INTRODUCTION

Diabetic retinopathy (DR) is the frequent microvascular complication of diabetes mellitus, affecting 7.7 million people globally and is the common cause of blindness among people of working age in the developed world. Chances of DR in diabetic adult’s ≥40 years old are 28.5% and risk of vision loss is 4.4% in United States. Studies originating from Pakistan have reported variable prevalence of retinopathy ranging from 15.7 to 55%. Gaddap study reported 27.43% patients with DR and 7.51% with sight threatening diabetic retinopathy (STDR) requiring urgent intervention for vision threatening complications. Laser photocoagulation became the standard treatment.
for DR including DME after publication of results
from the Early Treatment Diabetic Retinopathy
Study in 1990.10-13

“The Royal College of Ophthalmologists’ Clinical
Guidelines for Diabetic Retinopathy” recommends
laser alone if patients’ compliance is doubtful.14
Introduction of vascular endothelial growth factor
inhibitors (anti-VEGF) have changed the scenario
of the treatment especially of DME,15 there is marked
shift towards use of anti-VEGF.16 Availability,
cost, safety, need for repeated injection and strict
monitoring and follow-up compliance of 21.2%17
does not make drug therapy a favorable choice
for treatment of DME. Purpose of this study was
to evaluate the effect of IVB and standard macular
photocoagulation (MPC) in management of DME.

METHODS

This quasi-experimental study was conducted at
Al Ibrahim Eye Hospital (AIEH) from April 2015
to December 2015. Approval of this study was
obtained by ethical/research committee of Isra
Postgraduate Institute of Ophthalmology. Patients
with Type-2 Diabetes mellitus of either gender, ≥
35 years age group, having macular edema (DME)
> than 250µ confirmed by retinal Optical Coherent
Topography (OCT) was recruited for the study.
Fundus Florence Angiography was done to
identify margins of foveal avascular zone, to rule
out macular ischemia and determine the boundaries
for macular grid laser application. Patients were
randomly selected for both the treatment however;
choice was given to the patient for opting any
of the two treatments. Those who were having
cardiac or cerebro-vascular problem were placed in
Group-B. Sampling method carried out was “Non-
probability, purposive” type.

Informed consent was taken after explaining
the pros and cons of laser application and intra-
vitreal injection. Seventy-two eyes of 59 patients
were included in the study.13 subjects were treated
bilaterally and 46 received unilateral treatment
MPC was used in 31 eyes and intra-vitreal injection
in 41 eyes.

After taking history, “Best corrected visual acuity”
(BCVA) was taken at the time of recruitment.
Detailed ocular examination was performed, a
retina-trained ophthalmologist with slit lamp and
dilated fundus was examined with 90D (Volk) lens
FFA and retinal OCT was done using 3D OCT – 2000
FA plus by a trained technician. Central Macular
Thickness (CMT) measured as mean thickness on
the 1-mm circle centered on the fovea. BCVA was
taken on each follow up visit and entered into
database, at one month, second month, third month
and sixth month follow up visits.

Group-A received a total of three-intravitreal
injections of bevacizumab (Genentech), 1.25 mg
/ 0.05 ml at one monthly interval. After ensuring
proper sterilization; injection given through the
inferior-temporal pars plana, 4 mm from the limbus
in phakic and 3.5mm in pseudo-phakic eyes. All
the injections were given by the principle investigator.
After the injection patients were prescribed topical
moxifloxacin 0.5% eye drops four times a day for
one week.

Group-B received laser treatment on Pascal
double frequency YAG laser. Modified grid laser
photocoagulation was performed delivering 2 to 3
rows of 100-micron spots, 100 micron apart in the
para-foveal region. Then, 150 to 200 micron spots
were applied 200 micron apart to the remaining
areas of retinal thickening and capillary non-
perfusion. Focal leaks outside or within the zones
of diffuse leakage were treated with 100 to 150
micron spots to achieve a mild whitening of the
micro-aneurysms. No patient received Pan retinal
photocoagulation.

• Follow up pattern for both the Groups A&B
was 1 month, 2, 3 and 6 months.

• BCVA was recorded on each visit.

Main Outcome Measures: The change in best-
corrected visual acuity (BCVA) at the end of 6 months
considered as “primary outcome” (functional)
Statistical Analysis: The data was analyzed
through the software SPSS version 20.0. The
entire continuous variable w presented in Mean ±
Standard Deviation. The entire categorical variable
was shown in frequency and Percentages. To see the
significance between the groups at different visits
of baseline to 1st, 2nd, 3rd & 6th monthly intervals for
BCVA. Paired sample t-test was applied. P-value
≤0.05 considered statistically significant.

RESULTS

This study consisted of 59 diabetes Type-2
patients (72 eyes) Mean age of the patients was 53.76
± 8.82 with range of 36-71 years. Out of 59 patients,
40 (67.8%) were male and 19 (32.2%) were female.
Respondents were divided in two groups. Group-A
included 41 eyes who received Intravitreal Injection
and Group-B had 31 eyes who received laser
application.

This study of eyes with DME showed that therapy
with IVB at 3 months appeared to be superior to
MPC in improving visual acuity. The improvement
in BCVA in both groups was statistically equal and significant at 6 months (Table-I). There was a significant difference found in mean BCVA in both groups while comparing their follow-up with significant P-values 0.001, 0.000, 0.000, 0.000 (Fig.1). Visual acuity which was recorded in terms of improved, stable and worse is shown in Fig.2.

**DISCUSSION**

Present study showed functional improvement in injection group and laser group at the end of 6 months. There were 24 eyes which were improved in injection group and 20 eyes in laser group, 12 eyes were stable and 9 eyes in laser group were stable while BCVA in 5 eyes in injection group were worsened and BCVA in 2 eyes in laser group were deteriorate (Fig.2).

| Factor (Laser = 31 & Injection = 41) | Mean | Std. Deviation | P-value |
|-------------------------------------|------|----------------|---------|
| BCVA Re Distance Pre Treatment      |      |                |         |
| Laser Group                         | 0.7542 | 0.30041        | 0.391   |
| Injection Group                     | 0.8137 | 0.28062        |         |
| BCVA.R.D. 1st Month Laser           |      |                |         |
| Laser Group                         | 0.7458 | 0.31049        | 0.618   |
| Injection Group                     | 0.7815 | 0.29029        |         |
| BCVA.R.D. 2nd Month Laser           |      |                |         |
| Laser Group                         | 0.7029 | 0.32842        | 0.634   |
| Injection Group                     | 0.7395 | 0.31662        |         |
| BCVA.R.D. 3rd Month Laser           |      |                |         |
| Laser Group                         | 0.6500 | 0.33926        | 0.626   |
| Injection Group                     | 0.6883 | 0.31962        |         |
| BCVA.R.D. 6th Month Laser           |      |                |         |
| Laser Group                         | 0.5987 | 0.36368        | 0.259   |
| Injection Group                     | 0.6890 | 0.30877        |         |

In the present study there was a significant difference found in both groups while comparing their follow-up. Subjects were with 24 eyes showed improved vision in injection group and 20 eyes in laser group, 12 eyes were stable in injection group and 9 eyes in laser group, while 5 eyes in injection group were deteriorate and 2 eyes in laser group were deteriorate (Fig.2) From 1st, 2nd, 3rd & 6th month BCVA improved at follow up with significant P-values 0.001, 0.000, 0.000, 0.000 (Fig.1).

BOLT study found that intravitreal bevacizumab has a greater effect than macular laser treatment in patients with center-involving persistent CSME. At 12 months, there was a significant difference in the mean BCVA ($P = 0.0006$). At 2 years, the mean BCVA was also increased in the bevacizumab group compared to the macular laser therapy group ($P = 0.005$).

**Table-I: Mean BCVA comparison between the groups.**
Improvement in vision was seen early with IVB at 1st and 2nd month while other group started to show improvement at 3rd month. Both groups have almost statistically equal improvement of BCVA at 6 months.

Masoud Soheilian et al. reported that Intravitreal bevacizumab injection in patients with DME yielded a better visual outcome at 24 weeks compared with macular photocoagulation.\textsuperscript{26} Danial kook MD et al. reported that in cases with chronic diffuse ischemic diabetic macular edema (a long-term decrease of central retinal thickness) can be observed following repeated intravitreal injections of bevacizumab, he also added that “treatment with bevacizumab at an earlier stage of diabetic macular edema without ischemia may be associated with an even better functional outcome”.\textsuperscript{27}

In this study, we also found that both IVB and MPC treatments improve VA of DME eyes, at 1st post op. month VA with IVB being significantly superior to MPC. This superiority of VA with IVB appears to wane over longer follow-up periods. At other follow-up points the significant difference was not observed in VA may be limited by effective time of bevacizumab, because its half-life in the eyes is only 9.8 days. The effectiveness of IVB on VA was greater in patients with macular edema in an early follow-up period as indicated in study by Yilmaz et al.\textsuperscript{28} Pharmacokinetic data suggesting a single intravitreal injection of 1.25mg bevacizumab is effective for 6-7 weeks.\textsuperscript{29} Limitations of IVB include regression of visual acuity within a few weeks after treatment, indicating the need for more frequent injections. Studies have reported that MPC had the ability to stabilize VA in long term and it had a significant improving effect on VA.\textsuperscript{30} Considering medical expenses, MPC appear to be more acceptable for the majority of DME patients, especially those in under privileged countries.

Masoud Soheilian et al. reported that Primary outcome measure was change in best-corrected VA (log MAR) at week 24. Secondary outcomes were VA changes at 6, 12, and 36 weeks, as well as CMT changes by optical coherence tomography and potential injection-related complications.\textsuperscript{26} In this study no significant difference was found in both the groups (Table-I).

CONCLUSION

This study of eyes with DME showed that therapy with IVB at 1 and 3 months appeared to show better improvement in best corrected vision than the laser however both modes of treatment are found to improve BCVA equally at the end of six months. Further studies over a period of 2-3 years are needed to see if the initial benefit is sustained over the time. This was a six month follow up study in order to determine stability in both vision BCVA, a long term follow up study is recommended. Sample size of this study is rather small to see the significance in difference of effect of the treatment.

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Authors’ Contribution:

ASJ and AHM: Conceived, designed, writing of manuscript and takes all the responsibility.

SM and AR: Did final review for publication.