		Groups			Total
		Group-A	Group-B	Group-C	
VA	<b>6/18</b>	4(8.3%)	3(6.2%)	1(2.1%)	8(5.6%)
	<b>6/24</b>	22(45.8%)	26(54.2%)	1(2.1%)	49(34%)
	<b>6/36</b>	16(33.3%)	10(20.8%)	9(18.8%)	35(24.3%)
	<b>6/60</b>	6(12.5%)	9(18.8%)	37(77.1%)	52(36.1%)
<b>Total</b>		48(100%)	48(100%)	48(100%)	144(100%)

Chi-square = 60.020

P-value  $\leq 0.001$  (Highly significant)

According to VA in Right eye, in group-A there were 4(8.3%) cases who had 6/18, 22(45.8%) cases had 6/24, 16(33.3%) cases had 6/36 and 6(12.5%) cases had 6/60 or below visual acuity. In group-B 3(6.2%) cases had 6/18, 26(54.2%) cases had 6/24, 10(20.8%) cases had 6/36 and 9(18.8%) cases had 6/60 or below. In group-C 1(2.1%) case had 6/18, 1(2.1%) had 6/24, 9(18.8%) had 6/36 and 37(77.1%) 6/60 or below visual acuity. There was a significant difference of visual acuity in different study groups of the right side, p-value < 0.05.

**Table-4: Comparison of visual acuity in LEFT eye in all study groups**

		Groups			Total
		Group-A	Group-B	Group-C	
VA	6/18	10(20.8%)	7(14.6%)	2(4.2%)	19(13.2%)
	6/24	22(45.8%)	26(54.2%)	3(6.2%)	51(35.4%)
	6/36	12(25%)	11(22.9%)	16(33.3%)	39(27.1%)
	6/60	4(8.3%)	4(8.3%)	27(56.2%)	35(24.3%)
<b>Total</b>		48(100%)	48(100%)	48(100%)	144(100%)

Chi-square = 54.22, P-value ≤ 0.001 (Highly significant)

According to VA in Left eye, in groups A, B and C there were 10(20.8%), 7(14.6%) and 2(4.2%) cases who had 6/18 visual acuity, 22(45.8%), 26(54.2%) and 3(6.2%) cases had 6/24 visual acuity, 12(25%), 11(22.9%) and 16(33.3%) cases 6/36 visual acuity and 4(8.3%), 4(8.3%) and 27(56.2%) had 6/60 visual acuity. There was a significant difference of visual acuity of the left side in different study groups shown by p-value < 0.05.

**Table-5: Comparison of Intraocular pressure (right eye) in study groups**

Study groups	Intraocular pressure (right)				p-value
	Mean	S.D	Minimum	Maximum	
Group-A	25.67	1.55	22	30	<0.001**
Group-B	25.38	1.63	18	28	
Group-C	28.21	1.65	22	30	
<b>Total</b>	26.42	2.05	18	30	

**Pair wise comparison**

Dependent variable	(I) Group	(J) group	p-value
<b>Intraocular pressure (right)</b>	Group-A	Group-B	0.377
		Group-C	<0.001**
	Group-B	Group-C	<0.001**

\*\*Highly significant, \*Significant

The mean intraocular pressure of the right side was 25.67 ± 1.55 in group-A, 25.38 ±

1.63 in group-B and 28.21 ± 1.65 in group-C, with significant difference, p-value < 0.001. On applying multiple comparison test, a significant difference was present in group-A compared to group-C and group-B compared to group-C shown by p-value <0.05.

**Table-6: Comparison of Intraocular pressure (left eye) in study groups**

Study groups	Intraocular pressure (left)				p-value
	Mean	S.D	Minimum	Maximum	
<i>Group-A</i>	25.50	1.58	22	30	<0.001**
<i>Group-B</i>	24.83	1.62	18	28	
<i>Group-C</i>	27.48	2.21	19	30	
<i>Total</i>	25.94	2.14	18	30	

*Pair wise comparison*

Dependent variable	(I) Group	(J) Group	p-value
<i>Intraocular pressure (left)</i>	<i>Group-A</i>	Group-B	0.076
		Group-C	<0.001**
	<i>Group-B</i>	Group-C	<0.001**

\*\*Highly significant

The mean intraocular pressure of the left side was  $25.50 \pm 1.58$  in group-A,  $24.83 \pm 1.62$  in group-B and  $27.48 \pm 2.21$  in group-C, with significant difference, p-value < 0.001. On applying multiple comparison test, significant difference was seen in group-A as compared to group-C and group-B as compared to group-C, p-value <0.05.

**Table-7: Comparison of CCT before topical therapy in study groups**

Study groups	CCT before topical therapy (right)				p-value
	Mean	S.D	Minimum	Maximum	
<i>Group-A</i>	540.12	4.10	536	557	0.261
<i>Group-B</i>	539.25	3.35	535	548	
<i>Group-C</i>	538.98	3.17	534	548	
<i>Total</i>	539.45	3.57	534	557	
Study groups	CCT before topical therapy (left)				p-value
	Mean	S.D	Minimum	Maximum	
<i>Group-A</i>	539.75	3.43	535	548	0.219
<i>Group-B</i>	538.71	2.47	535	546	
<i>Group-C</i>	538.98	3.09	534	546	
<i>Total</i>	539.15	3.03	534	548	

At baseline the mean CCT of the right side in group-A, group-B and group-C was  $540.12 \pm 4.10$ ,  $539.25 \pm 3.35$  and  $538.98 \pm 3.17$  respectively with no significant difference as shown by p-value >

0.05. The mean CCT for left side in group-A, group-B and group-C was  $539.75 \pm 3.43$ ,  $538.71 \pm 2.47$  and  $538.98 \pm 3.09$  respectively showing no significant difference as shown by  $p\text{-value} > 0.05$ .

**Table-8: Comparison of CCT of right side at 1 month after topical medication in all study groups**

Study groups	CCT 1 month after topical medication (right)				p-value
	Mean	S.D	Minimum	Maximum	
<i>Group-A</i>	534.69	3.35	530.0	543.0	<0.001**
<i>Group-B</i>	537.83	3.37	534.0	547.0	
<i>Group-C</i>	539.66	3.11	536.0	548.9	
<i>Total</i>	537.39	3.85	530.0	548.9	

*Pair wise comparison*

Dependent variable	(I) Group	(J) group	p-value
<i>CCT of right side after 1 month</i>	<i>Group-A</i>	Group-B	<0.001**
		Group-C	<0.001**
	<i>Group-B</i>	Group-C	0.007*

\*\*Highly significant, \*Significant

At 1 month follow up, the mean CCT of the right side in group-A, group-B and group-C was  $534.69 \pm 3.35$ ,  $537.83 \pm 3.37$  and  $539.66 \pm 3.11$  respectively, with significant difference,  $p\text{-value} < 0.001$ . On applying multiple comparison test, significant difference was seen in group-A when compared with group-B and group-C and group-B as compared to group-C,  $p\text{-value} < 0.05$ .

**Table-9: Comparison of CCT of left side at 1 month after topical medication in all study groups**

Study groups	CCT 1 month after topical medication (left)				p-value
	Mean	S.D	Minimum	Maximum	
<i>Group-A</i>	535.23	3.46	530.0	545.0	<0.001**
<i>Group-B</i>	537.48	2.74	532.0	545.0	
<i>Group-C</i>	539.64	3.08	535.0	548.0	
<i>Total</i>	537.45	3.58	530.0	548.0	

*Pair wise comparison*

Dependent variable	(I) Group	(J) group	p-value
<i>CCT of left side after 1 month</i>	<i>Group-A</i>	Group-B	0.001*
		Group-C	<0.001**
	<i>Group-B</i>	Group-C	0.001*

\*\*Highly significant, \*Significant

Comparison Of Change In Central Corneal Thickness In Patients Of Primary Open Angle Glaucoma On Prostaglandins Monotherapy, Beta Blockers Monotherapy And Carbonic Anhydrase Inhibitor-Beta Blocker Combination Therapy

At 3 months of follow up, the mean CCT of right side in group-A, group-B and group-C was  $535.23 \pm 3.46$ ,  $537.48 \pm 2.74$  and  $539.64 \pm 3.08$  respectively, with significant difference, p-value < 0.001. On applying multiple comparison test, a significant difference was found in group-A as compared to group-B and group-C and group-B compared to group-C with p-value < 0.05.

**Table-10: Comparison of CCT of right side at 3 month after topical medication in all study groups**

Study groups	CCT 3 month after topical medication (right)				p-value
	Mean	S.D	Minimum	Maximum	
<i>Group-A</i>	535.69	7.73	530.0	583.0	0.010*
<i>Group-B</i>	537.12	3.42	533.0	546.0	
<i>Group-C</i>	539.00	3.39	535.0	548.0	
<i>Total</i>	537.27	5.40	530.0	583.0	

*Pair wise comparison*

Dependent variable	(I) Group	(J) group	p-value
<i>CCT of right side at 3 month</i>	<i>Group-A</i>	Group-B	0.183
		Group-C	0.002*
	<i>Group-B</i>	Group-C	0.082

\*Significant

At 3 months of follow up, the mean CCT of the right side in group-A, group-B and group-C was  $535.69 \pm 7.73$ ,  $537.12 \pm 3.42$  and  $539.00 \pm 3.39$  respectively, with significant difference, p-value < 0.001. On applying multiple comparison test, significant difference was found in group-A as compared to group- C only, p-value <0.05.

**Table-11: Comparison of CCT 3 month after topical medication (left) in study groups**

Study groups	CCT 3 month after topical medication (left)				p-value
	Mean	S.D	Minimum	Maximum	
<i>Group-A</i>	535.33	3.37	530.0	545.0	<0.001**
<i>Group-B</i>	536.92	3.04	532.0	547.0	
<i>Group-C</i>	538.64	3.22	534.0	547.1	
<i>Total</i>	536.96	3.47	530.0	547.1	

*Pair wise comparison*

Dependent variable	(I) Group	(J) group	p-value
<i>CCT of left side at 3 month</i>	<i>Group-A</i>	Group-B	0.017*
		Group-C	<0.001**
	<i>Group-B</i>	Group-C	0.009*

\*\*Highly significant, \*Significant



Comparison Of Change In Central Corneal Thickness In Patients Of Primary Open Angle Glaucoma On Prostaglandins Monotherapy, Beta Blockers Monotherapy And Carbonic Anhydrase Inhibitor-Beta Blocker Combination Therapy

At 3 months of follow up, the mean CCT of the left side in group-A, group-B and group-C was  $535.33 \pm 3.37$ ,  $536.92 \pm 3.04$  and  $538.64 \pm 3.22$  respectively, with significant difference, p-value < 0.001. On applying multiple comparison test, significant difference was found in group-A as compared to group-B and group-C and group-B when compared to group-C, p-value < 0.05.

**Table-12: Comparison of CCT 6 months after topical medication (right) in study groups**

Study groups	CCT 6 months after topical medication (right)				p-value
	Mean	S.D	Minimum	Maximum	
<i>Group-A</i>	532.38	3.36	527.0	541.0	<0.001**
<i>Group-B</i>	539.17	3.20	534.0	548.0	
<i>Group-C</i>	538.28	3.45	527.0	547.0	
<i>Total</i>	536.61	4.48	527.0	548.0	

**Pair wise comparison**

Dependent variable	(I) Group	(J) group	p-value
<i>CCT of right side after 6 months</i>	<i>Group-A</i>	Group-B	<0.001**
		Group-C	<0.001**
	<i>Group-B</i>	Group-C	10.94

\*\*Highly significant, \*Significant At 6 months of follow up, the mean CCT of right side in group-A, group-B and group-C was  $532.38 \pm 3.36$ ,  $539.17 \pm 3.20$  and  $538.28$

$\pm 3.45$  respectively, with significant difference, p-value < 0.001. On applying multiple comparison test, significant difference was found in group-A versus group-B and group-C, p-value < 0.05. While group-B and C were statistically same, p-value > 0.05.

**Table-13: Comparison of CCT 6 months after topical medication (left) in study groups**

Study groups	CCT 6 months after topical medication (left)				p-value
	Mean	S.D	Minimum	Maximum	
<i>Group-A</i>	532.60	3.48	526.0	540.0	
<i>Group-B</i>	538.52	2.97	532.0	545.0	
<i>Group-C</i>	538.14	3.06	534.0	546.8	
<i>Total</i>	536.42	4.17	526.0	546.8	

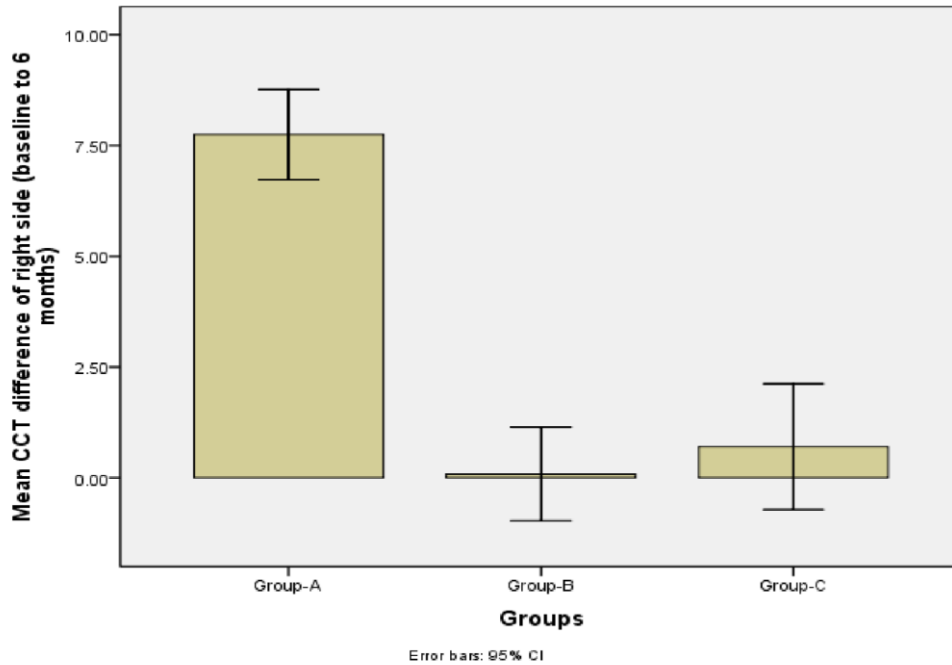
**Pairwise comparison**

Dependent variable	(I) Group	(J) group	p-value
<i>CCT of left side at 6 months</i>	<i>Group-A</i>	Group-B	<0.001**
		Group-C	<0.001**
	<i>Group-B</i>	Group-C	0.554

\*\*Highly significant, \*Significant

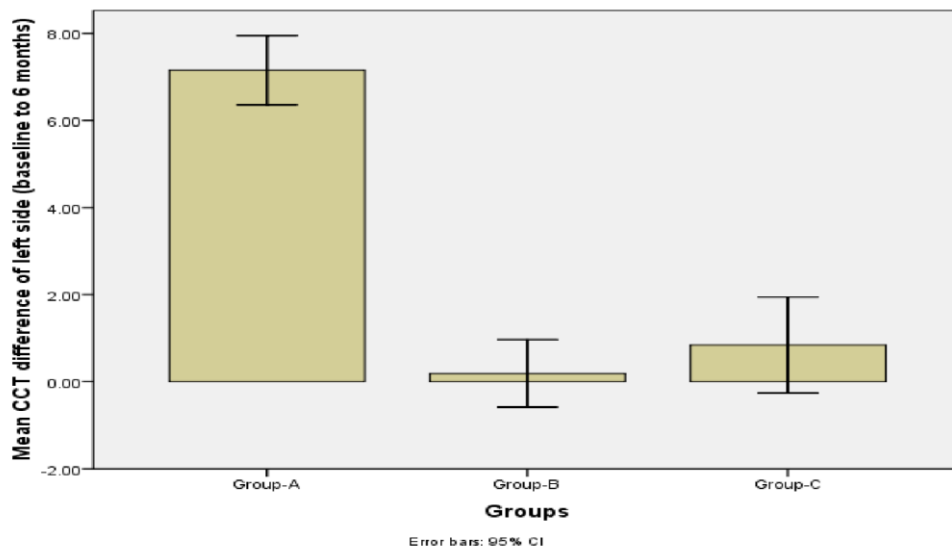
Comparison Of Change In Central Corneal Thickness In Patients Of Primary Open Angle Glaucoma On Prostaglandins Monotherapy, Beta Blockers Monotherapy And Carbonic Anhydrase Inhibitor- Beta Blocker Combination Therapy

At 6 months of follow up, the mean CCT of the left side in group-A, group-B and group-C was  $532.60 \pm 3.48$ ,  $538.52 \pm 2.97$  and  $538.14 \pm 3.06$  respectively, with significant difference, p-value  $< 0.001$ . On applying multiple comparison test, significant difference was found in group-A versus group-B, and group-C p-value  $< 0.05$ , while group-B and C were statistically same.



**Fig-5: Comparison of mean difference of CCT (Baseline – 6 months follow ups) of right side in all study groups**

The mean difference of CCT from baseline to 6 months follow ups on the right side in group-A, group-B and group-C was  $7.75 \pm 3.50$ ,  $0.08 \pm 3.64$  and  $0.70 \pm 4.90$  respectively with significant difference, p-value  $< 0.05$ . On applying multiple comparison test, it was found that reduction was significant of Group-A when compared with group B and C p-value  $< 0.05$ .



**Fig 6-: Comparison of mean difference of CCT (Baseline – 6 months follow ups) of left side in all study groups**

Comparison Of Change In Central Corneal Thickness In Patients Of Primary Open Angle Glaucoma On Prostaglandins Monotherapy, Beta Blockers Monotherapy And Carbonic Anhydrase Inhibitor-Beta Blocker Combination Therapy

The mean difference of CCT from baseline to 6 months follow ups on the right side in group-A, group-B and group-C was  $7.15 \pm 2.74$ ,  $0.19 \pm 2.68$  and  $0.84 \pm 3.79$  respectively with significant difference,  $p$ -value  $< 0.05$ . On applying multiple comparison test, it was found that reduction was significant of Group-A when compared with group B and C  $p$ -value  $< 0.05$ .

**Table – 14: Comparison of difference (from baseline to 6<sup>th</sup> months) of CCT in left and right side among all study groups**

Groups	Comparison of difference (from baseline to 6 <sup>th</sup> months) of CCT in left and right side among all study groups	Mean	S.D	p-value
Group-A	CCT before topical therapy (right)	540.12	4.10	<0.001
	CCT 6 months after topical medication (right)	532.37	3.36	
	CCT before topical therapy (left)	539.75	3.43	<0.001
	CCT 6 months after topical medication (left)	532.59	3.48	
Group-B	CCT before topical therapy (right)	539.25	3.20	8.75
	CCT 6 months after topical medication (right)	539.16	2.46	
	CCT before topical therapy (left)	538.71	2.97	6.30
	CCT 6 months after topical medication (left)	538.52	3.19	
Group-C	CCT before topical therapy (right)	538.98	3.16	0.326
	CCT 6 months after topical medication (right)	538.27	3.44	
	CCT before topical therapy (left)	538.98	3.09	0.130
	CCT 6 months after topical medication (left)	538.13	3.06	

The mean CCT after 6 months ( for right and left) was significantly reduced in group-A,  $p$ -value  $< 0.05$  while its change was statistically insignificant in both group-B and group-C,  $p$ -value  $> 0.05$ .

**DISCUSSION**

Throughout the world, glaucoma is an important cause of irreversible blindness and ocular morbidity. Approximately worldwide people expected to have been afflicted with POAG by year 2020 is 65.5 million people. The highest prevalence of this disease is present in the blacks for all the age groups with the exception of Hispanics in more than 80 years age group. The accurate diagnosis and monitoring of glaucoma is largely dependent on accurate measurement of the IOP. GAT is the gold standard currently for this purpose. However, its readings are affected by variations in the CCT<sup>20</sup>. In OHTS, thinner CCT was found to be a strong predictor for developing POAG. It could be due to missing out of initial glaucomatous changes due to underestimation of the IOP in thinner corneas or possibly there might be other biomechanical risk factors in play. IOP is underestimated in thin corneas and overestimated in thicker ones. The relative risk of POAG in the OHTS was found to be 1.71 with every 40. microns decrease in the CCT and thinner CCT<sup>99</sup>. Relatively thin CCT is seen in people with normal tension glaucoma whereas higher values for CCT are seen for POAG suspects, so CCT corrected IOP is important as it helps us to avoid misdiagnosing this condition. CCT is a variable factor among various ethnicities and is one of the most heritable ocular features. More recently, various researchers have given more weightage to the corneal dynamics and properties, arguing

against the significance of CCT corrected IOP in glaucoma treatment and follow up. However, applanation tonometry is still relied on in most of the underprivileged countries for diagnosis and management purposes and so CCT corrected IOP does hold value<sup>21</sup>.

Certain topical ocular hypotensive drugs might lead to thickening of cornea and lowering of corneal clarity. Wirtitsch et al. studied such effects of dorzolamide in patients with cornea guttata. It caused increased corneal thickness in such patients. On the other hand, some other ocular hypotensive agents lower the CCT thus, underestimating the IOP<sup>22</sup>. In a trial conducted by Maruyama et al. topical latanoprost was seen to lead to significant reduction in CCT during the first 2 years of use. Various longitudinal and cross-sectional studies have been carried out in this regard assessing change in CCT with ocular hypotensive agents.<sup>23</sup> However, they had their own limitations like a short follow-up period, use of monotherapy or a single pharmacological group.

In the current study the mean age of all patients was  $51.65 \pm 9.62$  years with minimum and maximum age as 40 and 85 years. In this study there were 65(45.1%) male and 79(54.9%) female cases. Mean age in current study was consistent with another study but it had different male to female ratio i.e. a study reported that mean age of the study population was  $51.49 \pm 7.00$  years (range: 40–67 years) and sixty-six patients (63.5%) were male.<sup>103</sup>

At 6 months of follow up, the mean CCT of right side in group-A, group-B and group-C was  $532.38 \pm 3.36$ ,  $539.17 \pm 3.20$  and  $538.28 \pm 3.45$  respectively, with significant difference,  $p$ -value  $< 0.001$ . At 6 months of follow up, the mean CCT of the left side in group-A, group-B and group-C was  $532.60 \pm 3.48$ ,  $538.52 \pm 2.97$  and

$538.14 \pm 3.06$  respectively, with significant difference,  $p$ -value  $< 0.001$ . The mean CCT after 6 months after (right and left) was significantly reduced in group-A,  $p$ -value  $< 0.05$  while it was remained same in both group-B and group-C,  $p$ -value  $> 0.05$ . Our findings are consistent with another study which reported that Mean CCT in prostaglandins group was  $521.79 \pm 34.94$  and in beta-blockers group was  $535.17 \pm 27.98$ .<sup>23</sup> Recently, there was a study carried out in persons having normal tension glaucoma (NTG) to determine the efficacy of prostaglandins on CCT. The results showed a declining trend in the CCT. The mean CCT showed a significant difference at 1, 2, and 3 years compared with baseline. The subgroup analysis confirmed this decline in CCT. In the 0.005% latanoprost group, mean CCT was decreased at 1 year ( $p = 0.11$ ), 2 years ( $p = 0.00$ ), and 3 years ( $p = 0.02$ ). In the 0.0015% tafluprost group and the 0.004% travoprost group, mean CCT was also significantly decreased at all years ( $p = 0.00$ ). In conclusion, topical PGAs cause a remarkable reduction in CCT<sup>24</sup>.

A study was carried out enrolling patients with ocular hypertension, glaucoma suspects and perimetric glaucoma. Rate of change of CCT per year was studied with the patients receiving prostaglandin analogues, beta-blockers, CAI monotherapy and combined antiglaucoma therapy. The study concluded that CCT needs to be measured regularly before therapy as well as during therapy while using PGs and a combination therapy with PGs, beta-blockers and CAI. If not done so, CCT variation affects IOP measurements<sup>25</sup>. There was a study done to estimate the long-term effect of prostaglandin analogues on CCT and association of CCT changes with IOP values. This study was carried out for 4 years. According to the results, there was a significant decrease in mean CCT from  $537 \pm 34 \mu\text{m}$  at pre-treatment to  $526 \pm 32 \mu\text{m}$  at the final follow-up ( $P < 0.0001$ ). There was a significant reduction during the first two years to  $529 \pm 32 \mu\text{m}$  ( $P = 0.0015$ ). However, mean CCT at the midpoint of the study and that measured at the last follow up showed no significant difference ( $P = 0.17$ ). Thus, we see from this study that topical latanoprost causes significant reduction of CCT<sup>26</sup>. In the current study the mean intraocular pressure of the right side was  $25.67 \pm 1.55$  in group-A,  $25.38 \pm 1.63$  in group-B and  $28.21 \pm 1.65$  in group-C, with significant difference,  $p$ -value  $< 0.001$ .

Our study showed significant change in CCT in prostaglandins analogue group only, not in other two groups. Increase in CCT by Beta blockers and carbonic anhydrase inhibitors as documented in some studies was not observed in our study as these reversible changes in CCT occur temporarily within approximately one-two weeks in those studies while reverting back to approximately same levels after

a month (the time of our first follow up). The limitations of our study include sporadic follow up interval, short study time, less number of patients and many hidden factors which may have altered results especially the patients' compliance including due to drug affordability.

## CONCLUSION

It is concluded that the mean change in central corneal thickness and IOP was statistically in patients on prostaglandins monotherapy when compared with the patients on beta-blockers monotherapy and those on combination therapy of beta-blockers and carbonic anhydrase inhibitors for primary open angle glaucoma. Hence in future the effect of drugs must be in consideration to maintain the IOP and central corneal thickness.

## REFERENCES

1. Bowling B. Kanski's clinical ophthalmology. A systemic approach. 18<sup>th</sup> Edition. Edinburgh: Elsevier; 2016. Chapter 10: Glaucoma; p.305-394.
2. Martin E, Patrianakos T, Giovengo M. Medication induced glaucoma. *Dis Mon.* 2017;63(2):54-7.
3. Bourne RR, Taylor HR, Flaxman SR, Keeffe J, Leasher J, Naidoo K, et al. Number of People Blind or Visually Impaired by Glaucoma Worldwide and in World Regions 1990 - 2010: A Meta-Analysis. *PLoS One.* 2016;11(10):1-16.
4. Chan EW, Li X, Tham YC, Liao J, Wong TY, Aung T, et al. Glaucoma in Asia: regional prevalence variations and future projections. *Br J Ophthalmol.* 2016;100(1):78-85.
5. Tham Y-C, Li X, Wong TY, Quigley HA, Aung T, Cheng C-Y. Global prevalence of glaucoma and projections of glaucoma burden through 2040: a systematic review and meta-analysis. *Ophthalmology.* 2014;121(11):2081-90.
6. Palmer JJ, Chinanayi F, Gilbert A, Pillay D, Fox S, Jaggernath J, et al. Trends and implications for achieving VISION 2020 human resources for eye health targets in 16 countries of sub-Saharan Africa by the year 2020. *Hum Resour Health.* 2014;12(45):1478-4491.
7. Carvalho CG, Procianny RS, Neto EC, Silveira RC. Preterm Neonates with Respiratory Distress Syndrome: Ventilator-Induced Lung Injury and Oxidative Stress. *J Immunol Res.* 2018;2018:6963754.
8. Jacobs DS. Open-angle glaucoma: Treatment, [Updated 2018; cited 2018]. Available from: URL <https://www.uptodate.com/contents/open-angle-glaucoma-treatment>. UpToDate.com. 2013.
9. Khawaja A, Kozak A, Jindal AP, Salim S. Primary open-angle glaucoma. Eyewiki [internet]. [updated 2017; cited 2018]. Available from: URL [http://eyewiki.aao.org/Primary\\_Open-Angle\\_Glaucoma](http://eyewiki.aao.org/Primary_Open-Angle_Glaucoma). 2017.
10. Schmid K, Irak I. Primary Open-Angle Glaucoma (POAG) Treatment & Management. Medscape. [updated 2018; cited 2018]; Available from: URL <https://emedicine.medscape.com/article/1206147-treatment#showall>. 2009.
11. Stefan C, Dumitrica DM, Tebeanu E, Nae I, Sapundgieva A, Dragomir L. [Prostaglandin analogues and central corneal thickness]. *Oftalmologia.* 2007;51(4):95-9.
12. Viestenz A, Martus P, Schlötzer-Schrehardt U, Langenbacher A, Mardin CY. [Impact of prostaglandin-F(2alpha)-analogues and carbonic anhydrase inhibitors on central corneal thickness -- a cross-sectional study on 403 eyes]. *Klin Monbl Augenheilkd.* 2004;221(9):753-6.
13. Grueb M, Rohrbach JM. Effect of timolol on central corneal thickness. *Eur J Ophthalmol.* 2013;23(6):784-8.
14. Brandt JD, Gordon MO, Beiser JA, Lin SC, Alexander MY, Kass MA. Changes in central corneal thickness over time: the ocular hypertension treatment study. *Ophthalmology.* 2008;115(9):1550-6.
15. Kocabeyoglu S, Mocan MC, Irkec M. Decreased keratocyte density and central corneal thickness in primary open-angle glaucoma patients undergoing treatment with topical prostaglandin analogues. *Indian J Ophthalmol.* 2015;63(1):15-9.

16. Panos GD, Konstantinidis A, Mendrinou E, Kozobolis V, Perente I, Gatzoufas Z. Effect of tafluprost 0.0015% on central corneal thickness in patients with primary open-angle glaucoma. *Curr Eye Res.* 2013;38(9):977-82.
17. Maruyama Y, Mori K, Ikeda Y, Ueno M, Kinoshita S. Effects of long-term topical prostaglandin therapy on central corneal thickness. *J Ocul Pharmacol Ther.* 2014;30(5):440-4.
18. You JY, Cho BJ. Effect of latanoprost on central corneal thickness in unilateral normal-tension glaucoma. *J Ocul Pharmacol Ther.* 2013;29(3):335-8.
19. Viswanathan D, Goldberg I, Graham SL. Longitudinal effect of topical antiglaucoma medications on central corneal thickness. *Clin Exp Ophthalmol.* 2013;41(4):348-54.
20. Singh AK. Effect of Latanoprost Eye Drops on Central Corneal Thickness in North Indian Population. *International Journal of Science and Research (IJSR).* 2016;5(7):243-45.
21. Bafa M, Georgopoulos G, Mihas C, Stavrakas P, Papaconstantinou D, Vergados I. The effect of prostaglandin analogues on central corneal thickness of patients with chronic open-angle glaucoma: a 2-year study on 129 eyes. *Acta Ophthalmol.* 2011;89(5):448-51.
22. Tsikripis P, Papaconstantinou D, Koutsandrea C, Apostolopoulos M, Georgalas I. The effect of prostaglandin analogs on the biomechanical properties and central thickness of the cornea of patients with open-angle glaucoma: a 3-year study on 108 eyes. *Drug Des Devel Ther.* 2013;7:1149-56.
23. Aghaian E, Choe JE, Lin S, Stamper RL. Central corneal thickness of Caucasians, Chinese, Hispanics, Filipinos, African Americans, and Japanese in a glaucoma clinic. *Ophthalmology.* 2004;111(12):2211-9.
24. Wiggs JL, Pasquale LR. Genetics of glaucoma. *Hum Mol Genet.* 2017;26(R1):R21-R7.
25. Kapetanakis VV, Chan MP, Foster PJ, Cook DG, Owen CG, Rudnicka AR. Global variations and time trends in the prevalence of primary open angle glaucoma (POAG): a systematic review and meta-analysis. *Br J Ophthalmol.* 2016;100(1):86-93.