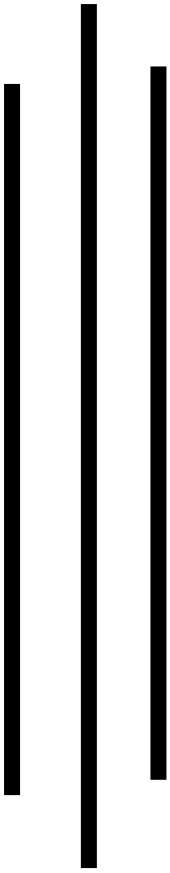
National Guidelines for Management of Diabetic Retinopathy

2017



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1. Foreword (Nepali)

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2. Foreword (Nepali)

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3. Acknowledgement (Nepali)

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Acronym

CSME	Clinically significant macular edema
DCEC	District Community Eye Center
DM	Diabetes mellitus
DR	Diabetic retinopathy
DME	Diabetic macular edema
DD	Disc diameter
EOM	Extra ocular movement
ETDRS	Early Treatment Diabetic Retinopathy Study
FCHV	Female community health volunteers
IOP	Intra ocular pressure
ME	Macular edema
MOH	Ministry of Health
NPDR	Non proliferative diabetic retinopathy
NVD	Neovascularization at disc
NVE	Neovascularization elsewhere
OCT	Optical coherence tomography
PDR	Proliferative diabetic retinopathy
PRP	Pan retinal photocoagulation
SDG	Sustainable Development Goal
TRD	Tractional retinal detachment
VA	Visual acuity
VEGF	Vascular Endothelial Growth Factor
WHO	World Health Organization

Contents

1. Introduction

Diabetes mellitus (DM) is a global epidemic with significant morbidity.[1] Diabetic retinopathy (DR) is the specific microvascular complication of DM and affects 1 in 3 persons with DM. DR remains a leading cause of vision loss in working adult populations. Patients with severe levels of DR are reported to have poorer quality of life and reduced levels of physical, emotional, and social well-being, and they utilize more health care resources.

Epidemiological studies and clinical trials have shown that optimal control of blood glucose, blood pressure, and blood lipids can reduce the risk of developing retinopathy and slow its progression. Timely treatment with laser photocoagulation, and increasingly, the appropriate use of intraocular administration of vascular endothelial growth factor (VEGF) inhibitors can prevent visual loss in vision-threatening retinopathy, particularly diabetic macular edema (DME). [2] Since visual loss may not be present in the earlier stages of retinopathy, regular screening of persons with diabetes is essential to enable early intervention.

Diabetes mellitus is a growing public health problem and the most important non communicable disease in the high and low income countries. Diabetes increases the risk of eye diseases, but the main cause of blindness associated with diabetes is diabetic retinopathy and constitutes 4.8% of the global blindness.[3,4] There are 386 million (8.3% of world adult population) people living with diabetes globally. [5] Diabetes is one of the leading causes of visual impairment and blindness in developed countries.[3,6] 80% of people with diabetes live in low-middle income countries and it has the capacity to become a leading cause of blindness in next 20 years.[1] Due to the prolific increase in diabetes, minimum of 3 million eyes will need to be evaluated each day by 2030 (35 exams per second). Despite 54% increase in the diabetes population there will be less than a 2% growth in the number of ophthalmologists by 2030.[3]

1.1. Diabetic Retinopathy in Nepal

In Nepal, diabetes mellitus has emerged as an epidemic health problem especially in the urban areas. As mentioned earlier, low level of awareness on diabetic ocular consequences including inadequate regular DR screening and treatment facilities has compounded the situation of blindness. Awareness on DR and regular DR screening is the only way of reducing its resulting blindness.[7,8]

Diabetes is increasing as an epidemic especially in the urban areas. The study from urban area reported diabetes of 19% at the age 40 years and above and 2.5% in rural areas.[9] A population based study from semi urban areas reported 4-7% prevalence of diabetes at the age 40 years and above.[10,11] The prevalence of diabetes was 25% at the age 60 years and above in another study conducted in urban areas of Nepal.[12] Population based studies have reported prevalence of diabetic retinopathy of 10 to 21% among the person with diabetes at the age 40 years and above.[10,11] The prevalence of diabetic retinopathy has been found higher in the hospital based study ranged from 18-43%. [8, 13, 14] Almost half to one third of the person with diabetes were not aware of the diabetic retinopathy.[7,8,14] Duartion of diabetes, poor glycaemic control and hypertension are the most important risk factors for the diabetic retinopathy in our diabetic population as in reported from other countries. [8,10, 13,14]

The low level of awareness among the people with diabetes, in the community, health professionals regarding the blinding sequelae of diabetes, and limited human resources have resulted in late presentation and increased blindness from diabetic retinopathy despite being a preventable cause of blindness. [7,8,14, 15]

There was no clear guideline for management of diabetic retinopathy in Nepal.[16] This national guideline for DR management has highlighted the four broad aspect of DR management; detailed DR screening and referral guideline, detailed ophthalmic assessment of DR, treatment modality of DR and diabetic macular edema, and DR management is special circumstances. The wide dissemination of this guideline in health care system will help in comprehensive management of DR to reduce from its avoidable blindness in Nepal.

1.2 Classification of Diabetic Retinopathy

The classic retinal micro vascular signs of DR include micro aneurysms, haemorrhages, hard exudates (lipid deposits), cotton-wool spots (ischemic retina related to accumulations of axoplasmic debris within adjacent bundles of ganglion cell axons), venous dilation and beading and intra retinal micro vascular abnormalities (i.e., dilated pre-existing capillaries) (**Annex Figures**). These signs can be classified into two phases of DR.

1.2.1 Non-proliferative Diabetic Retinopathy

Non proliferative DR is the early stage of DR. Recognition of non-proliferative retinopathy allows a prediction of risk of progression, visual loss and determination of a review interval. **Annex Table 1** shows the signs of non- proliferative DR.

1.2.2 Proliferative Diabetic Retinopathy

Proliferative diabetic retinopathy (PDR) is a severe stage of DR and represents an angiogenic response of the retina to extensive ischemia and capillary closure. Neovascularization has been divided into 2 groups: new vessels on the disc (NVD) and new vessels elsewhere (NVE). Typically NVE grow at the interface of perfused and non-perfused retina. **Annex Table 2** shows the signs of PDR. The stages of DR, from non-proliferative to proliferative DR. DR can be classified using the simple international classification of DR scale shown in Table 1. DME is an important complication that is assessed separately from the stages of retinopathy, as it can be associated with any of the DR stages and can run an independent course.

1.2.3 Diabetic Macular Oedema

It is important to assess the presence and severity of diabetic macular edema (DME) separately from stages of DR. The stages of DR can be classified using the International Classification of DR Scale shown in **Table 1**.

TABLE 1. INTERNATIONAL CLASSIFICATION OF DIABETIC RETINOPATHY AND DIABETIC MACULAR EDEMA

Diabetic Retinopathy	Findings Observable on Dilated Ophthalmoscopy abnormalities
No apparent DR No	No abnormalities

Mild Non proliferative DR	Microaneurysms only
Moderate nonprolifirative DR	Microaneurysms and other signs (e.g., dot and blot hemorrhages, hard exudates, cotton wool spots), but less than severe nonproliferative DR
Severe nonproliferative DR	Moderate nonproliferative DR with any of the following: • Intraretinal hemorrhages (=20 in each quadrant); • Definite venous beading (in 2 quadrants); • Intraretinal microvascular abnormalities (in 1 quadrant); • and no signs of proliferative retinopathy
Proliferative DR	Severe nonproliferative DR and 1 or more of the following: • Neovascularization • Vitreous/preretinal hemorrhage

Diabetic Macular Edema	Findings Observable on Dilated
No DME	No DME No retinal thickening or hard exudates in the macula
Non central-involved DME	Retinal thickening in the macula that does not involve the central subfield zone that is 1mm in diameter
Central-involved DME	Retinal thickening in the macula that does involve the central subfield zone that is 1mm in diameter

2. Screening guidelines, with referral pathway

2.1 Screening Guidelines

Screening for DR is an important aspect of DM management worldwide. A screening exam could include a complete ophthalmic examination with refracted visual acuity fundus photography. However, in a low-resource setting, the minimum examination components to assure appropriate referral should include a screening visual acuity exam and retinal examination adequate for DR classification. Vision should be tested prior to pupil dilation. Annex Figure 1 shows an example of the screening process for DR.

In existing health system of Nepal, various cadres should be utilized for DM and diabetic retinopathy (DR) screening at various levels.

Female Community Health Volunteers (FCHV's) can be utilized for referring any suspected cases of diabetes based on risk factors to the physician, and also to encourage for regular blood sugar test after 30 years of age, and known DM to district community eye centres (DCEC).

From Health Post, it is advisable to refer DM suspect to physician and known DM to DCEC. Primary health centres/ District hospital is to confirm the diagnosis of DM, treatment of DM, visual acuity testing

with pin hole, DR Screening/ refer to DCEC for DR screening as feasible, counsel for sugar control and regular follow up.

At the level of Zonal/ Regional hospital/ Central level hospital's Diabetic Clinic: they can confirm the diagnosis of DM, treatment of DM, VA testing, refer if subnormal, diagnosis of DR using trained allied medical personnel under the physician and Refer to tertiary eye hospital for DR management, counsel for sugar and other underlying risk factors control and regular follow up.

Eye care centers such as Primary and secondary eye care centers are able to confirm the DM diagnosis with the help of physician. If known DM, comprehensive eye examination with dilatation by trained allied ophthalmic personnel and ophthalmologist and cross referral of vision threatening retinopathy to tertiary eye hospital.

Physician, counsel for good glycaemic and other risk factor control and regular follow up under physician and eye centre.

Who should screen?

1. Ophthalmologist
2. Physician
3. Optometrist/ Ophthalmic assistant: Who have skill of screening of DR with training
4. Medical Officer after training on DR screening.
5. Allied medical personnel who have training on DR screening
6. Field level health worker or health volunteer who had training in grading images at any institution

Allied medical personnel or field workers should be trained with doctor engaged in active screening for at least 3 months.

How to screen?

1. Indirect Ophthalmoscopy
2. Slit-lamp bio microscopic examination
3. Dilated Direct Ophthalmoscopy
4. Non-Mydriatic photography
5. Mydriatic photography
6. Hand held fundus cameras

The screening vision exam should be completed by trained personnel in any of the following ways, depending on resources:

- Refracted visual acuity examination using a 3- or 4-meter visual acuity lane and a high contrast visual acuity chart, or 6 meters or 3 meters using mirror in Snellen visual acuity chart.
- Presenting visual acuity examination using a near or distance eye chart and a pin-hole option if visual acuity is reduced.
- Presenting visual acuity examination using a 6/12 (20/40) equivalent handheld chart consisting of at least 5 standard letters or symbols and a pin-hole option if visual acuity is reduced.

A retinal examination may be accomplished in the following ways:

Patients with less than adequate retinal assessment should be referred to an ophthalmologist unless it is obvious that there is no DR, or at the most, only mild non-proliferative DR (i.e., micro aneurysms only). In addition, persons with unexplained visual-acuity loss should be referred.

As part of a screening exam, persons with diabetes should be asked about their diabetes control, including blood glucose, blood pressure and serum lipids. In addition, women should be asked if they are or could be pregnant. Inadequate control and pregnancy may require further appropriate medical intervention. Doctor also should adopt holistic approach for the Diabetic patients and instruct nurses, dieticians, counselors and other cadres to take care of other diabetes related complications as well.

2.2 Referral Guidelines

Minimum referral guidelines are as follows: Visual acuity below 6/12 (20/40) or symptomatic vision complaints.

If DR can be classified according to the International Classification of DR or a Simplified scheme, they should be referred accordingly (Table 2)

TABLE 2. REFERRAL RECOMMENDATIONS BASED ON SIMPLIFIED CLASSIFICATION OF DIABETIC RETINOPATHY* AND DIABETIC MACULAR EDEMA FOR LOW-/INTERMEDIATE RESOURCE SETTINGS.

Classification	Referral to Ophthalmologist
No apparent DR, mild non proliferative DR and no DME	Referral not required
Mild non proliferative DR	Referral not required
Moderate nonproliferative DR	Referral required
Severe nonproliferative DR	Referral required
PDR	Referral required
Classification	Referral to Ophthalmologist
Noncentral-involved DME	Referral not required (referral recommended if laser resources available)
Central-involved DME	Referral required

* In cases where diabetes is controlled.

If visual acuity or retinal examination cannot be obtained at the screening examination: refer to ophthalmologist. Patients who have had laser treatment should also be referred for ophthalmic review.

3. Detailed ophthalmic assessment of Diabetic Retinopathy

3.1 Initial Patient Assessment

Detailed patient assessment should include a complete ophthalmic examination, including visual acuity and the identification and grading of severity of DR and presence of DME for each eye. The patient assessment should also include the taking of a patient history focused on diabetes and its modifiers.

3.1.1 Patient History (Key Elements)

- Duration of diabetes
- Past glycemic control (hemoglobin A1c)
- Medications (especially insulin, oral hypoglycemics, anti hypertensives, and lipid-lowering drugs), also to mention whether simply diet control or herbal.
- Systemic history (e.g., renal disease, systemic hypertension, serum lipid levels, pregnancy, Anemia, Cardiac condition)
- Ocular history
- Smoking history

3.1.2 Initial Physical Exam

- Visual acuity
- Extra ocular motility (EOM)
- Measurement of intraocular pressure (IOP)
- Gonioscopy when indicated (e.g., when neovascularization of the iris is seen or in eyes with increased IOP)
- Slit-lamp biomicroscopy for Anterior segment evaluation
- Fundus examination

3.1.3 Fundus Examination Assessment Methods:

Most sensitive methods for detecting DR are retinal photography and slit-lamp biomicroscopy through dilated pupils. Both depend on interpretation by trained eye health professionals.

Fundus photography has the advantage of creating a permanent record, and for that reason, it is the preferred method for retinopathy assessment. However, well-trained observers can identify DR without photography and documentation of an observation in form of diagram in absence of Fundus photograph can be done, however in the hands of non-ophthalmologists, photographs would be the examination of choice.

The use of all instruments requires training and competence but more skill is needed for indirect ophthalmoscopy and slit-lamp biomicroscopy than for fundus photography. Newer, semi-automatic nonmydriatic fundus cameras can be very easy to use. Media opacities will lead to image/view degradation and all photographs/images must be reviewed by trained personnel.

3.2 Follow-up Examination of Patients with Diabetic Retinopathy

In general, the follow-up history and examination should be is similar to the initial examination. The assessment of visual symptoms, visual acuity, measurement of IOP, and fundus examination are essential.

3.2.1 Follow-up History

- Visual symptoms
- Glycemic status (hemoglobin A1c)
- Systemic status (e.g., pregnancy, blood pressure, serum lipid levels, renal status)

3.2.2 Follow-up Physical Exam

- Visual acuity
- Measurement of IOP
- Gonioscopy when indicated
- Slit-lamp biomicroscopy
- Fundus examination

3.2.3 Ancillary Tests

Fluorescein angiography is not needed to diagnose DR, proliferative DR or DME, all of which are diagnosed by means of the clinical exam.

Fluorescein angiography can be used as a guide for treating DME and as a means of evaluating the cause(s) of unexplained decreased visual acuity. Fluorescein angiography can also identify macular capillary nonperfusion or sources of capillary leakage resulting in DME as possible explanations for visual loss.

OCT is the most sensitive method to identify sites and severity of DME, which are used only at the center with OCT facility

3.2.4 Patient Education

Discuss results or exam and implications.

Encourage patients with DM but without DR to have annual screening eye exams.

Inform patients that effective treatment for DR depends on timely intervention, despite good vision and no ocular symptoms.

Educate patients about the importance of maintaining near-normal glucose levels, near-normal blood pressure and to control serum lipid levels.

Communicate with the general physician (e.g., family physician, internist, or endocrinologist) regarding eye findings.

Provide patients whose conditions fail to respond to surgery and for whom treatment is unavailable with proper professional support (i.e., offer referrals for counseling, rehabilitative, or social services as appropriate).

Refer patients with reduced visual function for vision rehabilitation and social services.

TABLE 3. FOLLOW-UP SCHEDULE AND MANAGEMENT FOR DIABETIC RETINOPATHY SEVERITY IN OUR CONTEXT FOR ALL PATIENTS REGARDLESS OF DR SEVERITY, OPTIMIZE MEDICAL TREATMENT FOR GLYCEMIC CONTROL, HYPERTENSION, AND DYSLIPIDEMIA.

Follow up Schedule	**In our Settings**
No apparent DR	Repeat examination annually
Mild non proliferative DR	Repeat examination 6-9 months
Moderate non proliferative DR	Repeat examination within 4-6 months
Severe non proliferative DR or proliferative DR	Pan-retinal photocoagulation
DME	Laser / Intra-vitreal injections of anti-VEGF agents / Steroids

4. Treatment of Diabetic Retinopathy

Pan-retinal laser photocoagulation (PRP) should be performed in patients with proliferative DR. There are benefits of early panretinal photocoagulation at the severe non proliferative DR stage for patients with type 2 diabetes. Other factors, such as poor compliance with follow up, impending cataract extraction or pregnancy and status of fellow eye will help in determining the timing of the panretinal photocoagulation.

Informed consent with proper counseling required

- Very severe NPDR : PRP
- Unlikely to come for follow up (Econimical/Geographical): PRP
- Severe NPDR with Poor health : PRP
- If Blood Pressure is high, PRP to be reserved later as risk of haemorrhage

4.1 Panretinal Photocoagulation (PRP)

4.1.1 Pretreatment Discussion with Patients

Patients usually need numerous follow-up visits and may require supplementary laser treatment.

PRP reduces the risk of visual loss and blindness.

Although laser treatment is effective, some patients may still develop vitreous haemorrhage. The haemorrhage is caused by the diabetes and not by the laser; it may mean the patient needs more laser treatment.

Laser treatment often reduces peripheral and night vision; treatment may moderately reduce central vision. This short-term side effect is compensated by the significant long-term reduction in severe vision loss and blindness in laser-treated patients.

4.1.2 Lenses for PRP

The three-mirror Goldman contact lens has a central opening for treating the posterior pole, and side mirrors for treating the mid peripheral and peripheral retina. Disadvantages: small field of view, which requires continual manipulation of the lens to complete treatment. Spot size is set at 500μm.

Newer wide-angle contact lenses are often used. Although the image is inverted, there is a large field of view allowing for many burns with the field while easily maintaining orientation to the disc and macula. The optics of these wide-angle lenses will affect the laser spot size on the retina **(Table 4**). Wide-angle indirect ophthalmoscopy lenses provide an inverted image, but show a large field of view and a magnification of the spot in the retina **(Table 4)**. Scatter treatment can be applied to a large area of retina in a single image, and it is easy to visualize the disk and the macula.

TABLE 4. LASER SPOT SIZE ADJUSTMENT REQUIRED FOR DIFFERENT LENSES CONTACT

Lens	Field of Vision	Axial magnification	Spot magnification	Spot Size Setting for ~500 um
Mainster Wide-Field	125°	0.46	1.50x	300μm
Volk TransEquator	120-125°	0.49	1.43x	300μm
Volk Quad/Aspheric	130-135°	0.27	1.92x	200 to 300μm
Mainster PRP 165	160°	0.27	1.96x	200 to 300 μm

4.1.3 Technique for PRP

i. The pupil should be fully dilated and topical anesthesia is used. Retrobulbar or subtenons anesthesia to reduce pain and decrease eye motion can be employed as necessary.

ii. Typical initial settings on the Argon laser would be 500 μm spot size, a 0.1 second exposure and 250-270 mw power. The power is gradually increased until a whitish reaction is obtained on the retina. The lesions are placed 1 burn width apart. (Table 5)

iii. A total of 1600-3000 burns are placed in 1 or more sittings, carefully avoiding the macular area and any areas of tractional elevation of the retina. The burns are placed 2 to 3 disc diameters away from the center of the macula and 1 disc diameter away from the disc, usually outside the arcades and extended peripherally up to the equator and beyond.

iv. Laser treatment should not be applied over major retinal veins, preretinal hemorrhages, darkly pigmented chorioretinal scars, or within 1 DD (200-300 μm) of center of macula, so as to avoid

risk of hemorrhage or large scotomas.

v. Other considerations:

- Additional photocoagulation is needed if there is evidence of worsening of proliferative DR.
- Add laser burns in between scars of initial treatment further peripherally and also at the posterior pole, sparing the area within 500-1500 μm from the center of the macula.
- Favor quadrants with active new vessels or areas with intraretinal microvascular abnormalities where scars are more widely spaced and areas of severe ischemia not previously treated, such as the temporal part of the posterior pole.
- There is increasing use of multi-spot laser machine.

TABLE 5. THE BURN CHARACTERISTICS FOR PANRETINAL PHOTOCOAGULATION

Size (on retina):	**500 μm**
Exposure	0.05 to 0.1 seconds recommended. 0.02 or 0.03 seconds can be considered for use in High Resource Settings (in certain laser machines, where applicable).
Intensity	mild white (i.e. 2+ to 3+ burns)
Distribution	Mild and moderate PDR: Edges 1 burn width apart Severe PDR: Edges 0.5 to 0.75 burn width apart
Number of sessions/sittings	1 to 3
Nasal proximity to disk	No closer than 500 μm
Temporal proximity to center	No closer than 3000 μm
Superior/inferior limit	No further posterior than 1 burn within the temporal arcades
Extent	Arcades (~3000 μm from the macular center) to at least the equator

Total number of burns	1200 – 1600 There may be instances where 1200 burns are not possible such as the development of vitreous hemorrhage or inability to complete a sitting precluding completion of the PRP session. Similarly, there may be clinical situations in which more than 1600 burns are needed such as initial difficulty with laser uptake due to media opacity. Below is a guide for 20ms PRP and 100ms PRP: Mild PDR: 20ms PRP 2400-3500 burns Moderate PDR: 20ms PRP 4000-5000 burns Severe PDR: 20ms PRP 5500-6000 burns ETDRS laser 100ms 1200-1800 burns ETDRS laser 100ms 2000-2500 burns ETDRS laser 100ms 2000-2500
Wavelength	Green or yellow (red can be used if vitreous hemorrhage is present)

5. Treatment for Diabetic Macular Edema (DME)

5.1 Settings

- Optimize medical treatment: Improve glycemic control if HbA1c > 7.5% as well as associated systemic hypertension or dyslipidemia.

- Mild or moderate DME without centre involvement (e.g., circinate HE ring threatening the centre of the macula or when no vision loss has occurred in spite of centre involvement): Consider focal laser to leaking micro aneurysms. No treatment is applied to lesions closer than 300 μm from the centre of the macula.

- Severe DME with centre involvement and associated vision loss*: intra-vitreal anti- VEGF treatment (e.g., with ranibizumab [Lucentis] 0.3 or 0.5mg, bevacizumab [Avastin] 1.25mg, or Aflibercept [Eylea]) 2mg therapy). Consideration should be given to monthly injections followed by treatment interruption and re-initiation based on visual stability and OCT. Patients should be monitored almost monthly with OCT to consider the need for treatment. Persistent retinal thickening and leaking points: consider laser treatment after 24 weeks. Treatment with intra-vitreal triamcinolone may be considered, especially in pseudophakic eyes. (Annex Figures 3 and 4). Injections are to be given with all sterile precautions (Annexure).

  Intra-vitreal injection would depend on the availability at the corresponding centre of the treatment. Similarly, OCT to be performed depending upon the accessibility of the devices.

- DME associated with proliferative DR: combined intra-vitreal anti-VEGF therapy and PRP should be considered.

- Vitreomacular traction or epiretinal membrane on OCT: pars plana vitrectomy may be indicated.

5.2 Laser Technique for Macular edema

- Focal macular treatment includes focal laser treatment of micro aneurysms and grid treatment of areas of diffuse leakage and focal non-perfusion within 2DD of centre of the macula. (Table 6)

- Laser parameters used are 50-100 μm spot size, 120-150 mW energy and very light gray intensity of the burn. Care is taken to demarcate and avoid the foveal avascular zone.

- If DME is associated with large areas of macular ischemia, only the areas of retinal thickening are treated.

TABLE 6. MODIFIED-ETDRS AND THE MILD MACULAR GRID LASER PHOTOCOAGULATION TECHNIQUES

Focal direct laser treatment	
Directly treat all leaking microaneurysms in areas of retinal thickening between 500 and 3000 μm from the center of the macula (but not within 500 μm of disc). Change in microaneurysms color with direct treatment is not required, but at least a mild gray-white burn should be evident beneath all microaneurysms.	
Burn size	50-100 μm
Burn duration	0.05 to 0.1 sec
Wavelength	Green to yellow wavelengths
Grid laser treatment	
Applied to all areas with diffuse leakage or non-perfusion area. Treat the area 500 to 3000 μm superiorly, nasally and inferiorly from the center of the macula, and 500 to 3500 μm temporally from macular center. No burns are placed within 500 μm of disc. Aim barely visible (light gray) laser burn and each burn should be at least two visible burn widths apart.	
Burn size	50-100 μm
Burn duration	0.05 to 0.1 sec
Wavelength	Green to yellow wavelengths

6. Indications for Vitrectomy

- Severe vitreous haemorrhage of 1–3 months duration and that does not clear spontaneously. Earlier intervention may be warranted in low-/intermediate resource settings as the underlying PDR disease

may have been previously untreated and highly advanced. In these settings it may be reasonable to perform vitrectomy in eyes with vitreous hemorrhage of 4 -6 weeks duration that has not cleared spontaneously.

- Advanced active proliferative DR that persists despite extensive PRP. Surgery is reasonable in eyes with recurrent episodes of vitreous haemorrhage from PDR due to persistent vessels despite PRP or mechanical traction on NV.

- Traction macular detachment of recent onset.

- Combined traction-rhegmatogenous retinal detachment.

- Tractional macular oedema or epiretinal membrane involving the macula. This includes vitreomacular traction.

7. Management of Diabetic Retinopathy in Special Circumstances

7.1 Pregnancy

Progression of DR is a significant risk in pregnancy. The following are recommendations:

i. Patients with pre-existing diabetes planning pregnancy should be informed on the need for assessment of DR before and during pregnancy. Pregnant women with pre-existing diabetes should be offered retinal assessment following their first antenatal clinic appointment and again at 28 weeks if the first assessment is normal. If any DR is present, additional retinal assessment should be performed at 16-20 weeks.

ii. Diabetic retinopathy should not be considered a contraindication to rapid optimisation of glycaemic control in women who present with a high HbA1c in early pregnancy but retinal assessment is essential.

iii. Diabetic retinopathy should not be considered a contraindication to vaginal birth.

7.2 Management of Cataract

- DR progresses faster after cataract surgery, so principles of management are as follows:

- Mild cataract - carefully assess DR status. Patients without vision loss with clear fundus view may not require cataract surgery.

- Moderate cataract - carefully assess DR status. Attempt to treat any severe NPDR with laser PRP, and/or DME with focal/grid laser or anti-VEGF therapy, before cataract surgery. Once DR/DME is stable, consider cataract surgery to improve vision.

- Severe to advanced cataract with poor fundus view - if DR status cannot be adequately assessed, consider early cataract surgery followed by assessment and treatment as necessary. If DME is present, consider anti-VEGF before surgery, at the time of surgery, or after surgery if DME is discovered when the media is cleared.

8. Technique for PRP

If there is a significant anxiety and pain with slit-lamp PRP, then patient can undergo indirect PRP in theatre using subtenon's block. The eye movements are restricted by retrobulbar/subtenons anesthesia. The peripheral retinal zones may not be visualized adequately and remain poorly treated by laser. This is often evident by the posterior pole "pepper-pot" configuration of PRP laser.

Laser PRP Settings

- Pulse Duration and Spot Size Use a 400μm retinal spot size. Smaller retinal spot size, e.g. 200μm and 300μm may lead to excessive higher fluence and risks of Bruch's rupture at 20ms exposure time. Furthermore, following laser burn healing, the final laser spot (burn) may be <100-150μm and patient will require more PRP treatment.

- Laser burn spacing Laser burns should be placed 1-burn widths apart for mild and moderate PDR. The space between the laser burns can be reduced for example, 0.5-burn widths apart for severe PDR, TRD and vitreous hemorrhage, with a higher density and number of laser spots.

- Laser burn intensity Laser surgeon should aim for a barely-visible, grey/white burn reaction on retina after laser application as the designated threshold. The laser surgeon should be aware that the laser burn intensity at 20ms will increase up to 1 minute after retinal application.

- Retinal surface coverage The PRP should be applied as far peripheral as possible using the laser contact lens, up to the ora serrata as the main areas of retinal ischemia in PDR exist in the far-peripheral retina while areas of ischemic penumbra is likely to be in pre-equatorial zones.

Laser Strategy for Primary PRP

- Early PDR Primary PRP should be completed by 2 weeks, fractionated if needed (1200- 1800 burns ETDRS strategy). If shorter duration of laser pulse (20ms) used, consider increasing number of laser burns appropriately, Based on laser burn ablation studies, approximately 2400-3500 burns using 20ms PRP are recommended for early PDR. Patient review: 4 months [in non-pregnant patient].

- Moderate PDR/High-risk PDR Primary PRP should be completed by 2 weeks, fractionated if needed (2000 -2500 burns ETDRS strategy). If shorter duration of laser pulse (20ms) used, consider increasing number of laser burns.Based on laser burn ablation studies, approximately 4000-5000 burns using 20ms PRP are recommended for early PDR. A complete PRP treatment should be completed over 4 weeks with aiming to deliver more laser spots in the initial sessions. Patient review: 3 months [in non-pregnant patient], however in poorly controlled diabetics,

review interval should be shortened.

- Severe PDR/High-risk PDR. These cases are high risk of continued traction and hemorrhagic complications following PRP. Laser surgeon should aim to deliver full PRP coverage of peripheral retina (3000 burns ETDRS) over 2-3 sessions in 3-4 weeks. If shorter duration of laser pulse (20ms) used, consider increasing number of laser burns appropriately. Based on laser burn ablation studies, approximately 5500-6000 burns using 20ms PRP are recommended for early PDR. The complete PRP treatment should be completed over 4 weeks with aiming to deliver more laser spots in initial sessions.

9. Recommended Practice for Intravitreal Injection

Intravitreal injections may be performed in an office setting, or an operating room.

Bilateral Injections: Bilateral Injections are discouraged in view of infection in our set up

Gloves Sterile gloves may be used.

Talking and Use of Masks Minimizing speaking and/or by the use of surgical masks during the injection preparation and procedure is recommended.

Application of Povidone–Iodine to the Ocular Surface and Eyelids Povidone–iodine (5–10%) should be the last agent applied to the intended injection site before injection. Povidone–iodine may also be applied to the eyelid margins and eyelashes. After the final application of povidone–iodine, the eyelashes and lid margins should not be allowed to come into contact with the injection site until the injection has been completed.

Topical Anesthetics Topical anesthetics should be applied to minimize patient discomfort.

Site of Injection Intravitreal injections should be given between the horizontal and vertical rectus muscles at the pars plana, 3.5 to 4.0 mm posterior to the limbus. Quadrant selection should be dictated by both patient-specific considerations and injecting physician preference. A simple perpendicular injection approach is both convenient and preferred in most settings.

Needle Gauge and Length A 30-gauge or smaller needle is generally preferred for anti-VEGF agents or nonviscous solutions. Larger bore needles can be considered for suspensions (e.g., steroids) and for solutions of higher viscosity. Needle length should be 5/8 inch (18 mm) or shorter but long enough to allow for complete penetration of the pars plana.

Protocol: Sequence of Events

i. Either surgical masks should be used or both the patient and providers should minimize speaking during the injection preparation and procedure;

ii. Take a procedural time-out to verify patient, agent, and laterality;

iii. Apply liquid anesthetic drops to the ocular surface;

iv. Apply povidone–iodine to the eyelashes and lid margins (optional, most use 10%);

v. Retract the eyelids away from the intended injection site;

vi. Apply povidone–iodine (most use 5%) to the conjunctival surface, including the intended injection site, at least 30 seconds before injection;

vii. If additional anesthetic is applied, reapply povidone–iodine to the intended injection site immediately before injection (most use 5%);

viii. Insert the needle perpendicular to the sclera, 3.5 to 4.0 mm posterior to the limbus between the vertical and horizontal rectus muscles. [17,18]

10.References

1. Wild S, Roglic G, Green A, Sicree R and KingH. Global Prevalence of Diabetes. Estimates for the year 2000 and projections for 2030.*DiabetesCare* 2004; 27: 1047-1052.

2. Report of a WHO Consultation in Geneva. Prevention of Blindness from Diabetes Mellitus. 2005, Switzerland.

3. IAPB, an overview of Diabetic Retinopathy, ***Information and resources provided courtesy of The Fred Hollows*** *Foundation (FHF), available at:* http://www.iapb.org/vision-2020/what-is-avoidable-blindness/diabetic-retinopathy

4. Report of a WHO Consultation in Geneva: Prevention of Blindness from Diabetes Mellitus. 2005, Switzerland.
5. International Diabetes Federation, *IDF World Atlas Sixth Edition*, 'The Global Burden', (2014), available at: http://www.idf.org/diabetesatlas/5e/the-global-burden

6. Global status report on NCDs, World Health Organization, 2010, Chapter 1, 16:23

7. Thapa R, Paudyal G, Maharjan N, Bernstein PS:Demographics and awareness of diabetic retinopathy among diabetic patients attending the vitreo-retinal service at a tertiary eye care center in Nepal**.***Nepal J Ophthalmol*2012, **4**(7):10-16.

8. Thapa R, Joshi DM, Rizyal A, Maharjan N, Joshi RD.Prevalence, risk factors and awareness of diabetic retinopathy among admitted diabetic patients at a tertiary level hospital in Kathmandu.*Nepal J Ophthalmol*2014, 6(11):24-30.

9. Singh DL & Bhattarai MD. High prevalence of diabetes and impaired fasting glycemia in urban Nepal. *Diabetic Medicine* 2003;20:170-171.

10. Paudyal G, Shrestha MK, Meyer JJ, Thapa R, Gurung R, Ruit S. Prevalence of diabetic retinopathy following a community screening for diabetes.*Nepal Med CollJ*2008, 10(3):160-163.

11. Thapa SS, Thapa R, Paudyal I, Khanal S, Aujla J, Paudyal G, Rens G. Prevalence and pattern of vitreo-retinal diseases in Nepal: The Bhaktapur glaucoma study. *BMC Ophthalmology* 2013, 13:9.

12. Chhetri MR, Chapman RS. Prevalence and determinants of diabetes among the elderly population in the Kathmandu Valley of Nepal. *Nepal Med Coll J* 2009, 11(1):34-38.

13. Shrestha MK, Paudyal G, Wagle RR, Gurung R, Ruit S, Onta SR. Prevalence of and factors associated with diabetic retinopathy among diabetics in Nepal: a hospital based study. *Nepal Med Coll J* 2007;9:225-229.

14. Shrestha S, Malla OK, Karki DB, Byanju RN. Retinopathy in a diabetic population. Kathmandu University Medical Journal 2007, Vol. 5, No. 2, Issue 18, 204-209.

15. Thapa R, Bajimaya S, Paudyal G, Khanal S, Tan S, Thapa SS, Rens G. Population awareness of diabetic eye disease and age related macular degeneration in Nepal: the Bhaktapur Retina Study. BMC Ophthalmology 2015, 15:188.

16. Mishra SK, Jha N, Shankar PR et al. An assessment of diabetic retinopathy and diabetes management system in Nepal. J Nepal Health Res Council 2016;14(33):104-10)

17. International Council of Ophthalmology (ICO). Updated ICO Guidelines for Diabetic Eye Care, 2017

18. Diabetic Eye Care in India, Jan 2015

11. Annexes

Annex I: Diabetic Retinopathy Screening

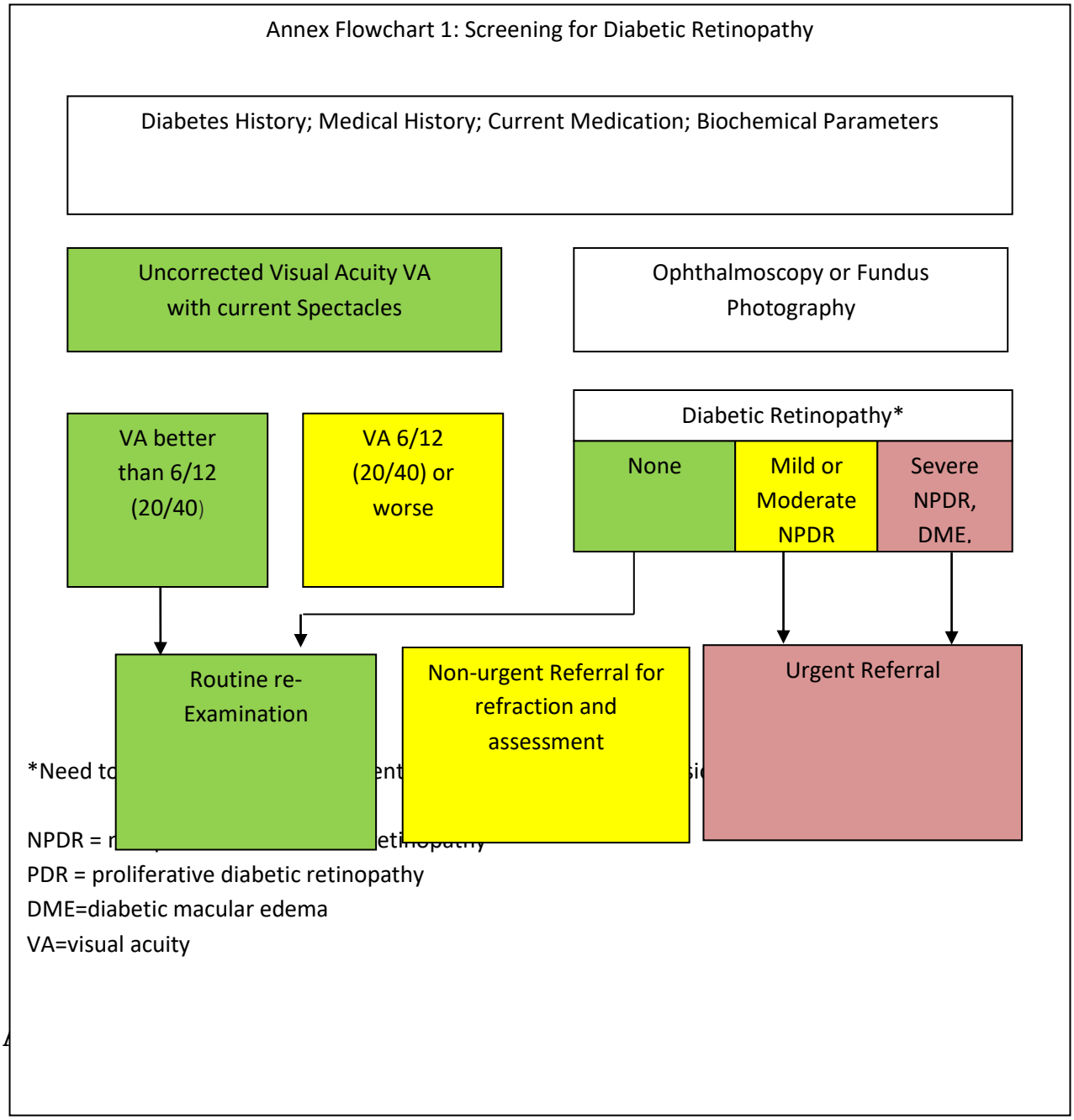

FIGURE 1: NORMAL RETINA

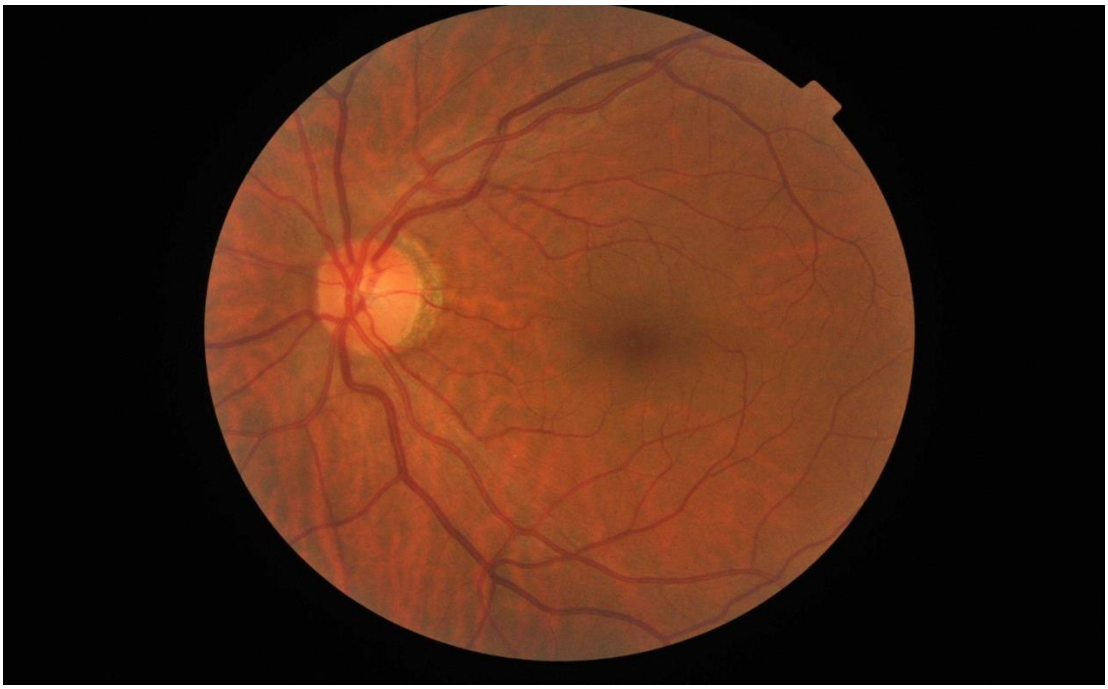

FIGURE 2: MILD NPDR

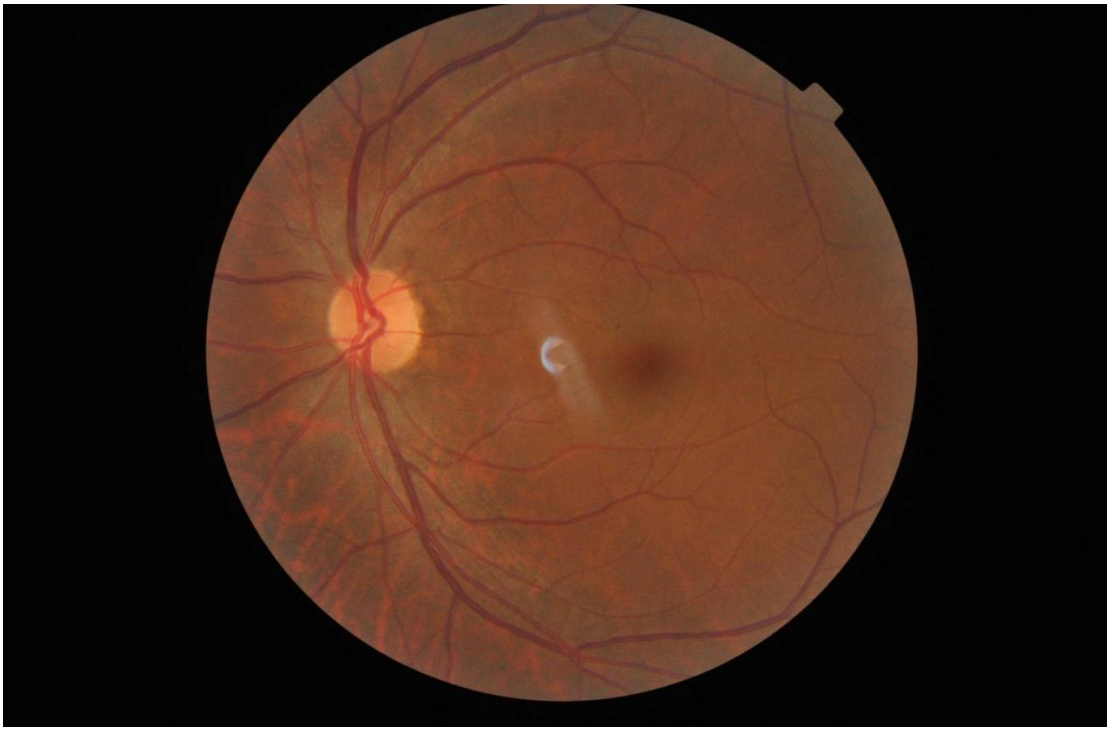

FIGURE 3: MILD NPDR WITH CSME

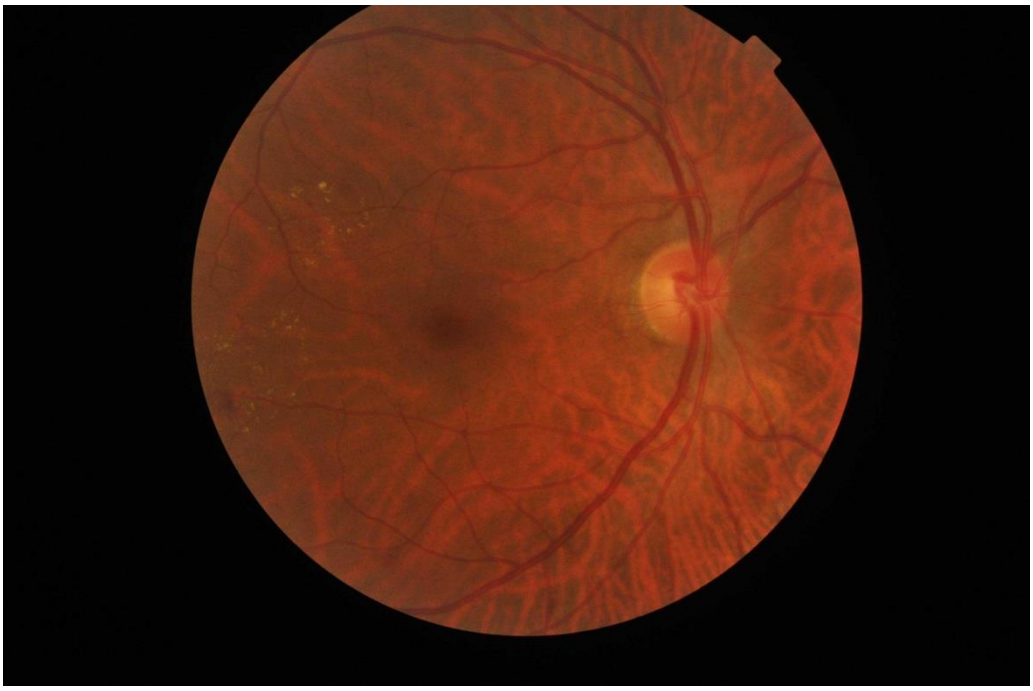

FIGURE 4: MODERATE NPDR WITH NO MACULAR EDEMA

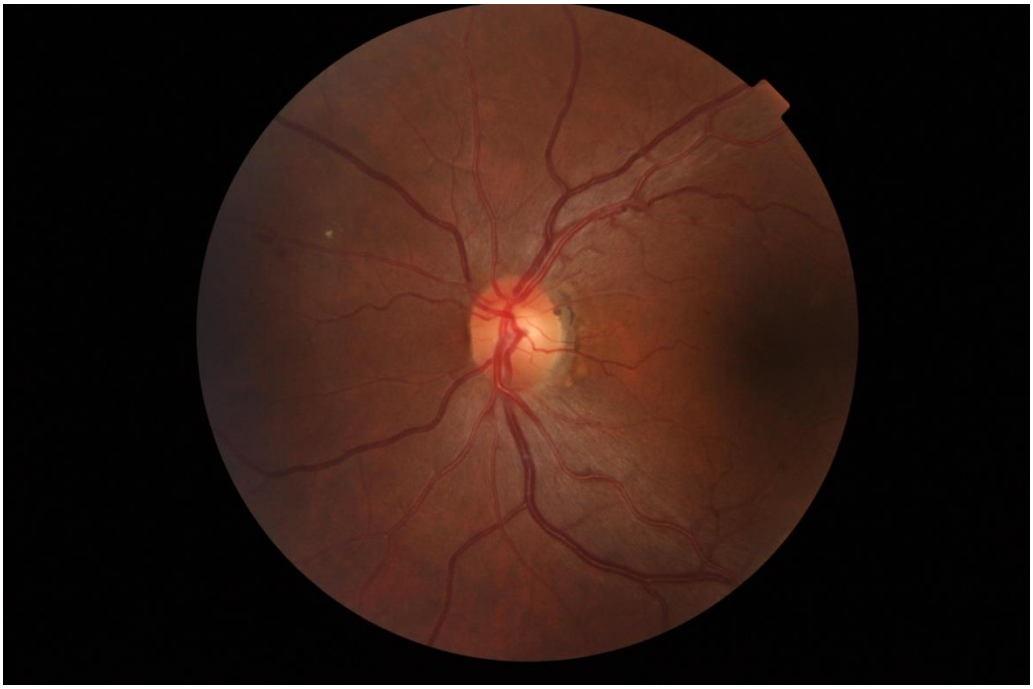

FIGURE 5: MODERATE NPDR WITH SEVERE MACULAR EDEMA

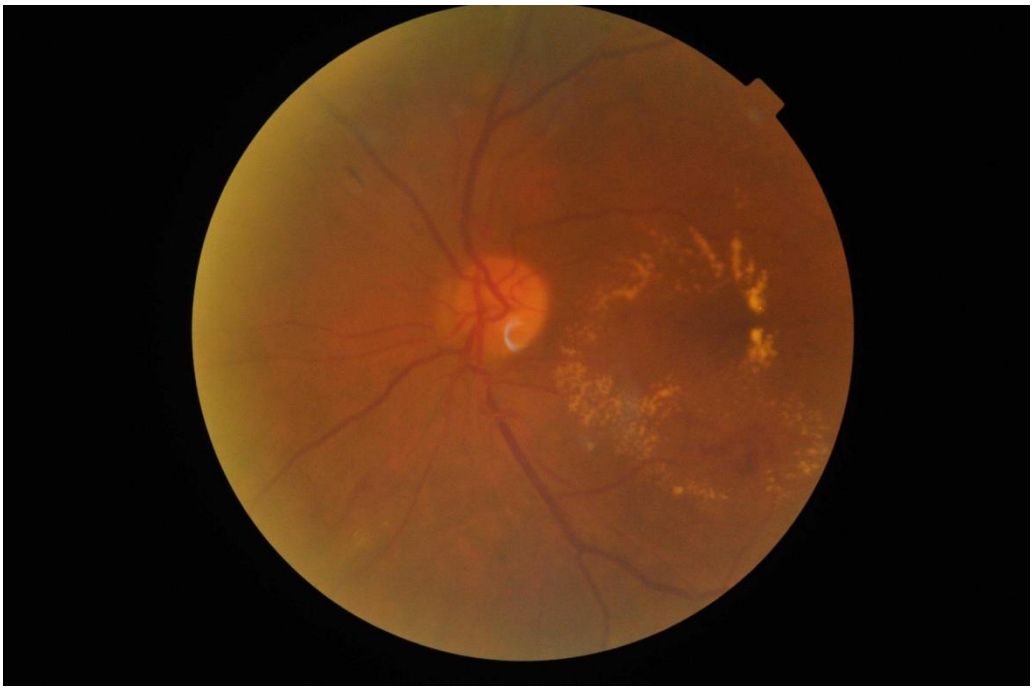

FIGURE 6: MODERATE NPDR WITH MODERATE MACULAR EDEMA

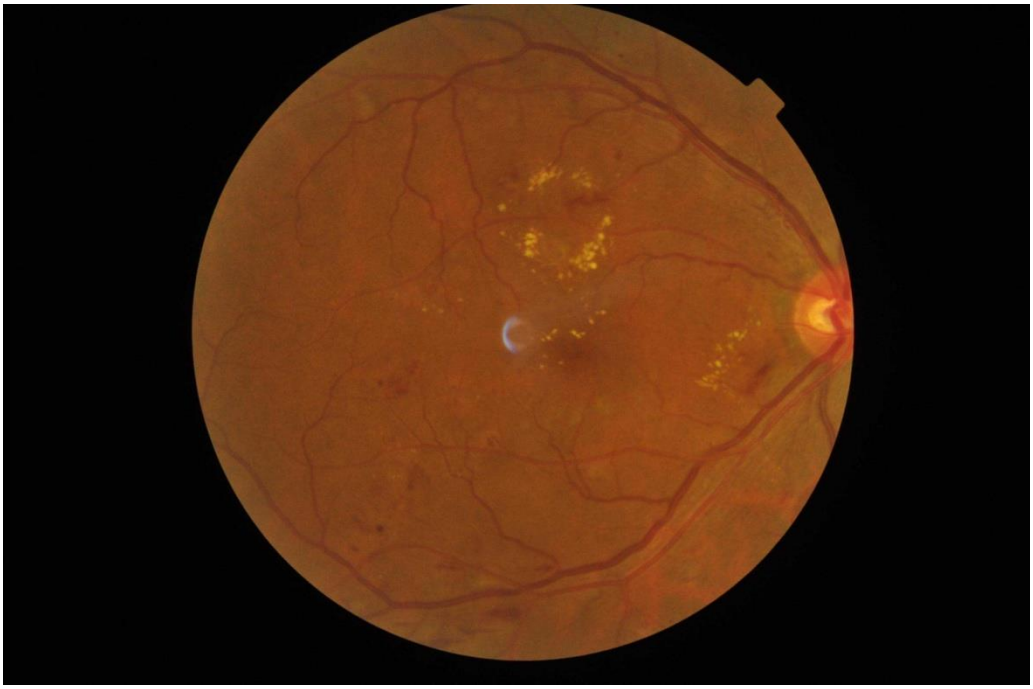

FIGURE 7: SEVERE NPDR WITH SEVERE DIABETIC MACULAR EDEMA

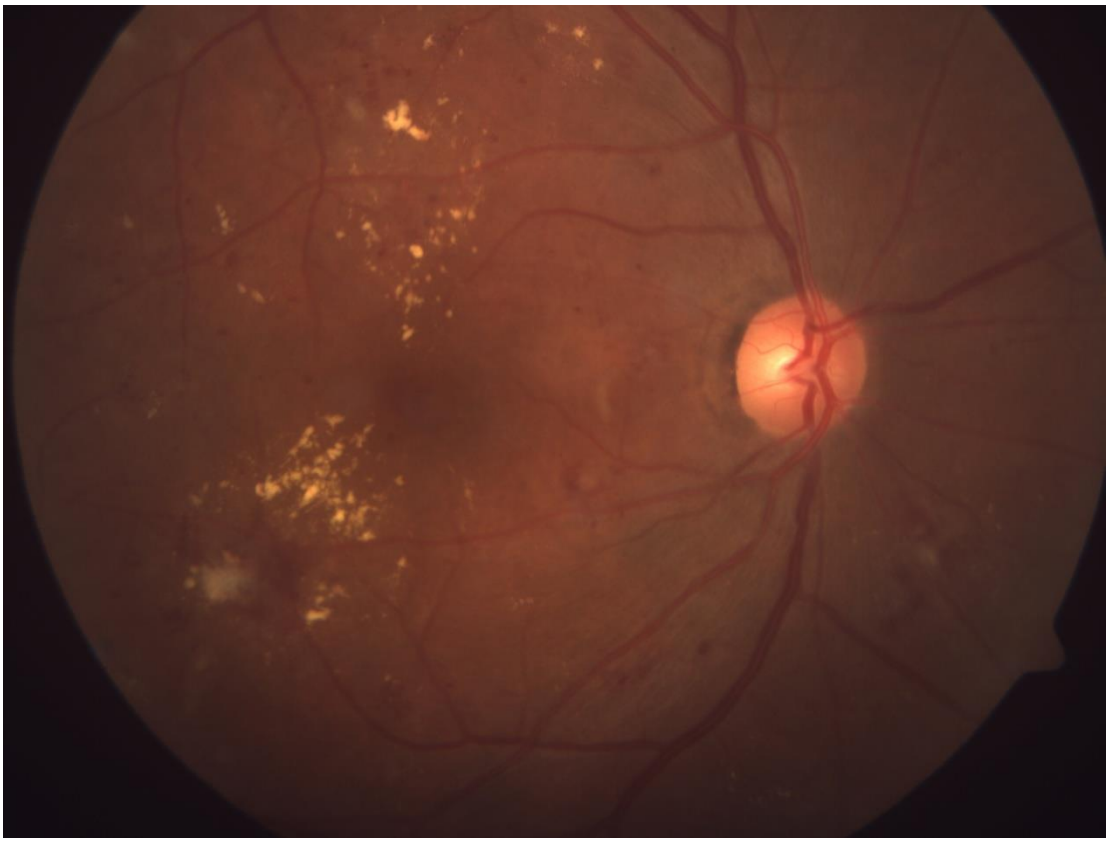

FIGURE 8: HIGH RISK PDR WITH NVD

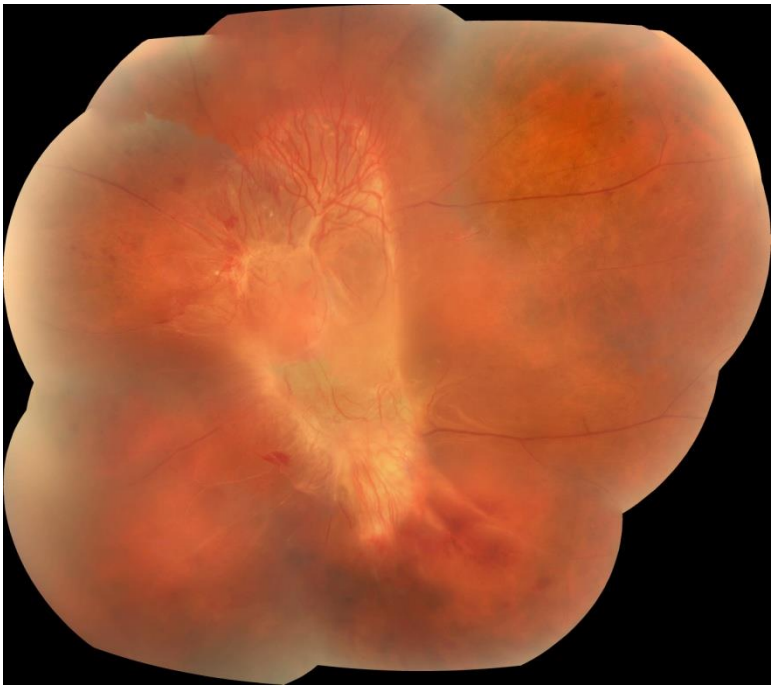

FIGURE 9: HIGH RISK PDR WITH PRERETINAL HEMORRHAGE BEFORE NEW VESSELS ON DISC

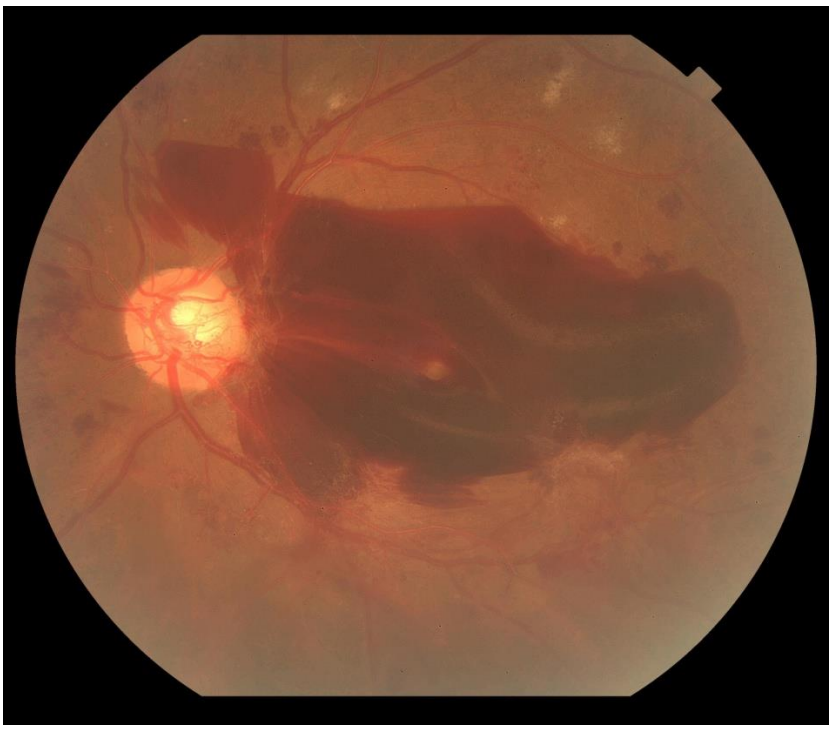

FIGURE 10: HIGH RISK PDR WITH NEW LASER SCARS

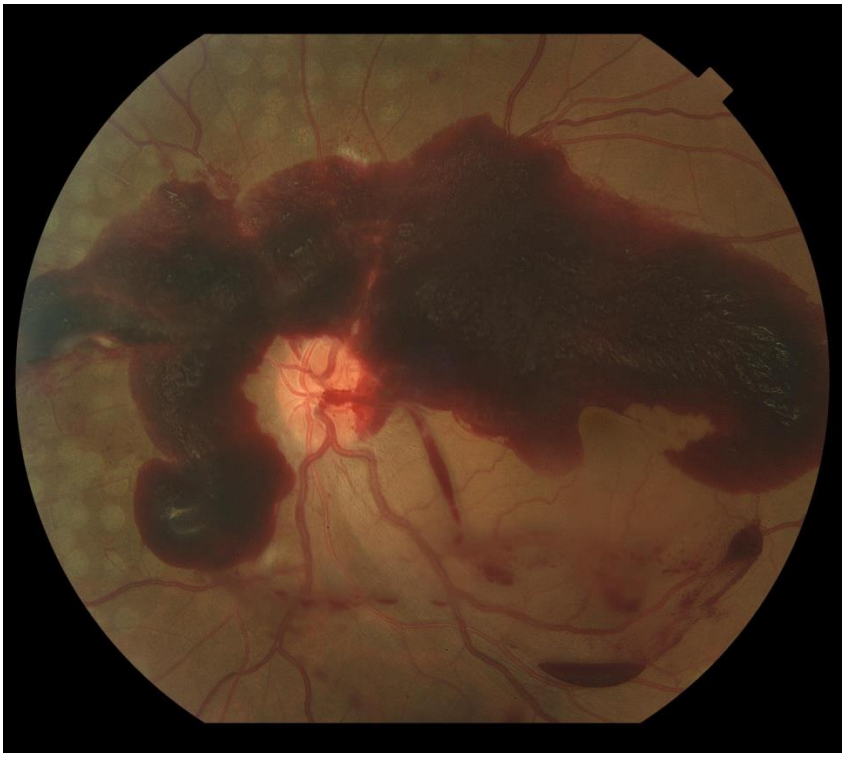

FIGURE 11: PDR WITH NEW VESSELS ON DISC AND ELSEWHERE

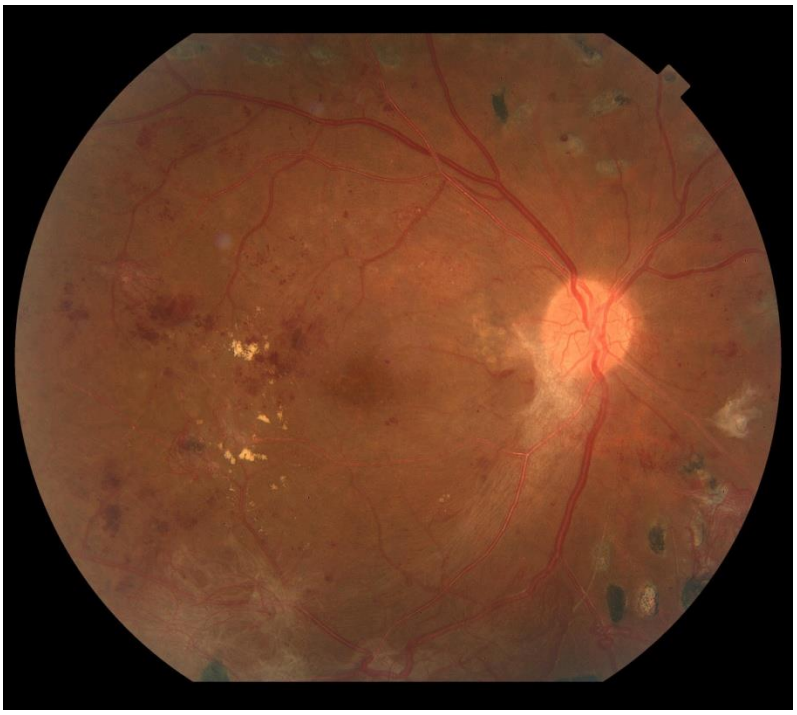

FIGURE 12: PERSISTENT DME AFTER PRP IN LEFT EYE

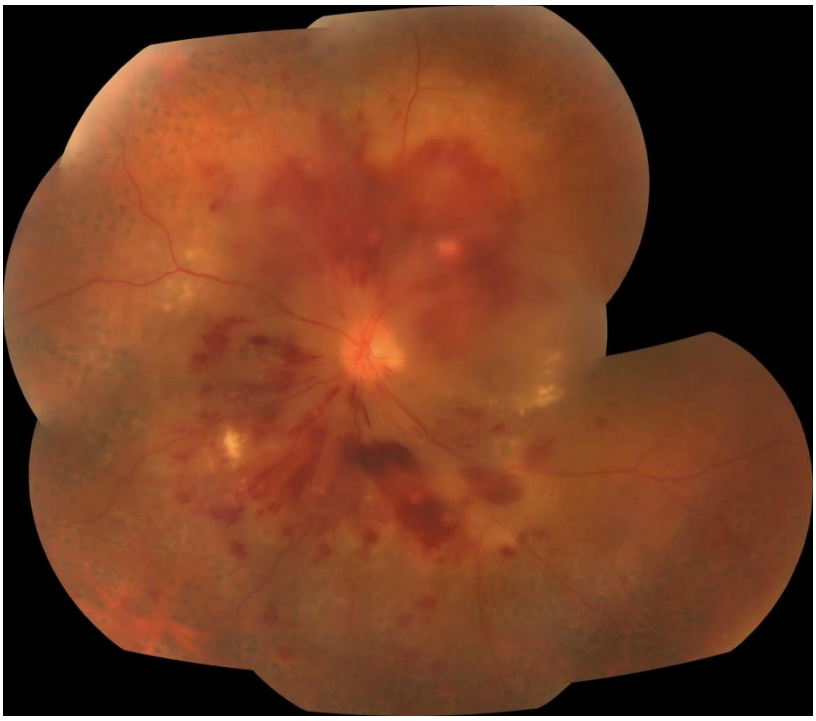

FIGURE 13: DME WITH PRP RIGHT

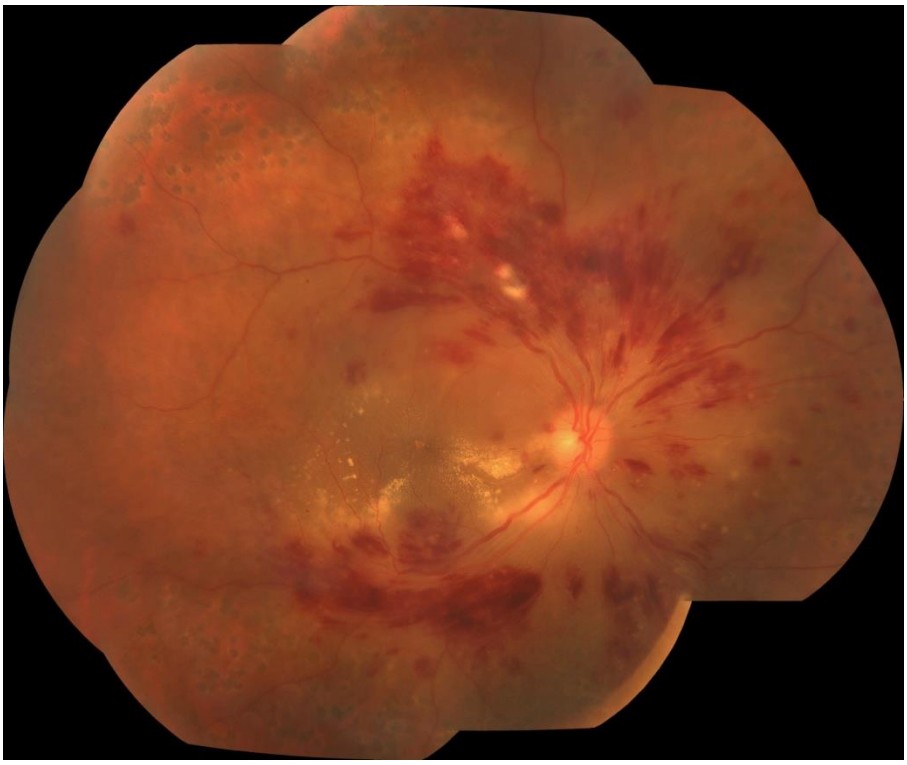

FIGURE 14: PERSISTENT DME AFTER FOCAL LASER TREATMENT

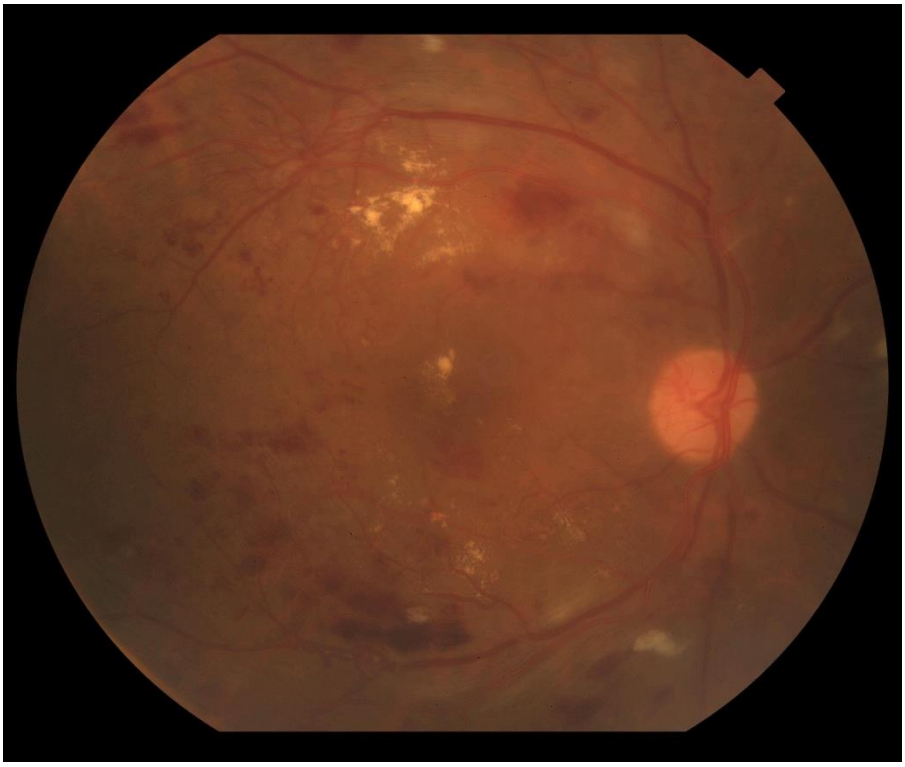

FIGURE 15: PERSISTENT DME AFTER FOCAL LASER TREATMENT

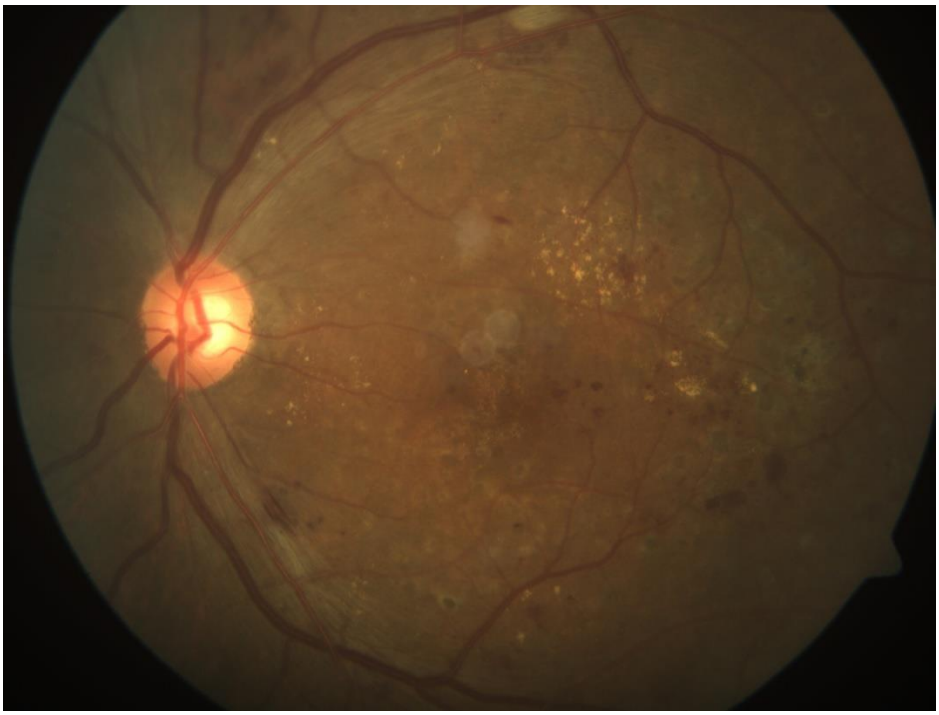

FIGURE 16: PDR WITH PRE RETINAL HEMORRHAGE

Annex: III Diabetic Retinopathy Subcommittee (Task Force)

Submitted by:

Diabetic Retinopathy Subcommittee (Task Force)

Apex Body of Eye Health

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Chief: Planning, Policy and International Co-Operation Division, Ministry of Health (MoH), Member Secretary, Apex Body of Eye Health

Members:

1. Dr. Bhola Ram Shrestha: Chief, Curative Service Division , MoH
2. Dr. Raba Thapa: Co-ordinator of diabetic retinopathy program, Consultant retina specialist, Tilganga Institute of Ophthalmology
3. Mr. Sailesh Kumar Mishra: National Program Co-ordinator, Apex Body of Eye Health
4. Prof. Dr. Madhur Dev Bhattarai: Ex Co-ordinator, DM Program, National Academy of Medical Science (NAMS), Vice President of Nepal Diabetes Association
5. Prof. Dr. Pradeep Shrestha: Chief Endocrinology Unit, Head, Department of Medicine, Tribhuvan University (TU) Teaching hospital
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- Dr. Suman S Thapa President, Nepal Ophthalmic Society
- Dr. Sanjay Singh, Ex-President, Nepal Ophthalmic Society
- Representative of Apex body for Eye Health

Logistic Management: Bal Bahadur Kshetri

ANNEX: V Major Contributing Agencies