

Microperimetry Changes after Intra-Vitreous Injection in Diabetic Macular Oedema.

¹Saeed Ahmed Saber, ¹Mahmoud Ahmed Kamal, ²Khaled Gamal Abu-Eleinen, ¹Ahmed Abdelkader Kottb

¹Departments of Ophthalmology Faculty of medicine - Fayoum University, Egypt.

²Departments of Ophthalmology Faculty of medicine - Cairo University, Egypt.

Abstract: Purpose: To focus on morphological macular changes and their impact on the visual acuity and Retinal sensitivity that occur in diabetic macular oedema before and after intra-vitreous injections like Bevacizumab, Ranibizumab and Triamcinolone Acetate using Microperimetry. Methods: Sixty eyes received preservative free intravitreal injection delivered through the pars plana. Thirty eyes with intra vitreal triamcinolone acetate and the other thirty with intravitreal Anti-VEGF. The best corrected visual acuity (BCVA), foveal thickness, and the average retinal sensitivity were considered in our study. Patients were instructed to attend for BCVA, OCT and microperimetry-1 follow-up at baseline, one and three months. Results: At the baseline, mean macular thickness was 447.58 ± 101.49 micron, mean visual acuity was 0.34 ± 0.16 dB and Mean macular sensitivity determined with the microperimetry-1 was 8.19 ± 4.57 dB. After the 3month follow-up, mean OCT macular thickness decreased to 272.35 ± 84.27 microns ($P < 0.001$); mean BCVA improved to 0.54 ± 0.16 dB (P -value < 0.001) and mean retinal sensitivity improved to 11.58 ± 3.67 dB (P -value < 0.001). Conclusions: In our study, we found that macular sensitivity is probably one of the most important predictors of visual function. MP-1 microperimetry seems to be a useful tool in evaluating visual outcome after intervention in eyes affected by DME.

[Saeed Ahmed Saber, Mahmoud Ahmed Kamal, Khaled Gamal Abu-Eleinen, Ahmed Abdelkader Kottb. **Microperimetry Changes after Intra-Vitreous Injection in Diabetic Macular Oedema.** *Biomedicine and Nursing* 2020;6(2): 49-64]. ISSN 2379-8211 (print); ISSN 2379-8203 (online). <http://www.nbmedicine.org>. 6. doi:[10.7537/marsbnj060220.06](https://doi.org/10.7537/marsbnj060220.06).

Keywords: Microperimetry (MP-1), Diabetic Macular Oedema, Intra-Vitreous Injection.

1. Introduction

Diabetic retinopathy is one of the major causes of permanent visual loss in the working population. Moreover, the prevalence of diabetes mellitus is dramatically increasing worldwide. Full-contrast visual acuity test doesn't reflect the real visual functional abnormalities due to the retinal involvement secondary to diabetes mellitus. Moreover, subtle and precocious neurosensory visual abnormalities have been quantified in diabetic patients in order to detect early visual retinopathy. The aim of these investigations is to try to identify among diabetic subjects a population at higher risk of developing vision threatening retinopathy (**Bresnick, 1986 and Midena et al., 1990**).

Psychophysical visual function testing may reflect the neural activity of the whole visual pathway, but it is known that these tests are valuable clinical indicators of retinal function derangements induced by the metabolic changes secondary to diabetes mellitus. In fact, in diabetic patients, impaired vision in dim light and difficulties in recognizing the contour of objects in low contrast conditions are common complaints even with good visual acuity and full visual fields (**Hyvärinen et al., 1983**).

Visual acuity is still considered the gold standard in clinical practice of vision testing, but it does not entirely reflect functional vision. Functional vision describes the impact of sight on the quality of life that represents the patient's point of view (**Owsley and Sloane, 1987; Sharma et al., 2005;; and Midena, 2006**).

Perimetry encompasses the assessment of differential light threshold of retinal locations from the fovea to the preplanned periphery. Static perimetry is particularly useful for detailed probing in carefully selected areas and represents the current cornerstone of visual field testing. Standard threshold static automated perimetry quantifies the differential light threshold required to detect a static white light stimulus in the visual field. Since standard threshold perimetry uses a static achromatic stimulus, it is thought to non-selectively evoke both major groups of retinal ganglion cells. Newer technologies are aimed at earlier detection of subtle deficits and enhancing diagnostic accuracy. In diabetic macular edema (DME), visual acuity loss is quite relevant and irreversible when long lasting edema involves the center of the macula; in these cases the outcome of laser treatment is poor. Before the loss of visual acuity

is reported by patients, they may suffer from other disturbances of visual function such as: waviness, blurring, relative scotoma and decrease of contrast sensitivity which are not assessed and quantified in routine examination (**Midena, 2006**).

Therefore, a visual function test aimed at identifying vision threatening retinopathy before visual acuity is affected would be of great value. One possible approach may be to identify decreased sensitivity in central and paracentral areas using microperimetry (**Midena, 2006**). As elegantly stated by Sunnes et al., conventional visual field examination is inadequate for the accurate functional evaluation of macular diseases and detection of small scotoma, particularly when foveal function is compromised and the patient may have unstable and extrafoveal fixation (**Sunnness et al., 1995**).

Accuracy of the conventional visual field rests on the assumption that fixation is foveal and stable. Moreover, the detection of the site and stability of retinal fixation (foveal or extrafoveal) and the quantification of retinal threshold over small and discrete retinal lesions are beyond the possibilities of conventional, automatic and non-automatic perimetry (**Midena and Radin, 2006**).

The integration of retinal details with function has been achieved by fundus-related perimetry, more widely known as microperimetry. **Microperimetry** allows for the exact topographic correlation between fundus abnormalities and corresponding functional alterations by integration, with different methods, of differential light threshold (more commonly known as retinal sensitivity) and fundus imaging. It also allows to quantify fixation characteristics, by exactly defining location and stability of any foveal or extrafoveal (PRL: preferred retinal locus) fixation site, as well as determination of size, site and shape of scotoma (**Midena and Radin, 2006**).

2. Patients and Methods

A prospective study of 60 study eyes of 56 patients, mean age 58 years (range: 45–70 years), with diabetic retinopathy were included in this study, 29 eyes of Females and 31 of males. 60 eyes with DME will have microperimetry then they will be subjected to intravitreal injection either bevacizumab, ranibizumab or triamcinolone. Then they will be followed up and microperimetry will be repeated at 1 and 3 months later.

Inclusion criteria:

Patients with clinically significant macular oedema according to ETDRS criteria as Retinal thickening within 500 μ m of the fovea; hard exudates within the same 500 μ m, if associated with retinal thickening; and ≥ 1 DD of retinal thickening, if any part of the thickened retina is within 1 DD from the

fovea are the candidates for this study.

Exclusion criteria:

Patients with the following criteria will be excluded:

- Uncontrolled diabetes.
- Elevated intraocular pressure
- Ocular infection
- Vitreomacular tractions
- Epiretinal membranes
- Previous macular laser photocoagulation

Therapy.

- Media Opacity

Evaluation:

Each patient will undergo detailed complete ophthalmic examination, including BCVA by Decimal, applanation tonometry, indirect ophthalmoscopy and fluorescein angiography. Central retinal thickness (CRT, i.e. thickness of foveal subfield) in micrometre was measured by Heidelberg SD-OCT software, double checked for accuracy and significant macular ischaemia was ruled out by FA, and none of the eyes had macular photocoagulation then microperimetry will be done.

Treatment consisted of monthly applied intravitreal injections with 0.5 mg Ranibizumab or bevacizumab 1.25 mg in 0.05 ml or 8 mg 0.2 mL preservative free triamcinolone injection combined with full retinal examinations, BCVA, SD-OCT volume scans and microperimetry. Patients will be evaluated post-injection using the same pre-injection tests. All data before and after three intravitreal injections were collected and analysed.

Microperimetry was performed with the Nidek MP1 microperimeter (MP1 Nidek Technologies, Japan). Because this test requires pupil dilation, it was performed after all of the tests requiring undilated pupils had been completed. At 15 min before microperimetry, the pupils were dilated with a drop of tropicamide 1% and phenylephrine 2.5%. The test was done with one eye patched at a time. In a darkened room, after a briefing trial test was initially performed, the test was performed with a 5- min gap between tests on each eye. All patients had a 30-s fixation test. In our study, these parameters were used: a fixation target consisting of a 2 degrees diameter red cross, a white monochromatic background at 4 asb, stimulus size Goldmann III with 200 milliseconds projection time. Decibel range was 0 to 20 (400 and 4 asb respectively). A strategy 4 to 2 double staircase was used; the initial level of retinal sensitivity was set at 8 dB. Stimuli with MP-1 were always projected exactly onto predefined retinal positions by means of an eye tracker that compensates the eye movements. All

subjects underwent microperimetry with dilated pupils.

Mean sensitivity of the perimetry was determined as the mean sensitivity of the 62 stimuli. The microperimetry thresholds were also divided based on the 9 ETDRS grid zones. An ETDRS grid was overlaid onto the microperimetry report chart, and thresholds were calculated separately for the central 1-mm zone and remaining 8 zones individually (Fig. (1)). Pointwise sensitivities of all of the points in the outer zones were summed to determine the peripheral sensitivity. The 5 points within the central 1- mm zone were summed to get the central zone sensitivity. Zones 2 to 5 were summed to get the parafoveal sensitivities and zones 6 to 9 for the perifoveal sensitivities. The follow-up protocol at 3 months was similar to the first.

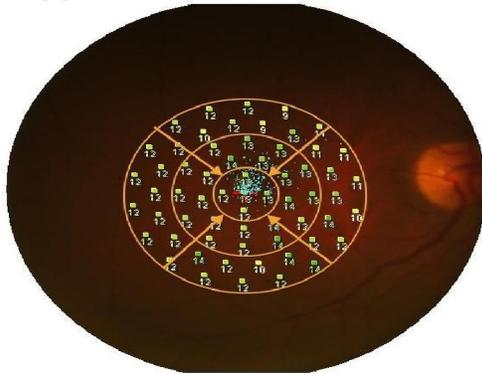


Fig. (1): ETDRS grid overlap on MP1. Inner circle represents central 1 mm of macula, and the outer most circle covers 6mm. The numerals represent point wise sensitivities. Central blue dots represent patient eye tracking.

The retinal thickness was defined as the distance between the vitreoretinal interface and the retinal pigment epithelium in the centre of the fovea, that is, the foveola, using SD-OCT.

The following figures belong to our study patients pre and post injections regarding microperimetric changes and OCT changes.

Case 1

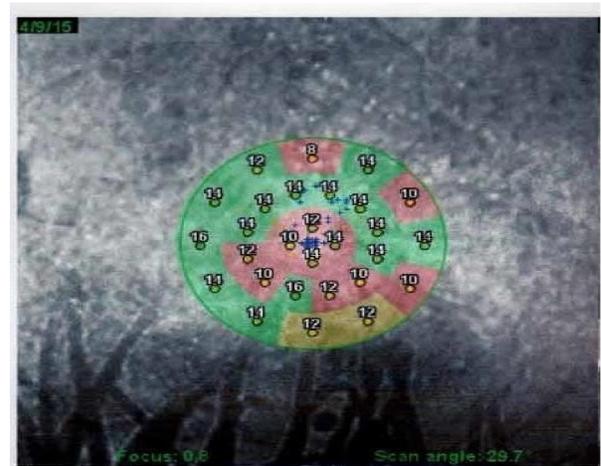


Fig. (2): Case 1: Left eye microperimetry pre Bevacizumab injection

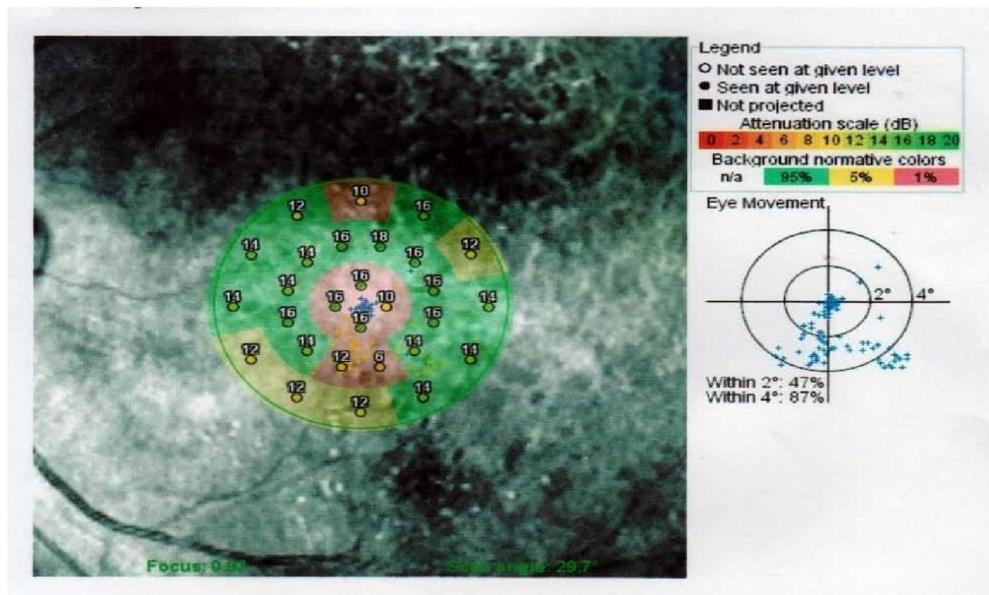


Fig. (3): Case 1: Left eye microperimetry post Bevacizumab injection

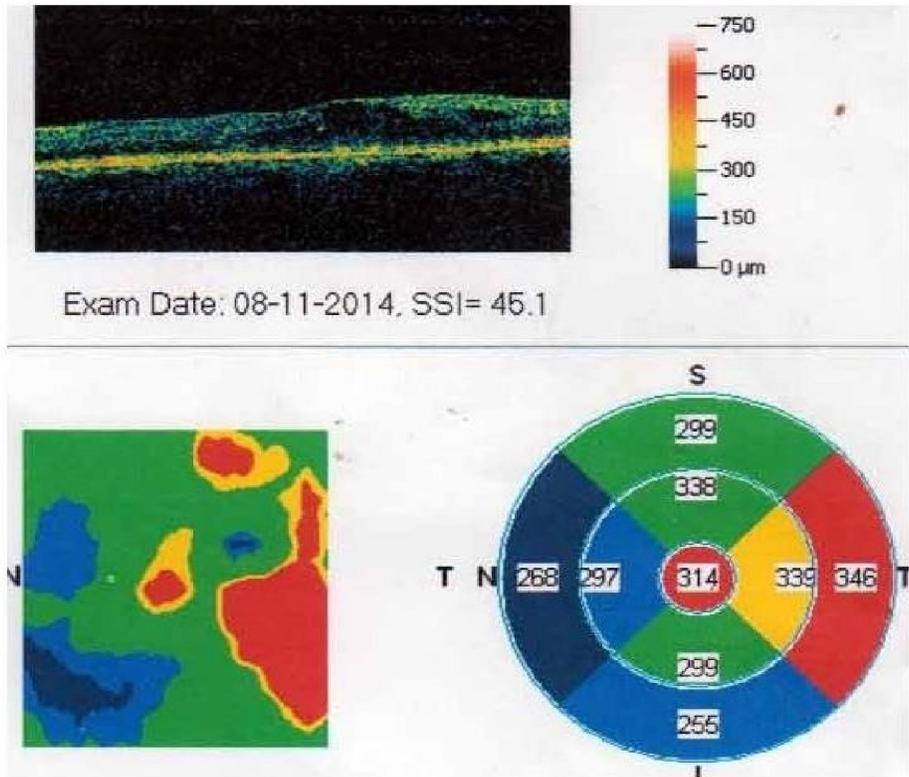


Fig. (4): Case 1: Left eye OCT pre Bevacizumab injection

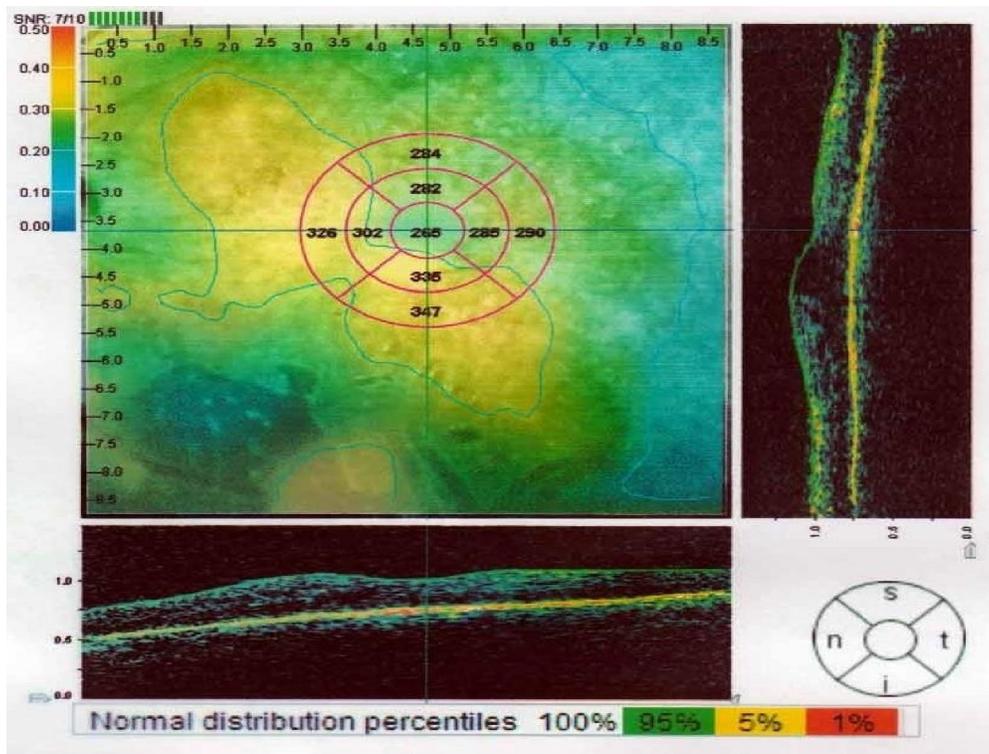


Fig. (5): Case 1: Left eye OCT post Bevacizumab injection

Case 2

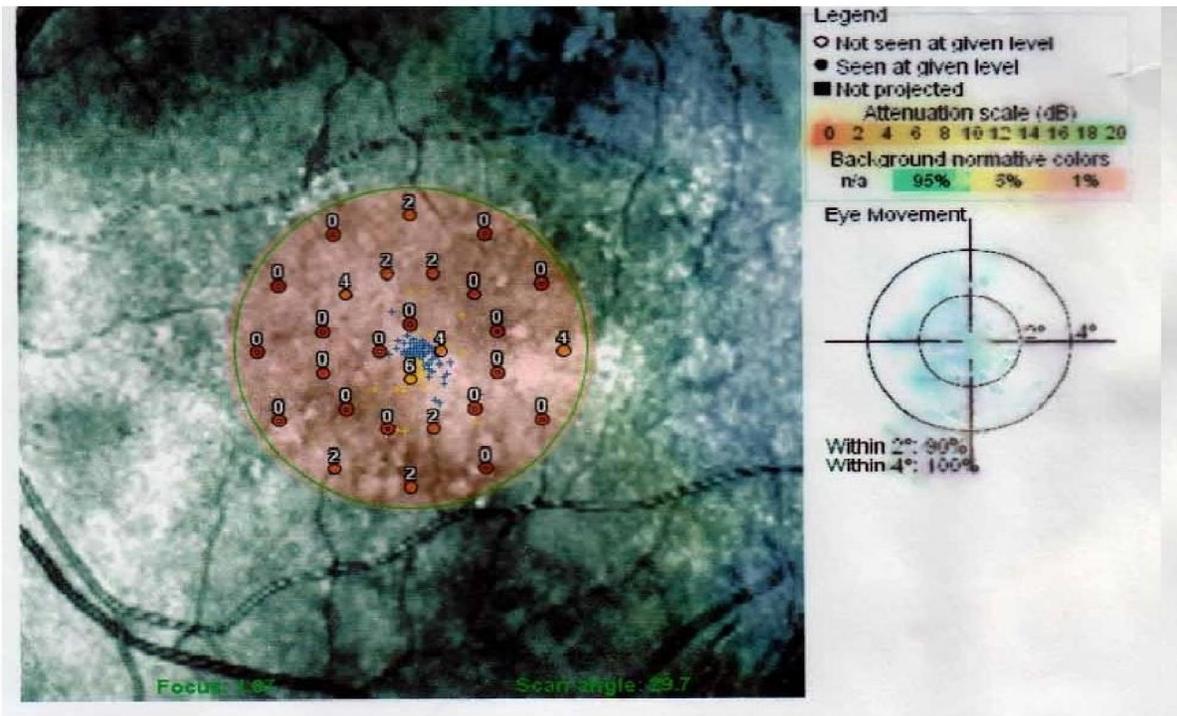


Fig. (6): Case 2: Left eye microperimetry pre Ranibizumab injection

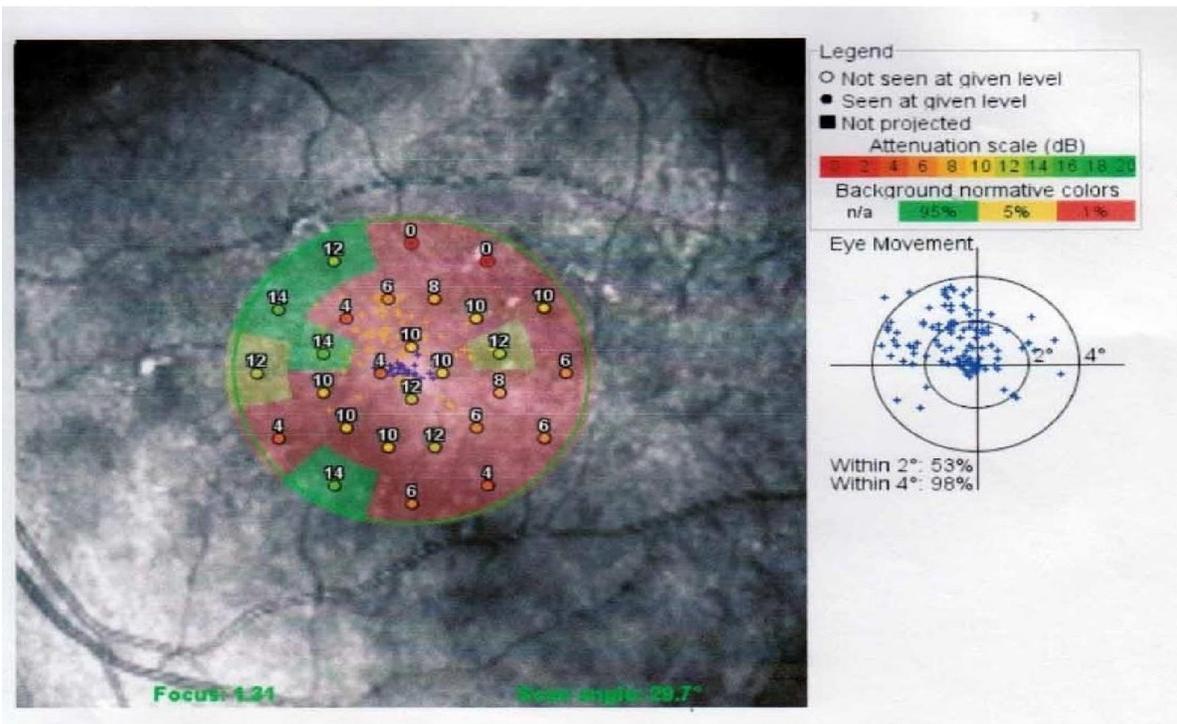
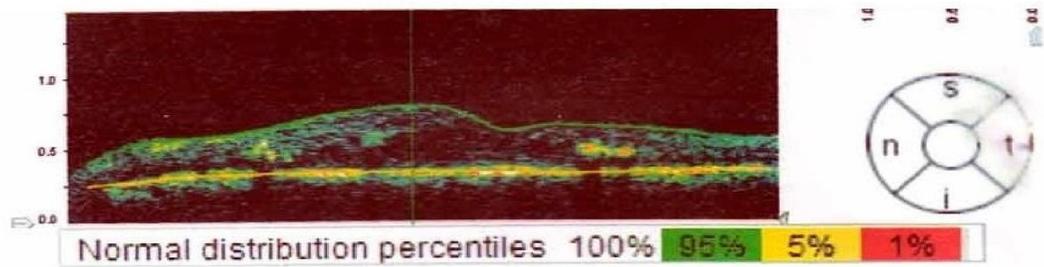
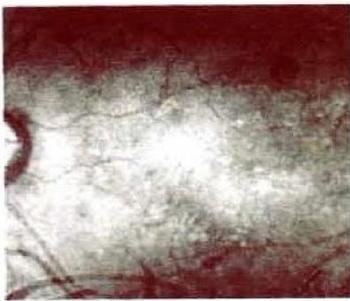


Fig. (7): Case 2: Left eye microperimetry post Ranibizumab injection

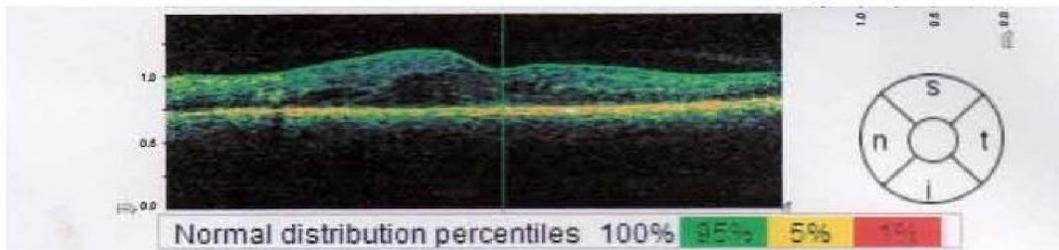


FullFieldImage



	Avg thick μ	Volume μ L
Center	467	
Center circle	453	0.35
Superior inner	393	0.29
Temporal inner	374	0.29
Inferior inner	400	0.30
Nasal inner	412	0.31
Superior outer	326	0.45
Temporal outer	327	0.45
Inferior outer	325	0.44
Nasal outer	349	0.48
Totals	363	3.37

Fig. (8): Case 2: Left eye OCT pre Ranibizumab injection



Full Field Image



	Avg thick μ	Volume μ L
Center	287	
Center circle	313	0.24
Superior inner	343	0.26
Temporal inner	333	0.25
Inferior inner	328	0.25
Nasal inner	401	0.31
Superior outer	343	0.47
Temporal outer	327	0.45
Inferior outer	317	0.43
Nasal outer	405	0.56
Totals	346	3.22

Fig. (9): Case 2: Left eye OCT post Ranibizumab injection

Case 3

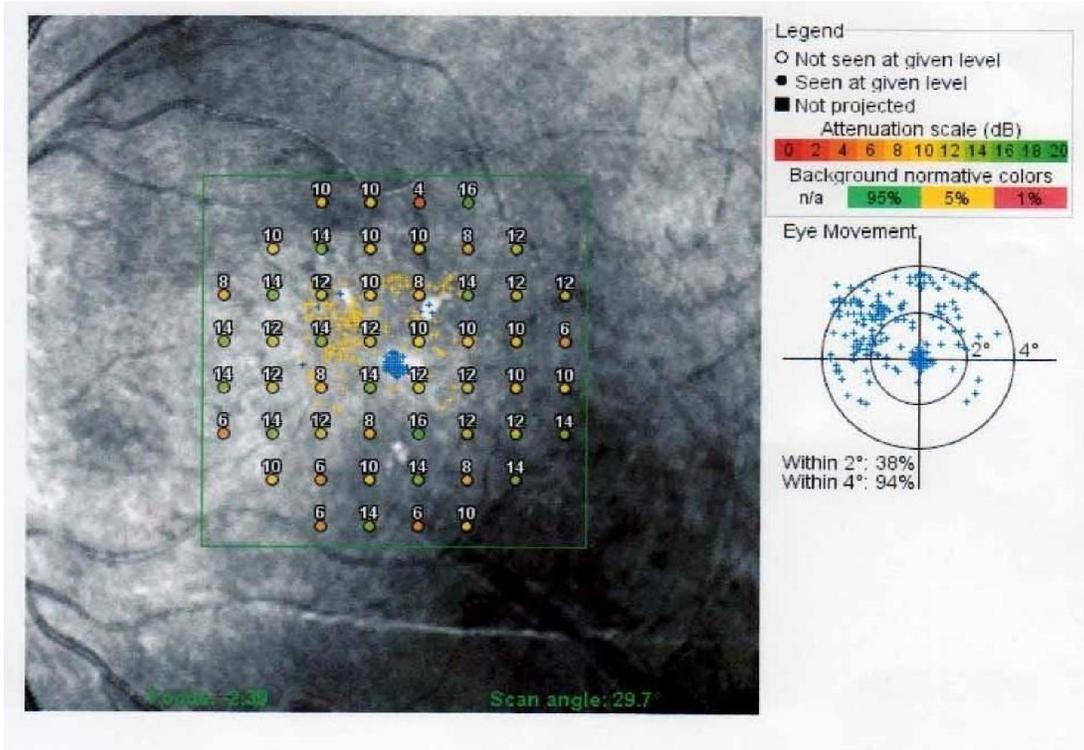


Fig. (10): Case 3: Left eye microperimetry pre Triamcinolone Acetate injection

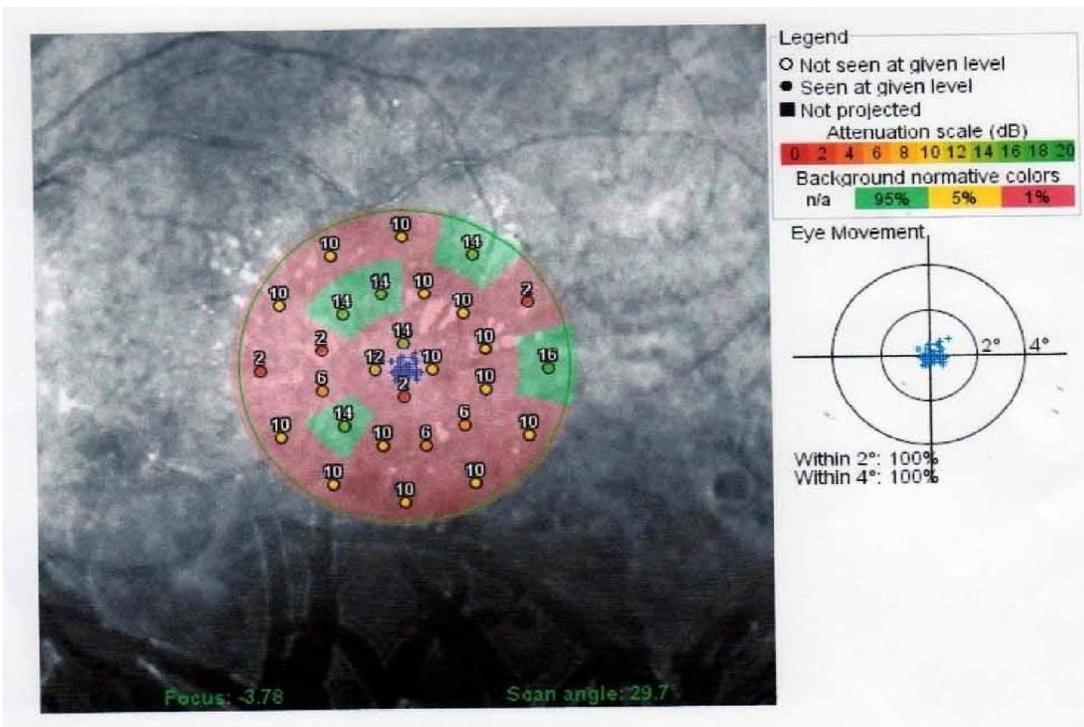


Fig. (11): Case 3: Left eye microperimetry post Triamcinolone Acetate injection

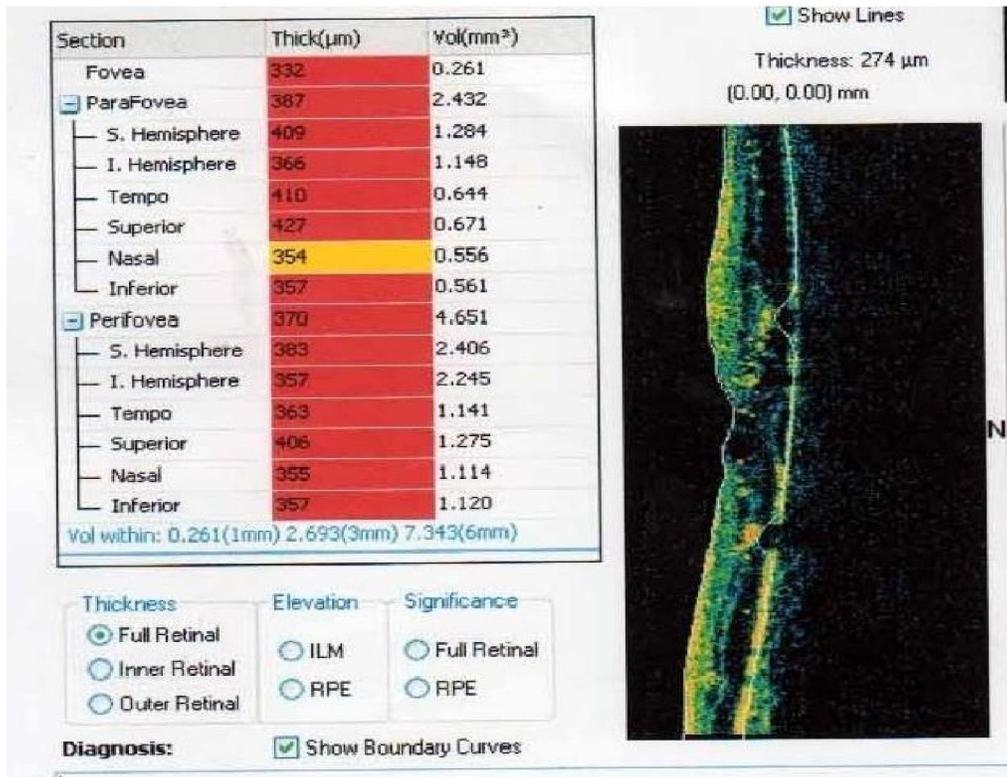


Fig. (12): Case 3: Left eye OCT pre Triamcinolone Acetate injection

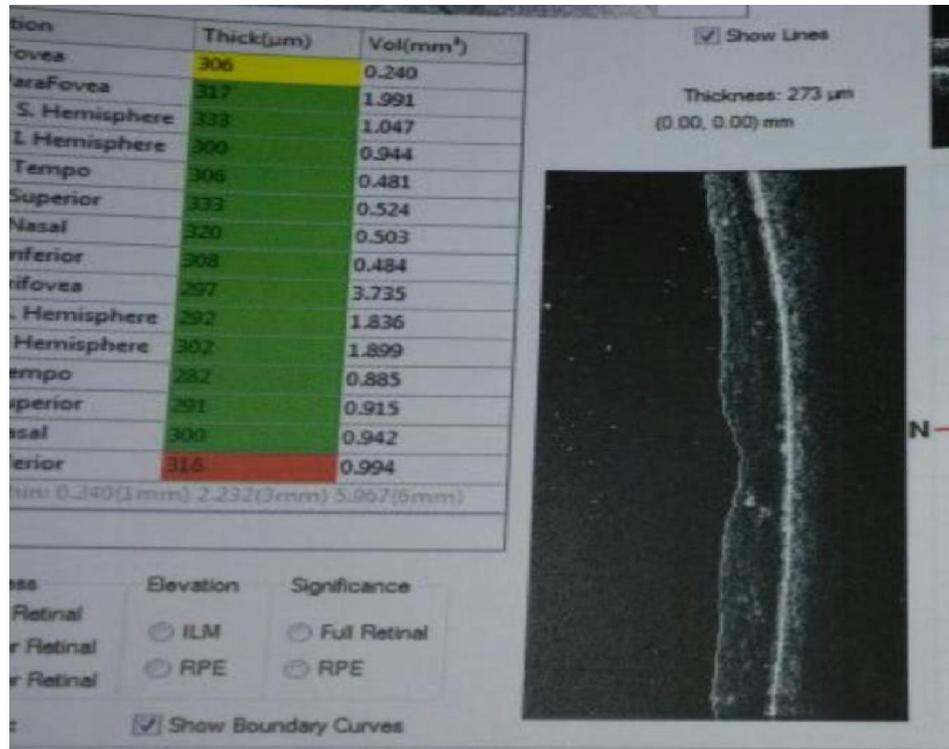


Fig. (14): Case 3: Left eye OCT post Triamcinolone Acetate injection

Data management:

The data had been coded to fit the program of statistical analysis (SPSS) Statistical Package for Special Sciences version 22 under windows 7.

Statistical tests:

- Description of qualitative variables by frequency and percentage.
- Description of quantitative variables in the form of mean and standard deviation (mean \pm SD).
- **The Paired Samples *t* Test** was used to compare means before and after injection.
- Correlation was done by **Spearman correlation**

Significance level (p) was expressed as following:

- ✓ P-value $>$ 0.05 is insignificant.
- ✓ P-value $<$ 0.05 is significant.

✓ P-value $<$ 0.001 is highly significant.

3. Results

This study was conducted on 56 diabetic patients (60 eyes). Who were referred to AL-Fayoum university hospital outpatient clinic for clinical evaluation. All are diagnosed as clinically significant macular oedema (criteria according to ETDRS). The duration of follow-up was 12 week.

Thirty eyes received intravitreal triamcinolone injection and the other thirty received intravitreal anti-VEGF (bevacizumab and ranibizumab).

Descriptive analysis of studied cases as regard age

Average age of study group is 58 years and the range varies from 45 to 70 years with mean 58.43 ± 6.16 SD. As shown in (Table.1) and (Fig.15).

Table (1). Descriptive analysis of studied cases as regard age

Age	Mean(Years)	Range(Years)	\pm SD
	58.43	45 to 70	6.16

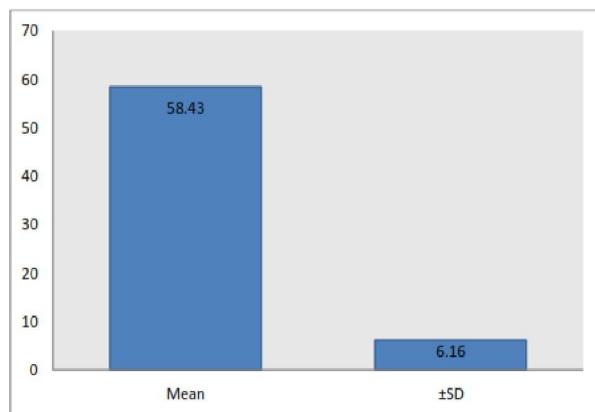


Fig. (15) Descriptive analysis of studied cases as regard age.

Descriptive analysis of the studied group as regard Gender

It shows that males representing 51.7% (31 of 60) while female represent 48.3% (29 of 60) of the study group. As shown in (Table 2) and (Fig.16).

Table (2) Descriptive analysis of the studied group as regard Gender

Gender	Male	Female
No. of Patients	31	29
Percentage	51.7%	48.3%

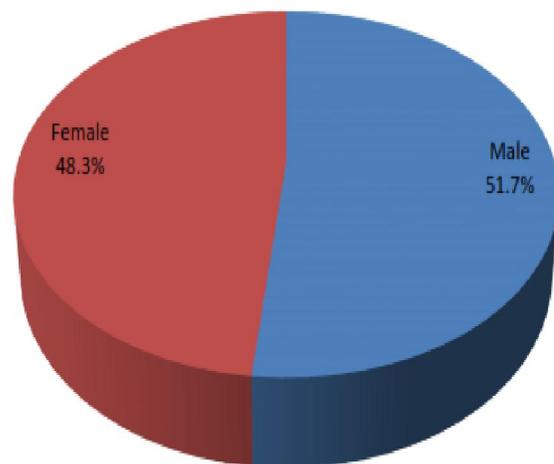


Fig. (16) Descriptive analysis of the studied group as regard Gender

Analysis of the studied group as regard Visual Acuity

Data regarding the change in patients' VA are shown in Fig. (17). Mean BCVA, expressed by decimal, was 0.34 ± 0.16 dB at baseline. At 12 weeks, BCVA improved to 0.54 ± 0.16 dB (P-value $<$ 0.001).

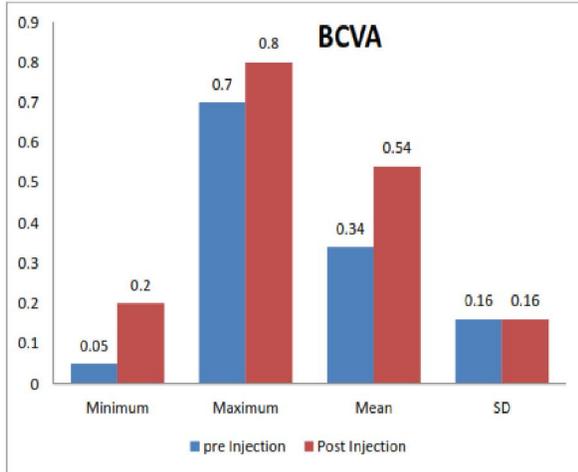


Fig. (17) Descriptive analysis of studied group as regard BCVA minimum, maximum, mean and SD pre and post injection.

Analysis of the studied group as regard Retinal sensitivity by Microperimetry

Mean macular sensitivity, determined with the MP-1 in the OCT- corresponding central field, was 8.19 ± 4.57 dB at baseline. At 4 weeks, macular sensitivity improved to 10.76 ± 3.86 dB (P-value < 0.001). At follow-up 12 weeks, macular sensitivity improved to 11.58 ± 3.67 dB (P- value < 0.001). As shown in (Fig.18).

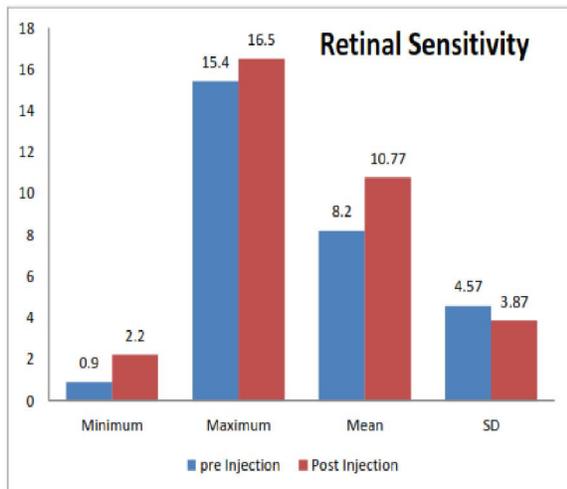


Fig. (18) Descriptive analysis of studied group as regard retinal sensitivity minimum, maximum, mean and SD pre and post injection.

The correlation between BCVA and macular sensitivity was statistically significant (P-value < 0.001).

Analysis of Correlation between retinal thickness and BCVA after injection:

Fig. (19) shows the correlation between retinal

thickness and BCVA after injection.

There is positive strong correlation between retinal thickness and BCVA after injection (p value= 0.001 – r= 0.714).

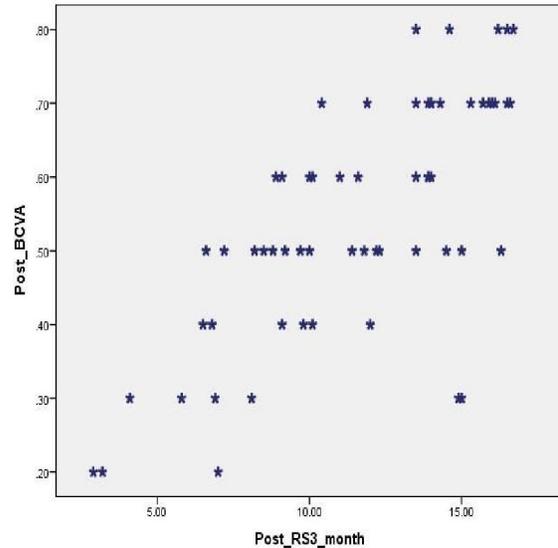


Fig. (19) Correlation between retinal sensitivity and BCVA post injection in the studied group.

Descriptive analysis of the studied group as regard Macular Thickness by OCT

On OCT examination, mean retinal thickness in the central field at baseline was 447.58 ± 101.49 microns (range 300–720).

At 12 weeks (12 weeks post injection I), central macular thickness decreased to 272.35 ± 84.27 microns (range 170–500) (P-value < 0.001). As shown in Fig. (20).

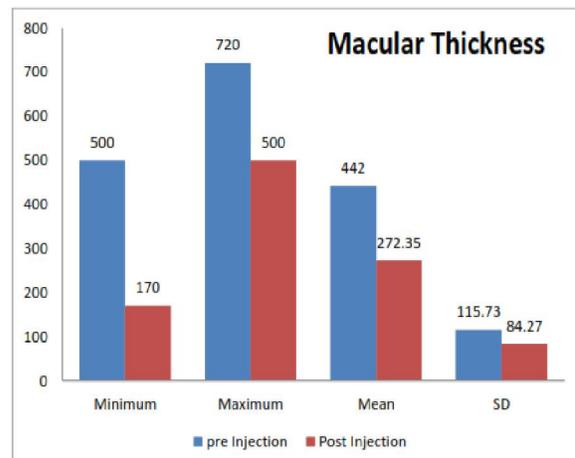


Fig. (20) Descriptive analysis of the studied group as regard Central Macular thickness minimum, maximum, mean and SD pre and post injection.

Analysis of Correlation between BCVA and retinal sensitivity after injection

The correlation between central macular thickness and macular sensitivity was statistically significant (P-value < 0.001). As shown in Fig. (21).

There is negative strong correlation between retinal thickness and macular sensitivity after injection (p value= 0.001 – r= -0.770).

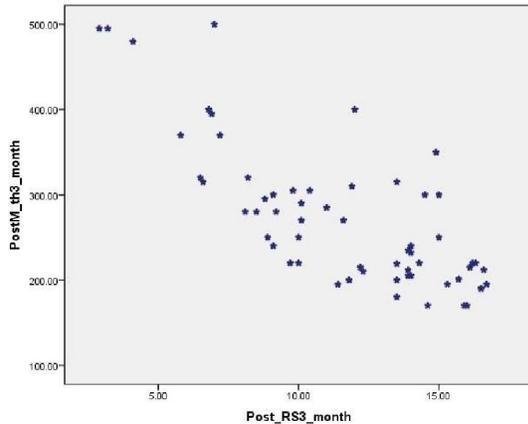


Fig. (21) Correlation between retinal thickness and retinal sensitivity after injection in the studied group.

Analysis of the studied group as regard Intraocular Pressure.

The change in patients’ IOP are shown in Fig. (22) with mean VA 16.1 ± 2.3 vs. 18.3±4.69 mmHg.

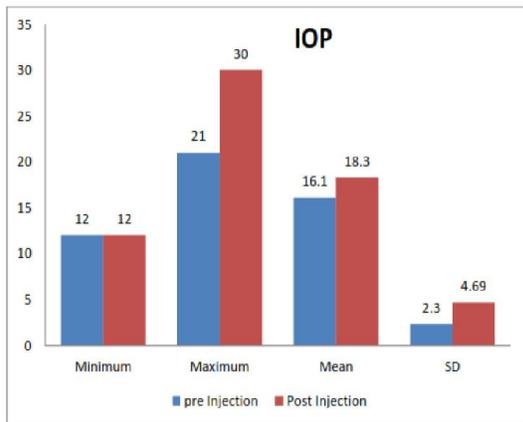


Fig. (22) Descriptive analysis of studied group as regard IOP minimum, maximum, mean and SD pre and post injection.

Analysis of the IV Triamcinolone group as regard Visual Acuity

Data regarding the patients’ VA are shown in Fig. (23) expressed by Decimal with mean VA 0.5 ± 0.18 vs. 0.33±0.15.

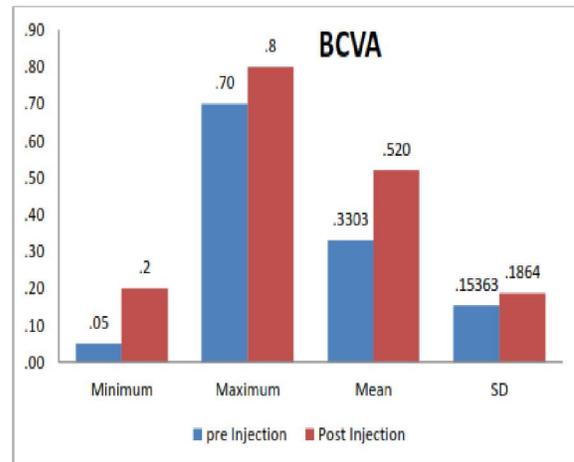


Fig. (23) Descriptive analysis of IV TA group as regard BCVA minimum, maximum, mean and SD pre and post IV TA injection.

Analysis of the IV Triamcinolone group as regard Retinal Sensitivity

Mean macular sensitivity, determined with the MP-1 in the OCT- corresponding central field, was 7.6 ± 4.1 dB at baseline. At follow-up 12 weeks, macular sensitivity improved to 10.6 ± 3.7dB (P-value < 0.001). As shown in Fig. (24).

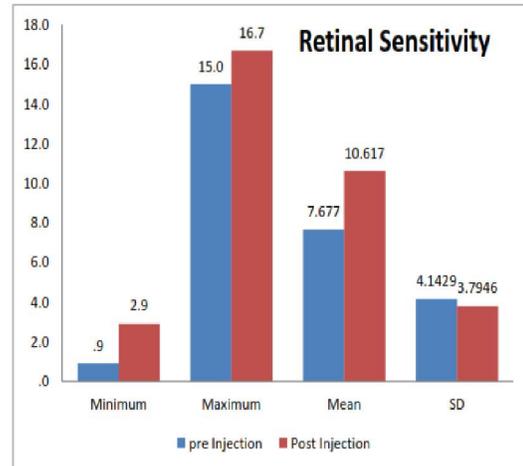


Fig. (24) Descriptive analysis of IV TA group as regard Retinal sensitivity minimum, maximum, mean and SD pre and post IV TA injection.

Analysis of Correlation between BCVA and retinal sensitivity after IV TA injection.

The correlation between central BCVA and retinal sensitivity shown in Fig. (25) was statistically significant (P-value < 0.001).

There is positive strong correlation between retinal sensitivity and BCVA after injection (p value= 0.001 – r= 0.759).

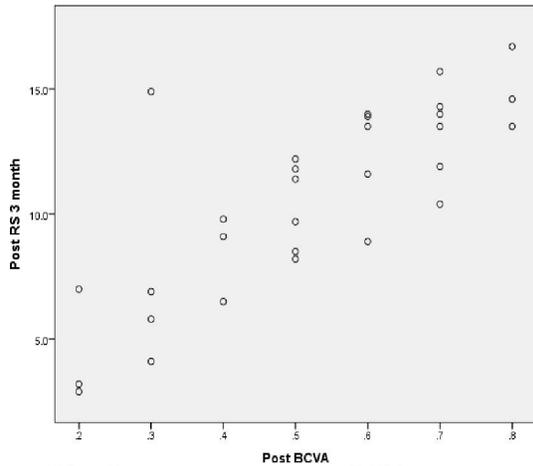


Fig. (25) Correlation between BCVA and retinal sensitivity after IVTA injection in IV TA group.

Analysis of the IV Triamcinolone group as regard Central macular Thickness

On OCT examination, mean retinal thickness in the central field at baseline was 469 ± 109 microns.

At 12 weeks (12 weeks post injection I), central macular thickness decreased to 290 ± 100 microns (P-value < 0.001). As shown in Fig. (26).

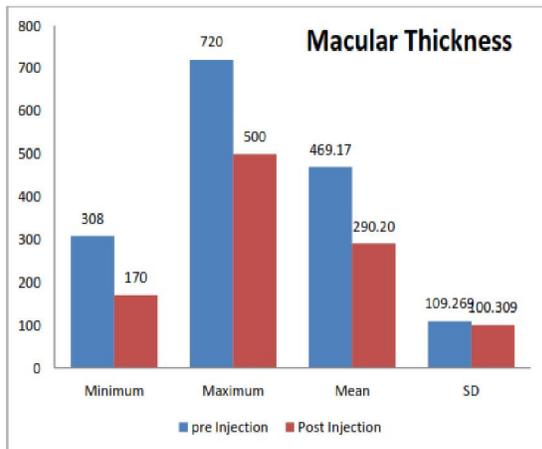


Fig. (26) Descriptive analysis of IV TA group as regard Macular thickness minimum, maximum, mean and SD pre and post IVTA

Analysis of Correlation between retinal thickness and retinal sensitivity after IV TA injection

The correlation between central macular thickness and retinal sensitivity was statistically significant (P-value < 0.001). As shown in Fig. (27).

There is negative strong correlation between macular thickness and retinal sensitivity after injection (p value= 0.001 – r= -0.718)

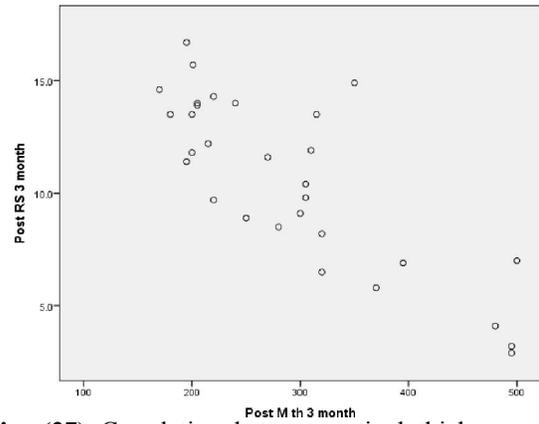


Fig. (27) Correlation between retinal thickness and retinal sensitivity after IV TA injection

Analysis of the IV TA group as regard IOP

As regard change in IOP after IVTA injection, data are shown in Fig. (28).

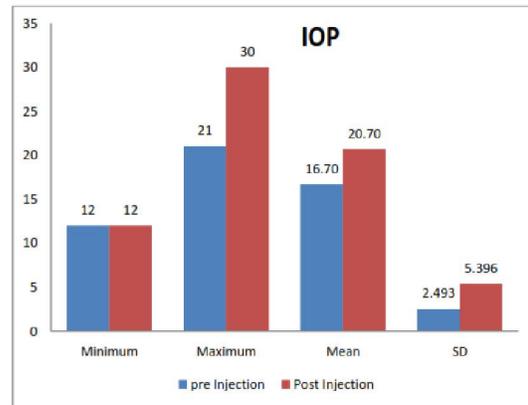


Fig. (28) Descriptive analysis of IV TA group as regard IOP minimum, maximum, mean and SD pre and post IV TA injection.

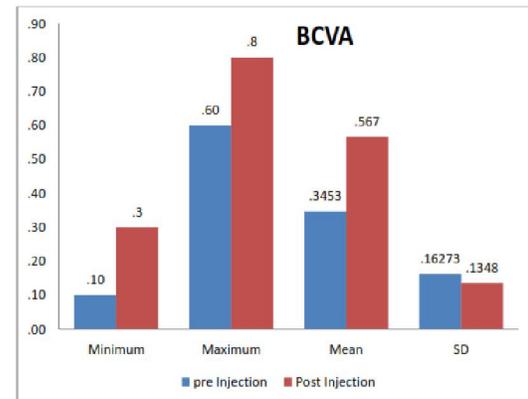


Fig. (29) Descriptive analysis of IV anti-VEGF group as regard BCVA minimum, maximum, mean and SD pre and post IV anti-VEGF injection.

Analysis of the IV Anti-VEGF group as regard Visual Acuity

The change in patients' VA expressed by decimal are shown in Fig. (29).

Analysis of the IV Anti-VEGF group as regard Retinal Sensitivity

Fig. (30) shows mean retinal sensitivity, determined with the MP-1 in the OCT-corresponding central field, was 8.717 ± 4.977 dB at baseline. At follow-up 12 weeks, macular sensitivity improved to 12.550 ± 3.3353 dB (P-value < 0.001).

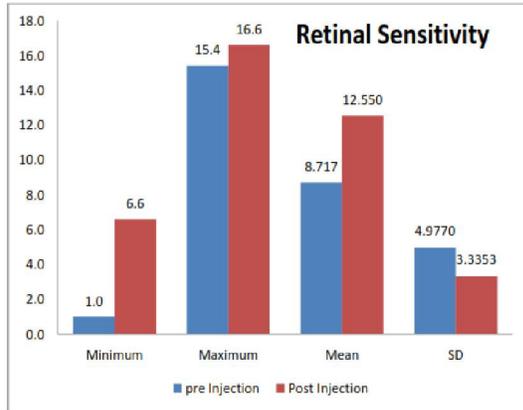


Fig. (30) Descriptive analysis of IV anti-VEGF group as regard Retinal sensitivity minimum, maximum, mean and SD pre and post IV anti-VEGF injection.

Analysis of correlation between BCVA and Retinal sensitivity after IV Anti-VEGF injection.

The correlation between central BCVA and macular sensitivity was statistically significant (P-value < 0.001).

There is positive strong correlation between retinal thickness and BCVA after injection (p value= 0.001 – r= 0.617). As shown in Fig. (31).

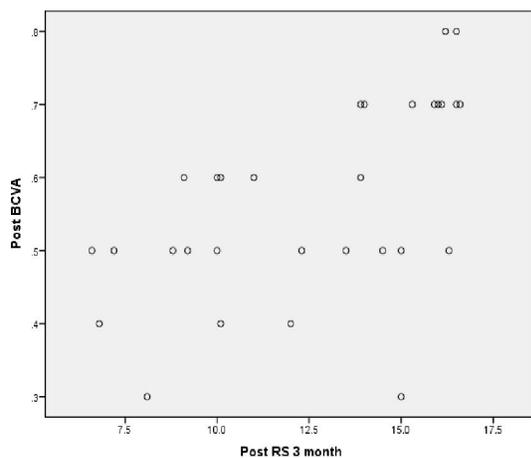


Fig. (31) Correlation between retinal sensitivity and BCVA after IV Anti- VEGF injection.

Analysis of the IV Anti-VEGF group as regard Central macular Thickness

On OCT examination, mean retinal thickness in the central field at baseline was 426 ± 89.754 microns (range 300–650).

At 12 weeks (12 weeks post injection I), central macular thickness decreased to 254.5 ± 61.058 microns (range 170–400) (P-value < 0.001). As shown in Fig. (32).

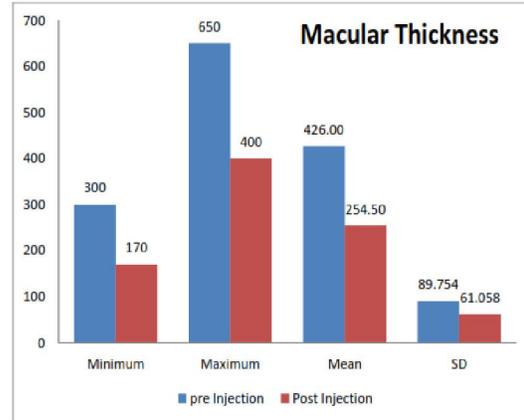


Fig. (32) Descriptive analysis of IV anti-VEGF group as regard Macular thickness minimum, maximum, mean and SD pre and post IV anti-VEGF injection.

Analysis of correlation between Reti sensitivity and central macular thickness after IV Anti-VEGF injection.

The correlation between retinal sensitivity and central macular thickness was statistically significant (P-value < 0.001).

There is negative strong correlation between retinal sensitivity and central macular thickness after IV Anti-VEGF injection (p value= 0.001 – r= 0.699). As shown in Fig. (33).

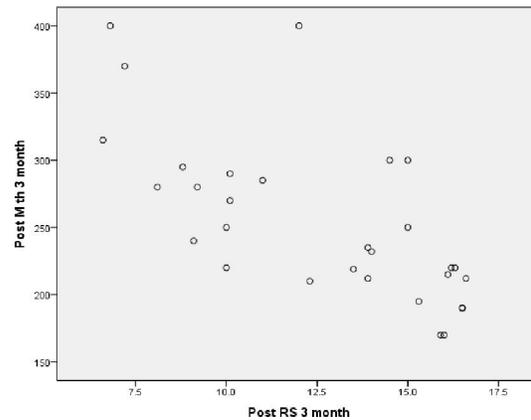


Fig. (33) Correlation between retinal sensitivity and central macular thickness after IV Anti-VEGF injection.

Analysis of the IV Anti-VEGF group as regard IOP

The changes in IOP after IV anti-VEGF injection are shown in Fig. (34).

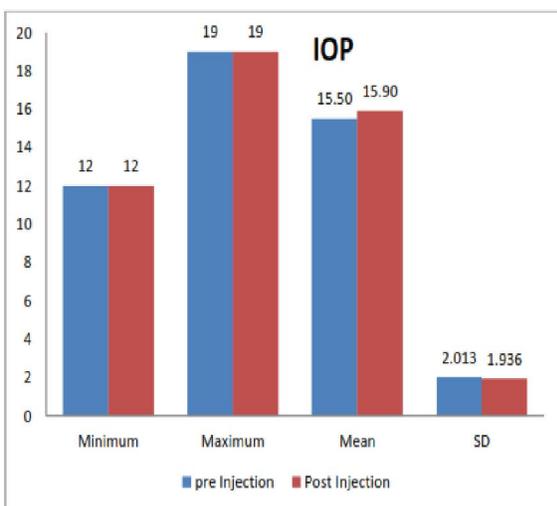


Fig. (34) Descriptive analysis of IV anti-VEGF group as regard IOP minimum, maximum, mean and SD pre and post IV anti-VEGF injection.

4. Discussion

Macular edema is a major cause of VA impairment in diabetic patients, frequently leading to legal blindness (Ooi & Hardy, 1999). Laser photocoagulation is a useful treatment for managing DME, but in eyes with diffuse DME, focal treatment cannot be performed on localized areas because the whole macular region is involved (Grenga, Lupo, Domanico, & Vingolo, 2008).

Recommended treatment is grid macular laser treatment. It is however known that diffuse macular edema is more resistant to laser treatment compared to focal macular edema.

During recent years, in order to reduce the breakdown of the inner blood–retinal barrier and extravasation from leaking vessels, several pharmacological therapies have been used, such as intravitreal triamcinolone acetate and intravitreal anti-VEGF drugs (bevacizumab, pegaptanib, ranizumab) [(Ooi & Hardy, 1999), (Grenga, et al., 2008), (Starita, Patel, Katz, & Adamis, 2007) and (Kumar & Sinha, 2007)].

Microperimetry, particularly MP-1, allows quantifying macular sensitivities and fixation in an exact fundus related fashion, adding detailed information about degree and pattern of macular function alteration, thus MP-1 is a useful tool for a qualitative evaluation of the retinal function. MP-1 has been successfully used in the diagnosis and follow-up of different macular disorders, including age-related macular degeneration, myopic maculopathy, macular

dystrophies, and diabetic macular edema (Vujosevic et al., 2006) (Midena et al., 2007) (Kube, Schmidt, Toonen, Kirchhof, & Wolf, 2005) (Rohrschneider, 2000).

We report the results of 60 consecutive eyes with diffuse DME treated with intravitreal injection (30 eyes with IV Triamcinolone and 30 eyes with IV Anti-VEGF (Bevacizumab & Ranibizumab) which resulted in both anatomic and functional improvement. Our results also show that bevacizumab and Ranibizumab were well tolerated and no systemic adverse events were noticed during the study. Ocular tolerance was also high and no ocular inflammation was noted.

Intravitreal steroids reduce macular edema for which several theories were proposed, including local reduction of inflammatory mediators, lower levels of VEGF, increased diffusion by an effect on calcium channels and improved blood retinal barrier function; (Vedantham Vasumathy, 2006) it however remains plagued by a considerably high percentage of side-effects, namely cataract progression in a number of eyes and rise in IOP (37%) (Konstantopoulos, Williams, Newsom, & Luff, 2007). Pascale Massin et al reported that the main side effect observed was IOP elevation, which occurred in 6 of 12 injected eyes (50%), at intervals ranging from 2 days to 6 weeks after injection (Massin et al., 2004).

In this study which was carried out in an Egyptian population, the mean central macular thickness reduced to 272.3 μ from 447.5 μ and the visual acuity also showed a modest improvement from a baseline of 0.3 to 0.5 at the end of 3 months. Also, retinal sensitivity has shown improvement from 8.1 \pm 4.5 dB to 11.5 \pm 3.6 dB.

We reported 30 diabetic eyes treated with intravitreal triamcinolone acetate injection and another 30 diabetic eyes with intravitreal.

Bevacizumab or Ranibizumab injection so we will discuss each group separately aiming for accurate comparison.

Beginning with IV TA injection group, we reported that the mean retinal thickness in the central field at baseline was 479 \pm 109 microns (range 308–720), at 12 weeks, mean central macular thickness changed to 290 \pm 100 microns in agreement with the reported mean retinal thickness in the central field in a similar study at baseline was 692 \pm 70microns, at 12 weeks, mean central macular thickness changed to 363.7 \pm 123.52 microns (Grenga, et al., 2008). and also to the reported data by Murat Karacorlu et al which informed that mean retinal thickness in the central field at baseline was 452.73 \pm 108.29 microns, but at 30 days, mean central macular thickness changed to 254.00 \pm 40.29 microns (Karacorlu, Ozdemir, Senturk, Karacorlu, & Uysal, 2010).

In our study, macular sensitivity improved (10.6

± 3.7 dB vs. 7.6 ± 4.1 dB) while Grenga P et al reported slightly lower results (8.54 ± 2.78 dB vs. 6.85 ± 2.1 dB), confirming a positive effect of the treatment on macular function (Grenga, et al., 2008).

The reported study of Karacorlu M et al comparing mean retinal sensitivity Thirty days after IVTA showing that it had increased from 8.45 ± 2.52 dB to 11.68 ± 3.25 dB in agreement to ours (9.9 ± 3.7 dB vs. 7.6 ± 4.1 dB).

Regarding BCVA, our study demonstrated significant improvement from 0.3 ± 0.15 to 0.5 ± 0.18 compared to data reported by Grenga P et al which also showed similar results with improvement from 0.13 ± 0.09 to 0.23 ± 0.15 (Grenga, et al., 2008).

Grenga p et al. and Karacorlu et al. reported significant improvements in macular sensitivity after intravitreal triamcinolone (Grenga, et al., 2008) (Karacorlu, et al., 2010). Thus, MP-1 microperimetry offers the possibility of a direct comparison of retinal pathology with the psychophysical measurements (Vujosevic, et al., 2006).

This finding was consistent with the MP-1 microperimetry data, confirming a good correlation between retinal sensitivity and perceived visual performance.

As regard IV Anti-VEGF injection group, On OCT examination, In our study mean retinal thickness in the central field at baseline was 426 ± 89 microns (range 300– 650), at 12 weeks (4 weeks post injection III), mean central macular thickness changed to 254 ± 61 microns in agreement with the reported mean retinal thickness in the central field in a similar study at baseline was 447.08 ± 143.01 microns (range 244–600), at 12 weeks (4 weeks post injection III), mean central macular thickness changed to 311.09 ± 83.9 microns (Malagola, Spinucci, Cofone, & Pattavina, 2013).

Similar to the study published by Comyn O et al. (Comyn et al., 2014) which informed that the central OCT subfield thickness decreased from 455 ± 79 mm to 350 ± 78 mm, our study also demonstrated significant improvement in VA.

Microperimetry In our study, macular sensitivity improved (10.77 vs. 8.2 dB) while Romualdo Malagola et al reported higher results (14.26 vs.

8.29 dB), confirming a positive effect of the treatment on macular function (Malagola, et al., 2013). Comyn O et al reported similar results to ours (11.9 ± 3.9 vs. 10.8 ± 3.7) (Comyn, et al., 2014).

Our data suggest that macular sensitivity is probably one of the most important predictors of visual function. MP-1 microperimetry seems to be a useful tool in evaluating visual outcome after intervention in eyes affected by DME.

This finding was consistent with the MP-1 microperimetry data, confirming a good correlation

between retinal sensitivity and perceived visual performance; patients described this improvement in terms of higher comfort during activities such as reading or manual work. This finding expressly demonstrates improved macular function and its strong impact on patients' general or perceived health status, independent of objective measurements. Our data suggest that macular sensitivity is probably one of the most important predictors of visual function. MP-1 microperimetry seems to be a useful tool in evaluating visual outcome after intervention in eyes affected by DME.

Conclusion

Diabetes has a relevant impact on visual function, up to permanent visual acuity loss, when retinopathy is clinically evident. Visual acuity cannot represent the only functional way of quantifying visual function loss. Microperimetry has the major advantage of integrating the functional parameter (sensitivity threshold) to the morphologic status of the retina (biomicroscopy, fluorescein angiography and OCT.).

60 Diabetic eyes were enrolled, with diffuse DME treated with intravitreal injection and divided into two groups; group I was injected with intravitreal triamcinolone acetate. Group II was injected with intravitreal Anti VEGF either Bevacuzimab or Ranibizumab.

According to IV TA injection group, we reported that the mean retinal thickness in the central field at baseline was 479 ± 109 microns (range 308–720), at 12 weeks, mean central macular thickness changed to 290 ± 100 microns.

Also macular sensitivity improved (10.6 ± 3.7 dB vs. 7.6 ± 4.1 dB) as well as BCVA, our study demonstrated significant improvement from 0.3 ± 0.15 to 0.5 ± 0.18 .

As regard IV Anti-VEGF injection group, On OCT examination, In our study mean retinal thickness in the central field at baseline was 426 ± 89 microns (range 300– 650), at 12 weeks (4 weeks post injection III), mean central macular thickness changed to 254 ± 61 microns Also macular sensitivity improved (10.77 vs. 8.2 dB) with significant improvement in VA.

Thus, MP-1 microperimetry offers the possibility of a direct comparison of retinal pathology with the psychophysical measurements.

Our data suggest that retinal sensitivity of the macular area determined by the MP1 was significantly correlated with visual acuity and with morphological changes revealed by OCT. The combination of OCT and MP1 can be easily performed in routine clinical settings, and may provide other methods to evaluate and assess DME.

Our data suggest that macular sensitivity is probably one of the most important predictors of

visual function. MP-1 microperimetry seems to be a useful tool in evaluating visual outcome after intervention in eyes affected by DME.

References

- Comyn, O., Sivaprasad, S., Peto, T., Neveu, M. M., Holder, G. E., Xing, W.,... Hykin, P. G. (2014). A Randomized Trial to Assess Functional and Structural Effects of Ranibizumab versus Laser in Diabetic Macular Edema (the LUCIDATE Study). *AJOPHT American Journal of Ophthalmology*, 157(5), 960-970.e962.
- Grenga, P., Lupo, S., Domanico, D., & Vingolo, E. M. (2008). Efficacy Of Intravitreal Triamcinolone Acetonide In Long Standing Diabetic Macular Edema: A Microperimetry and Optical Coherence Tomography Study. *Retina*, 28(9), 1270-1275.
- Karacorlu, M., Ozdemir, H., Senturk, F., Karacorlu, S. A., & Uysal, O. (2010). Macular function after intravitreal triamcinolone acetonide injection for diabetic macular oedema. *Acta ophthalmologica*, 88(5), 558-563.
- Konstantopoulos, A., Williams, C. P. R., Newsom, R. S., & Luff, J. (2007). Ocular morbidity associated with intravitreal triamcinolone acetonide. *Eye*, 21(3), 317-320.
- Kube, T., Schmidt, S., Toonen, F., Kirchhof, B., & Wolf, S. (2005). Fixation Stability and Macular Light Sensitivity in Patients with Diabetic Maculopathy: A Microperimetric Study with a Scanning Laser Ophthalmoscope. *Ophthalmologica*, 219(1), 16-20.
- Kumar, A., & Sinha, S. (2007). Intravitreal bevacizumab (Avastin) treatment of diffuse diabetic macular edema in an Indian population. *Medknow Publications*.
- Malagola, R., Spinucci, G., Cofone, C., & Pattavina, L. (2013). Prospective microperimetry and OCT evaluation of efficacy of repeated intravitreal bevacizumab injections for persistent clinically significant diabetic macular edema. *International ophthalmology*, 33(3), 261-267.
- Massin, P., Audren, F., Haouchine, B., Erginay, A., Bergmann, J. F., Benosman, R.,... Gaudric, A. (2004). Intravitreal triamcinolone acetonide for diabetic diffuse macular edema. *Ophthalmology -Rochester And Hagerstown*, 111(2), 218-224.
- Midena, E. (2006). Perimetry and the fundus: an introduction to microperimetry. Thorofare, NJ: SLACK Inc.
- Midena, E., Vujosevic, S., Convento, E., Manfre, A., Cavarzeran, F., & Pilotto, E. (2007). Microperimetry and fundus autofluorescence in patients with early age-related macular degeneration. *Br J Ophthalmol British Journal of Ophthalmology*, 91(11), 1499.
- Ooi, C. G., & Hardy, K. J. (1999). Treatment of severe proliferative retinopathy and diabetic maculopathy. *Diabetes Metab. Res. Rev. Diabetes/Metabolism Research and Reviews*, 15(5), 373-377.
- Rohrschneider, K. (2000). Scanning laser ophthalmoscope fundus perimetry before and after laser photocoagulation for clinically significant diabetic macular edema. *American Journal of Ophthalmology*, 129(1), 27-32.
- Starita, C., Patel, M., Katz, B., & Adamis, A. (2007). Vascular Endothelial Growth Factor and the Potential Therapeutic Use of Pegaptanib (Macugen) in Diabetic Retinopathy. *Developments in ophthalmology.*, 39, 122-148.
- Sunness, J. S., Applegate, C. A., Haselwood, D., & Rubin, G. S. (1996). Fixation Patterns and Reading Rates in Eyes with Central Scotomas from Advanced Atrophic Age-related Macular Degeneration and Stargardt Disease. *Ophthalmology - Rochester And Hagerstown*, 103(9), 1458-1466.
- Vedantham Vasumathy, a. K. R. (2006). Intravitreal injection of triamcinolone acetonide for diabetic macular edema: Principles and practice.
- Vujosevic, S., Berton, M., Bini, S., Casciano, M., Cavarzeran, F., & Midena, E. (2016). Hyperreflective Retinal Spots and Visual Function After Anti-Vascular Endothelial Growth Factor Treatment In Center-Involving Diabetic Macular Edema. *Retina*, 36(7), 1298-1308.
- Midena E., Segato T., Giuliano M., Zucchetto M. Macular recovery function (nyctometry) in diabetics without and with early retinopathy. *Br. J. Ophthalmol.* 1990;74:106-108.
- Bresnick G.H. Diabetic retinopathy viewed as a neurosensory disorder. *Arch Ophthalmol.* 1986;104:989-990.
- Hyvärinen L., Laurinen P., Rovamo J. Contrast sensitivity in evaluation of visual impairment due to diabetes. *Acta Ophthalmol.* 1983;61:94-101.
- Sharma S., Oliver-Fernandez A., Liu W. The impact of diabetic retinopathy on health-related quality of life. *Curr. Opin. Ophthalmol.* 2005;16:155-159.
- Owsley C., Sloane M.E. Contrast sensitivity, acuity, and the perception of 'real-world' targets. *Br. J. Ophthalmol.* 1987;71:791-796.
- Midena E., Radin P.P. Liquid crystal microperimetry. In: Midena E., editor. *Perimetry and the Fundus: An Introduction to Microperimetry*. Slack incorporated; Thorofare, NJ: 2006. pp. 1-7.