Achieving Target IOP

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ABSTRACT

Purpose: Evaluation of progression of glaucoma in patients after achieving their target IOP using SAIF target IOP table

Materials and Methods: This is a retrospective non randomized comparative interventional study that was performed on 216 eyes of 108 patients with Primary open angle (POAG).and Normal tension glaucoma from the outpatient clinics at Fayoum University hospital and MISR University hospital, from 2009 till 2014 . We calculated the target IOP according to Saif's table[4] of prediction and C/D ratio. Patients were classiefied into two groups: **Group 1** : achieved target IOP(48 female& 24 male) patients. **Group 2** : didn't achieve target IOP (18 female& 18 male) patients.

Results: C/D ratio in group 1 was 0.373 ± 0.179, (ranged 0.3 - 0.8), while group 2: the mean C/D ratio was 0.860 ± 0.103 (ranged 0.6 -0.93) The V.F. difference in group 1: the mean (MD) was -1.90 ±4.92 , (ranged -16.60 to -1.90). and group 2: the mean (MD) was 0.27 ± 1.48 (ranged . -1.90 to 0.03)

Conclusion :After comparing mean deviation (MD) difference between two groups we found that there is statistically significant difference between both groups as regard the group that achieved target IOP there was regressive changes or stabilization of the visual field MD . Optimal target IOP may be different for different individuals depending on the severity of the disease and should be updated periodically as the disease progress

Keywords: Target IOP, primary open angle glaucoma, normal tension glaucoma, glaucoma suspect

INTRODUCTION

It is difficult to define glaucoma precisely, as it encompasses a diverse group of disorders. All forms of the disease have in common a potentially progressive and characteristic optic neuropathy which is associated with visual field loss as damage progresses, and in which intraocular pressure is usually a key modifying factor. Glaucoma is the second most prevalent eye condition, after cataract known to cause blindness worldwide.[1]

The actual etiology of the condition remains unknown.[2] Glaucoma consists of many eye disorders, such as congenital glaucoma, secondary glaucoma, primary angle closure glaucoma (PACG), normal tension glaucoma (NTG), pigmentary glaucoma, and primary open-angle glaucoma (POAG). These disorders destroy the optic nerve, leading to blindness.[3]

The risk factors for getting glaucoma include age, race, sex, heredity, family history, systemic (Diabetes, Obesity, Hypertension, Hypotension, Arteriosclerosis and Smoking) and socioeconomic factors as well as local factors (myopia, corneal thickness and scleral rigidity) all will channel into disc damage for the systemic factors and level of IOP for the local factors. So calculation of the combined probability of getting glaucoma for these 2 factors alone will include all the above mentioned variables.[4-9]

Target IOP can be defined as the intraocular pressure level which is necessary to prevent glaucomatous damage of visual field and optic nerve head in an individual patient, and hinder the progression of already established, structural or functional deficits. The criteria to help choose the target IOP include; the morphology of the optic nerve head, the performance and stability of the visual field, and the overall physical health of the patient.[10]

The following are the main problems of Target IOP assessment:

1. It must be individualized to the patient and to each eye.

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No absolute level or percentage change from baseline will be correct for the majority of our patients.[11]

2. It must be an accurate estimate.[11]
3. It needs to be determined in advance. However we can only confirm the appropriateness of the chosen IOP level at a later date. Trial and error is an unavoidable part of the process.[11]

It is generally assumed that aiming to achieve a Target IOP with at least a 30% reduction from the initial pressure at which damage occurred is a useful starting point.[11]

Determining the Target IOP:

The target intraocular pressure is a "best guess" level of IOP. Below which further damage to the optic nerve is unlikely to occur. The estimate is based on the initial level of IOP, degree of existing damage (optic nerve cupping, reserving power of the optic nerve**,** visual field loss, nerve fiber layer thickness) age, presence of other risk factors (diabetes and arteriosclerotic vascular diseases), rate of progression if known, family history of glaucoma.[7]

In average patient, the European Glaucoma Society (EGS) recommends that an initial target intraocular pressure should be set at least 30% lower than the pressure at which the ocular damage originally occurred. The more advanced the glaucoma, the greater the number of risk factors and the greater the vascular components, the lower the target IOP should be. The target IOP also helps the physician to assess the success of the treatment. The earlier the target IOP reached the better the outcome for the patient. The target intraocular pressure should be reassessed periodically and lowered if progression, optic nerve hemorrhage, or increase in risk factors occurs.[13,14]

The aim of the current study is evaluation of glaucoma progression after achieving target IOP using SAIF target IOP table.

MATERIAL AND METHODS

This is a retrospective non randomized comparative interventional study that was performed on two hundreds and sixteen eyes of one hundred and eight patients. The ethical committee approval done before seeing the patients'records

Patient selection:

Inclusion criteria:

- Primary open angle (POAG).
- Normal tension glaucoma.

Exclusion criteria:

-Closed angle glaucoma patients.

-Secondary glaucoma patients.

-Any previous ocular surgery.

Patients:

All patients attending the outpatient clinics at Beni Suef University hospital Fayoum University hospital and MISR University hospital, from 2009 till 2014.

Examinations:

All patients must had Full ophthalmological examinations included,

- Visual acuity assessment by Snellen's Chart.
- IOP measurement by Goldman's applanation tonometer at least 8 visits
- Slit lamp examination and fundus examination for optic disc evaluation by 90D lens.
- 2 Visual field analysis was done (Humphrey& Octupus).
- OCT for evaluation of (C/D ratio).
- Full medical assessment.

Treatment:

In this study we depended on medical treatment. Patients were treated with the suitable line of treatment according to initial IOP of the patient and to maintain target IOP after reaching it.

Lines of treatment:

-Monotherapy: either

*Beta blocker (e.g: Timolol) or

*Alpha2 agonist (e.g: Brimonidine).

-Bitherapy:

* Beta blocker& Alpha2 agonist or

* Beta blocker& prostaglandin analogue (e.g:latanoprost) or

* Alpha2 agonist& prostaglandin analogue.

* Beta blocker& Carbonic anhydrase inhibitor.

-Triple therapy:

*Beta blocker& carbonic anhydrase inhibitor and

*Alpha2 agonist, or

*Prostaglandin analogue.

-Quadriple therapy:

*Beta blocker& carbonic anhydrase inhibitor and

*Alpha2 agonist and

*Prostaglandin analogue.

Calculation of target IOP:

We calculated the target IOP according to Saif's table[4] of prediction and C/D ratio. (Table 1)

Table 1: Shows SAIF target IOP guided by the C/D ratio[4].

C/D ratio	0	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9	1.0
Target IOP mmHg	20	18	17	16	15	14	13	11	10	9	8

According to calculation of target IOP of each eye patients were classiefied into two groups:

-Group (1): patients who achieved target IOP.

-Group (2): patients who didn't achieve target IOP.

We analyzed mean deviation (MD) of the visual field to assess V.F. progression with treatment.

RESULTS

Data were statically described in terms of mean, ± standard deviation SD, median and range, or frequencies (number of cases) and percentages when appropriate.

This study included one hundred and eight patients (two hundreds and sixteen eyes), (sixty six female patients& forty two male patients) with primary open angle (POAG) & normal tension glaucoma divided into:

Group 1: Patients who achieved target IOP (48 female& 24 male) patients.

Group 2: Patients who didn't achieve target IOP (18 female& 18 male) patients.

This study was done on 108 patients (216 eyes): 61,1% female patient (72.7% achieved target IOP & 27.3% didn't achieve target IOP) while 38.9% male patient (57.1% achieved target IOP & 42.9% didn't achieve target IOP). (Table 2)

Table 2: Demographic data (sex)

	Female		Male	
	Number(n)	(%)	Number(n)	(%)
Group 1	48	72.7%	24	57.1%
Group 2	18	27.3%	18	42.9%

N=number

The mean age among patients who achieved target IOP was 39 years old ±15years, min. age was 20 years old, max. age was 62 years old& among patients didn't achieve target IOP mean was 50 years old ±12 years, min. age was 39years old, max. age was 72 years as shown in table 3.

The mean visual acuity was 0.632 ± 0.310 in patients who achieved target IOP, in patients who didn't achieve target IOP mean was 0.435 ±0.292 ,with minimal visual acuity 0.05 & maximum visual acuity 1.00 as shown in table 3.

The mean C/D ratio in group 1 was 0.373 ± 0.179, (ranged 0.3 - 0.8) , while group 2: the mean C/D ratio was 0.860 ± 0.103 (ranged 0.6 -0.93) as shown in table 3 and figure 1.

As regard IOP changes among 8 visits;

At the **1st visit** the mean IOP was 16.12 ± 3.47 mmHg among the group that achieved target IOP and it was 19.80 ±7.27 mmHg among the group that didn't achieve target IOP.

Mean IOP at the **2nd visit** became 15.31 ±2.20 mmHg among the group of patients that achieved target IOP and it was 16.60 ±4.69 mmHg among the group that didn't achieve target IOP.

Mean IOP at the **3rd visit** became 14.04 ± 2.32 mmHg among the group of patients that achieved target IOP and it was 13.80 ±3.09 mmHg among the group that didn't achieve target IOP.

Mean IOP at the **4th visit** became 13.35 ± 2.61 mmHg among the group of patients that achieved target IOP and it was 14.60 ±4.06 mmHg among the group that didn't achieve target IOP.

Mean IOP at the **5th visit** became 14.23 ± 1.72 mmHg among the group of patients that achieved target IOP and it was 16.80 ± 4.41 mmHg among the group that didn't achieve target IOP.

Mean IOP at the **6th visit** became 14.00 ± 2.58 mmHg among the group of patients that achieved target IOP and it was 15.10 ± 2.83 mmHg among the group that didn't achieve target IOP.

Mean IOP at the **7th visit** became 12.38 ± 2.03 mmHg among the group of patients that achieved target IOP and it was 13.70 ± 3.88 mmHg among the group that didn't achieve target IOP.

Mean IOP at the **8th visit** (last visit) became 11.38 ± 1.97 mmHg among the group of patients that achieved target IOP

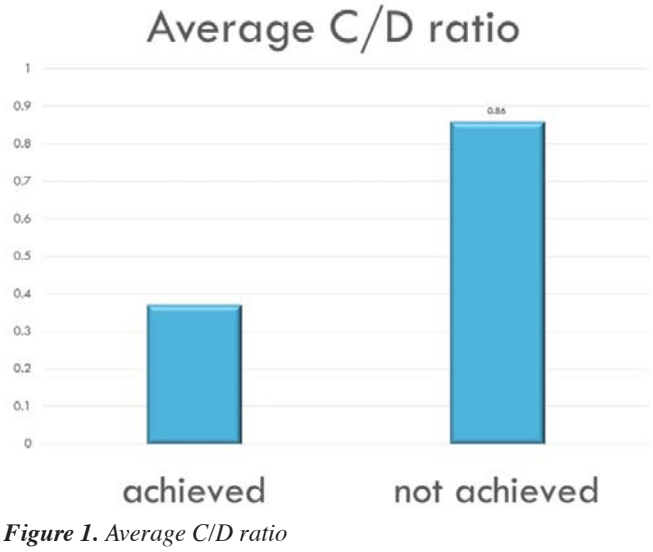

Figure 1. *Average C/D ratio*

Table 3: Statistical analysis of both groups.

group		Mean	Median	Standard Deviation	Minimum	Maximum
Group I	Age	39	47	15	14	57
	Visual Acuity	.632	.700	.310	.050	1.000
	Cup disc ratio	.373	.300	.179	.100	.800
	Visual Field baseline MD	6.691	3.080	7.335	.600	26.370
	Visual Field last visit MD	4.794	2.265	6.515	0.000	26.200
	Visual field difference	-1.90	-1.03	4.92	-16.60	7.10
	IOP visit 1	16.12	17.00	3.47	11.00	29.00
	IOP visit 2	15.31	14.50	2.20	12.00	22.00
	IOP visit 3	14.04	14.00	2.32	9.00	21.00
	IOP visit 4	13.35	13.00	2.61	9.00	23.00
	IOP visit 5	14.23	14.00	1.72	10.00	17.00
	IOP visit 6	14.00	14.00	2.58	9.00	20.00
	IOP visit 7	12.38	12.00	2.03	9.00	16.00
	IOP visit8	11.38	12.00	1.97	8.00	16.00
	IOP difference	4.73	4.50	2.95	0.00	13.00
	IOP decrease %	27.71	28.99	13.62	0.00	52.94
	Target IOP	15.192	16.000	1.987	10.000	18.000
Group 2	age	50	49	12	39	72
	Visual Acuity	.435	.400	.292	.050	1.000
	Cup disc ratio	.860	.900	.103	.600	1.000
	Visual Field baseline MD	17.687	19.875	9.981	1.200	30.370
	Visual Field last visit MD	17.957	19.020	9.335	3.500	29.080
	Visual field difference	.27	.03	1.48	-1.90	2.80
	IOP visit 1	19.80	20.00	7.27	8.00	31.00
	IOP visit 2	16.60	15.50	4.69	11.00	25.00
	IOP visit 3	13.80	12.50	3.09	11.00	22.00
	IOP visit 4	14.60	13.50	4.06	9.00	21.00
	IOP visit 5	16.80	17.00	4.41	10.00	24.00
	IOP visit 6	15.10	14.00	2.83	12.00	20.00
	IOP visit 7	13.70	12.00	3.88	9.00	20.00
	IOP visit8	14.70	14.00	2.26	10.00	18.00
	IOP difference	5.10	5.00	6.35	-6.00	13.00
	IOP decrease %	14.21	28.17	39.07	-75.00	46.15
	Target IOP	9.500	9.000	1.295	8.000	13.000

and it was 14.70 ± 2.26 mmHg among the group that didn't achieve target IOP.

IOP changes shown in table 3& 4 and figure 2

As regards IOP difference between the initial visit & the 8th visit patients who achieved target IOP the mean was 4.73 ±2.95 with min. difference zero and max difference 13.00mm Hg, patients who didn't achieve target IOP the mean was 5.10 ± 6.35 with min. difference 6.00 mmHg & max difference 13.00 mmHg, as shown in table 4 and figure 3.

As regards initial MD in patients who achieved target IOP the mean was 6.691 ±7.335, while patients didn't achieve target IOP the mean was 17.687 ±9.981 as shown in table 5.

As regards 2nd MD at the 8th visit in patients who achieved target IOP the mean MD was 4.794 ±6.515 and in patients who didn't achieve target IOP the mean MD was 17.957 ±9.335 as shown in figure 4.

As regards MD difference in patients who achieved target IOP the mean was -1.90 ±4.92 with min. difference -16.60

Table 4: IOP differences between the 8 visits.

		Paired Differences					t	df	Sig. (2-tailed)
		Mean	Std. Error Mean	Upp Std. Error Meaner	95% Confidence Interval of the Difference				
					Lower	Upper			
Group 1	MD1 - MD2	1.896923	4.922700	.394131	1.118361	2.675485	4.813	155	.000
	IOP1 - IOP2	.80769	2.11939	.16969	.47249	1.14289	4.760	155	.000
	IOP2 - IOP3	1.26923	1.95876	.15683	.95944	1.57902	8.093	155	.000
	IOP3 - IOP4	.69231	1.81966	.14569	.40451	.98010	4.752	155	.000
	IOP4 - IOP5	-.88462	3.02668	.24233	-1.36331	-.40592	-3.650	155	.000
	IOP5 - IOP6	.23077	2.17862	.17443	-.11380	.57534	1.323	155	.188
	IOP6 - IOP7	1.61538	2.29575	.18381	1.25229	1.97847	8.788	155	.000
	IOP7 - IOP8	1.00000	2.32795	.18639	.63182	1.36818	5.365	155	.000
	IOP1 - IOP8	4.73077	2.95197	.23635	4.26389	5.19765	20.016	155	.000
Group 2	MD1 - MD2	-.270000	1.479872	.191051	-.652291	.112291	-1.413	59	.163
	IOP1 - IOP2	3.20000	7.39400	.95456	1.28993	5.11007	3.352	59	.001
	IOP2 - IOP3	2.80000	5.31324	.68594	1.42744	4.17256	4.082	59	.000
	IOP3 - IOP4	-.80000	3.57392	.46139	-1.72324	.12324	-1.734	59	.088
	IOP4 - IOP5	-2.20000	5.91121	.76313	-3.72703	-.67297	-2.883	59	.005
	IOP5 - IOP6	1.70000	2.81822	.36383	.97198	2.42802	4.673	59	.000
	IOP6 - IOP7	1.40000	3.80544	.49128	.41695	2.38305	2.850	59	.006
	IOP7 - IOP8	-1.00000	3.15691	.40756	-1.81552	-.18448	-2.454	59	.017
	IOP1 - IOP8	5.10000	6.35317	.82019	3.45880	6.74120	6.218	59	.000

and max. difference -1.90. However in patients who didn't achieve target IOP the mean was 0.27 ± 1.48 with min. diff. -1.90 & max. diff. 0.03 as shown in figure 5.

As regards line of treatment there was four lines of treatment which were individualized according to each patient condition;

42 patients (38.8%) used monotherapy 39 patients (36.11%) of them achieve target IOP but 3 patients (2.8%) didn't achieve target IOP

Table 5: Mean deviation (MD) values in both groups

	Target IOP	
	Group 1	Group 2
MD (1)	6.691	17.687
MD (2)	4.794	17.957
P value	.000	.163
Mean difference	-1.90(±4.92)	0.27(±1.48)

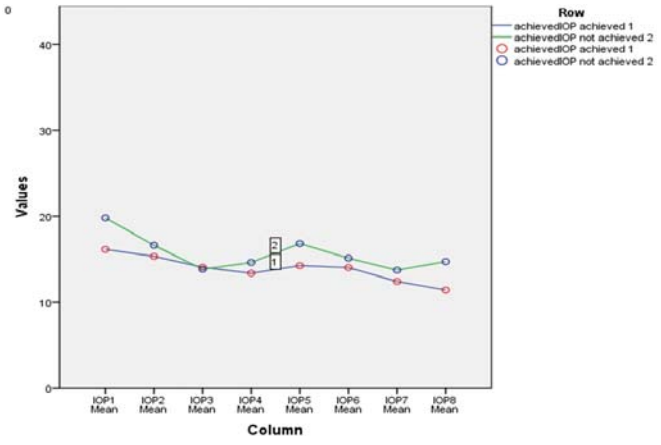

Figure 2. *IOP changes during follow up.*

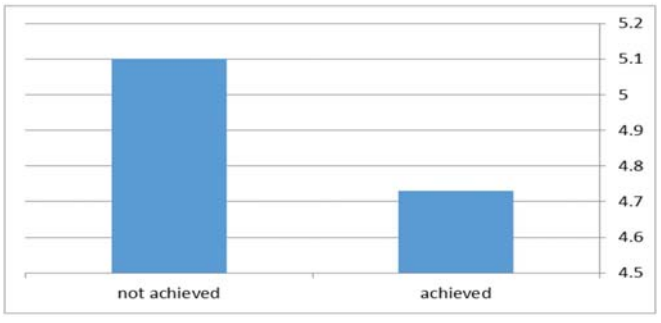

Figure 3. *Show mean of the IOP difference in patients who (1=achieved 2=non achieved) target IOP.*

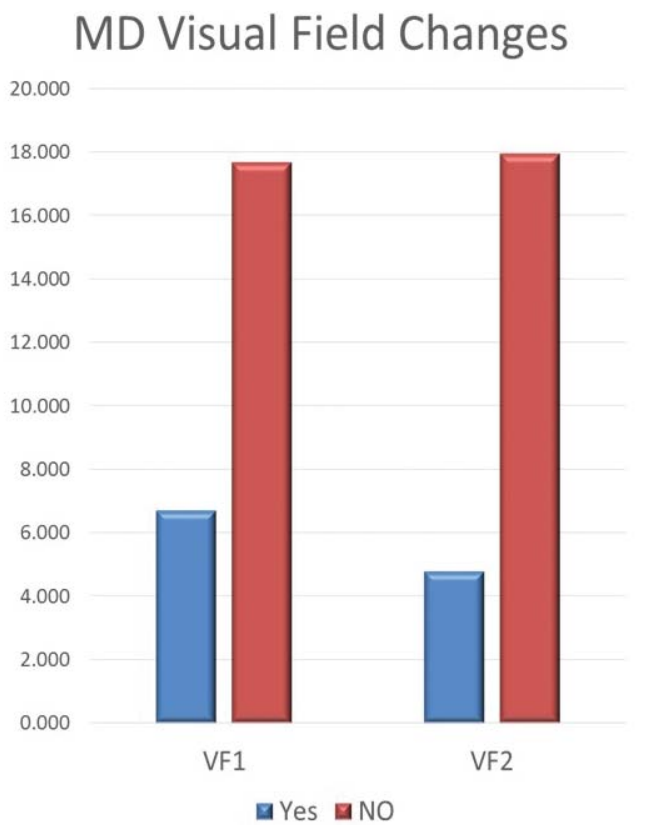

Figure 4. *V.F. MD change.*

36 patients (33.3%) used bitherapy 21 patients (19.4%) of them achieve target IOP but 15 patients (13.9%) didn't achieve target IOP

15 patients (13.89%) used triple therapy 12 patients (11.1%) of them achieved target IOP but 3 patients (2.8%) didn't achieve target IOP.

15 patients (13.89%) used quadriple therapy 6 patients(5.6%) of them achieved target IOP but 9 patients (8.3%) didn't achieve target IOP as shown in table 6.

As shown in Figure 6-9, right eye of 29 years of male patient, achieved the target IOP while the left eye did't achieve.

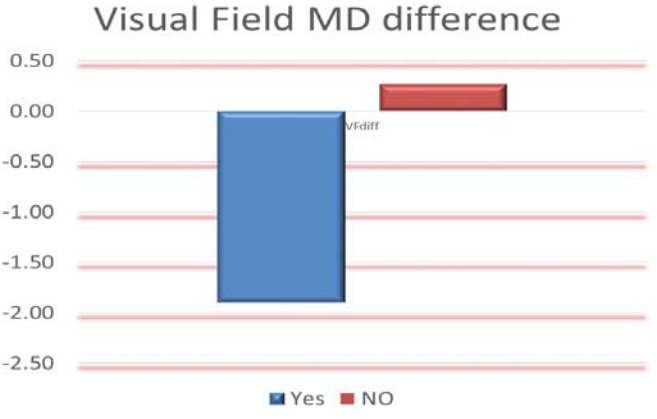

Figure 5. *Show V.F. MD difference.*

Table 6: Percentage of patients achieved& didn't achieve target IOP with different lines of treatment

	Line of treatment							
	Mono-therapy		Bi-therapy		Triple-therapy		Quadriple-therapy	
	Count	%	Count	%	Count	%	count	%
Group 1	78	36.1%	42	19.4%	24	11.1%	12	5.6%
Group 2	6	2.8%	30	13.9%	6	2.8%	18	8.3%

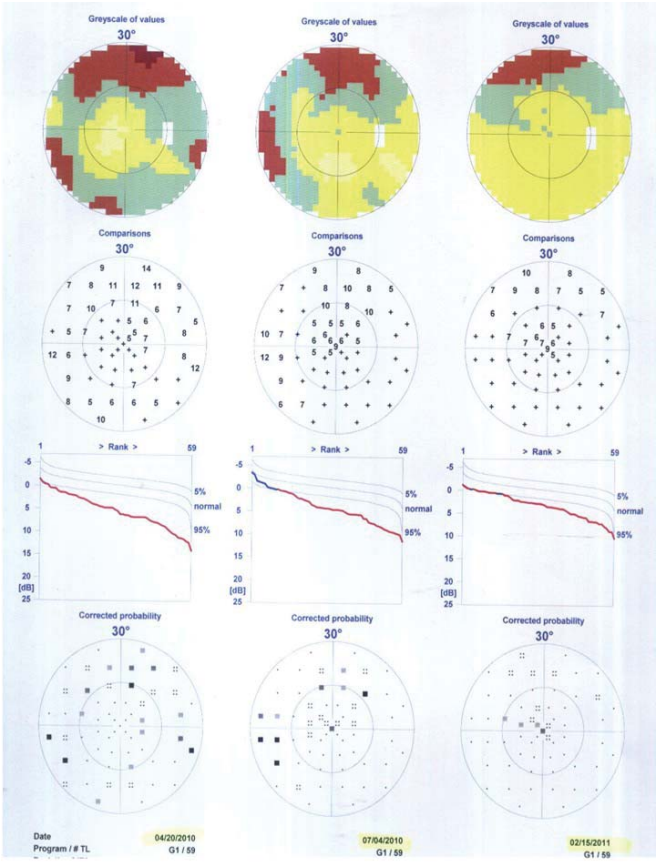

Figure 6. *Visual fields of the right eye.*

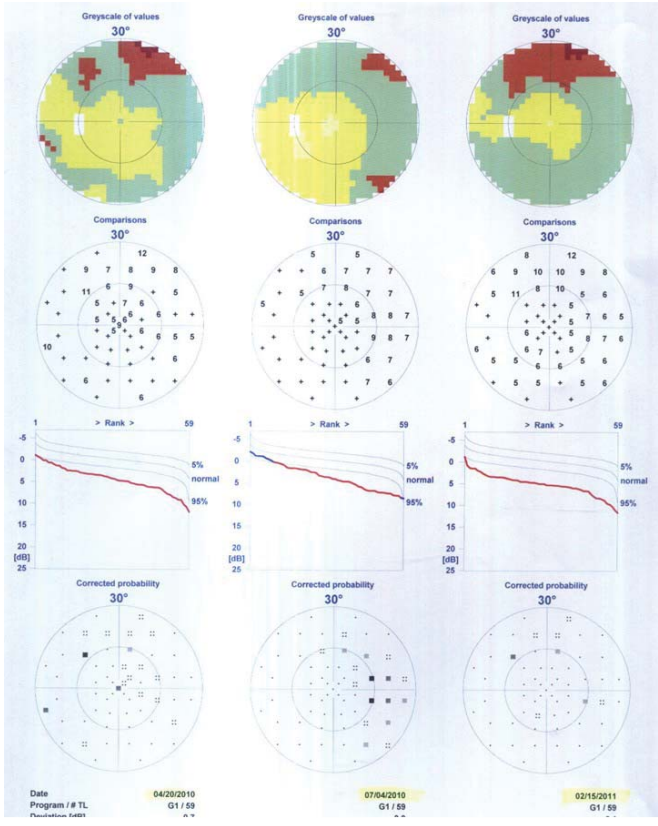

Figure 8. *Visual fields of the left eye.*

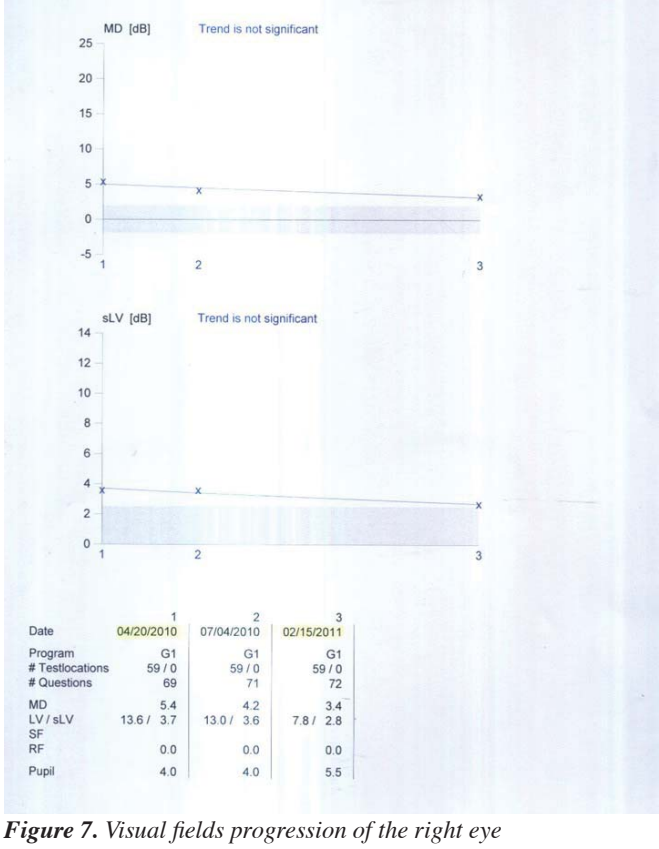

Figure 7. *Visual fields progression of the right eye*

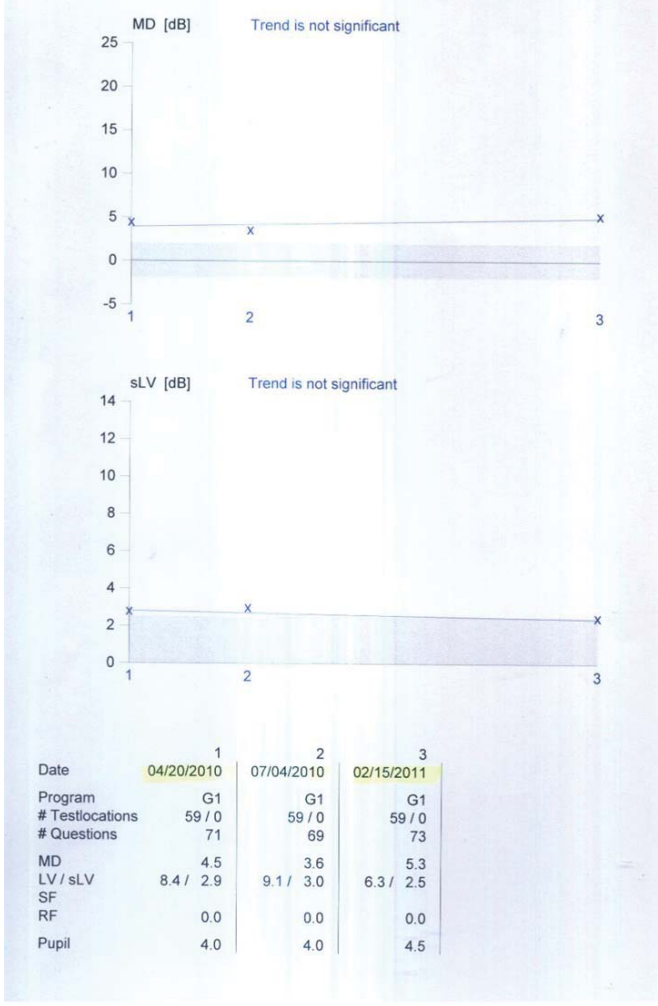

Figure 9. *Visual fields progression of the left eye*

DISCUSSION

Glaucoma is a progressive serious disease that ends up with-blindness. Early detection and diagnosis are no more dilemma. The dilemma will be how to stop or slow the progression of the disease.[6]

Assessment of glaucoma progression includes evaluation of three main items: IOP& optic disc and visual field.

Target IOP is defined as the mean intraocular pressure obtained with treatment that prevents further glaucomatous damage.[15]

The risk factors for getting glaucoma include age, sex, race, heredity, family history, systemic (Diabetes, Obesity, Hypertension, Hypotension, Arteriosclerosis and Smoking) and socioeconomic factors as well as local factors (Myopia, Corneal thickness and Scleral rigidity) all will channel into disc damage for the systemic factors and level of IOP for the local factors.[4-9]

For the above mentioned reasons we used in this study the Saif 's Table for the target IOP. The aim of this study was to evaluate the progression of glaucoma by the visual field changes and Cup disc ratio after reaching the target IOP by glaucoma medical treatment.

There were 108 patients included in this study with primary open angle glaucoma which was less than other studies and clinical trials that included larger number of patients as Tanuja& Rajiv on 150 cases of POAG and Normotensive glaucoma,[16] the Collaborative Initial Glaucoma Treatment Study (CIGTS) on 607 patients with newly detected simple glaucoma,[17-21] Early Manifest Glaucoma Trial (EMT) on 225 patients with newly diagnosed open angle glaucoma,[22,23] Advanced Glaucoma Intervention Study (AGIS) on 591 patients with advanced open angle glaucoma with poor medical control of IOP,[24-27] the Collaborative Normal Tension Glaucoma Study (CNTGS) on 230 patients with normal tension glaucoma,[28,29] and the Ocular hypertension treatment study(OHTS) on 1836 patients with ocular hypertension.[30-35]

The age of patients in this study ranged from 20 to 72 years which is relatively similar to the Collaborative Normal Tension Glaucoma Study (CNTGS) as the age of patients in that study ranged from 20-90 years.[28,29]

We had two groups of patients in this study the first group achieved our calculated target IOP while the other group didn't achieve the target IOP in two or more visits. In group 1, the IOP for the IOP for the achieved group ranged from 8-16 mmHg which was similar to the Advanced Glaucoma Intervention Study as the target IOP was set at <18 mmHg and the patients with lower IOP were free from visual field impairment, whereas those with higher values of IOP showed sustained visual field deterioration.[24-27]

Tanuja& Rajiv showed that cases with a follow up range of 14& less and 15-20 mmHg were stable.[16]

Early Manifest Glaucoma Trial (EMT) set target IOP using percent reduction and concluded that 25% reduction from the initial pressure decreased risk of progression by 25%.[22,23]

Collaborative Normal Tension Glaucoma study(CNTGS) said that patients with normal tension glaucoma (IOP<20 mmHg) with IOP reduction 30% showed a 12% rate of visual field impairment at 5 years.[28,29]

The mean C/D ratio was 0.37±0.179 (ranged 0.3-0.8) Which is slight larger than the mean C/D ratio of normal population (0.26 ± 0.14 ranged from 0.0 to 0.7) and less than the glaucomatous group (0.50 ± 0.23 ranged from 0.1 – 0.9) in Beni Suef area.[36-38]

In Group 2, the IOP ranged from 18-30 mmHg with deterioration of the visual field which was similar to the Advanced Glaucoma Intervention Study as the target IOP was set at <18 mmHg and the patients with higher values of IOP showed sustained visual field deterioration.[24-27]

Tanuja& Rajiv said that analysis of visual field and optic disc changes of cases with a follow up range of >20 mmHg showed deterioration.[16]

Early Manifest Glaucoma Trial (EMT) Study patients were divided into two groups. In one group, 25% reduction of intraocular pressure was attained treatment, whereas the other group was left untreated. Glaucoma progression measured by visual field impairment was statistically significantly greater in the group of untreated patients than in those with intraocular pressure reduction.[22,39]

Collaborative Normal Tension Glaucoma study (CNTGS) said that patients with normal tension glaucoma (IOP<20 mmHg) left without treatment showed a 35% rate of progression of glaucomatous visual field impairment at 5 years.[28,29]

The visual field changes showed decrease in the MD as the mean of MD was 6.691 before treatment and became 4.794 after achieving target IOP among the group that achieved target IOP. This may be due to removal of the pressure from the ganglion cells and optic nerve, also short duration between the visual fields (6months to 3.5 years) between the study groups may be a factor in these visual field improvements.

Musch DC et al[20] showed a, substantial visual field loss and improvement over 5 years of follow-up In the collaborative initial glaucoma treatment study.

In the non-achieving group the MD was 17.687and became 17.957 even with treatment in the group not achieving target IOP, this was not shown in other studies that demonstrating variable changes and progression of the visual field.[24,26,29,32,33,35]

CONCLUSION

After comparing visual field (MD) difference between two groups we found that there is statistically significant difference between both groups as regard the group that achieved target IOP there was regressive changes or stabilization of the visual field MD

Optimal target IOP may be different for different individuals depending on the severity of the disease and should be updated periodically as the disease progress

The information gained from the study, assist in estimating and modifying target IOP**.**

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