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Study of Diabetic Retinopathy In Terms Of Fundus Finding, OCT Changes and FFA Finding & Correlation with Biochemical Parameters Presenting To Eye OPD

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Background*: Diabetic Retinopathy (DR) is most important cause of legal blindness between 20-70yr age group. Periodic glycosylated haemoglobin (HbA1c) measurements can reflect the long-term control of hyperglycaemia. Intensive glycemic control had been proved to be effective in decreasing incidence rate of development and progression of DR in type 1 and type 2 DM.*
Hyperlipidaemia (LDL, TG) causes endothelial dysfunction due to reduced bioavailability of nitric oxide and breakdown of blood retinal barrier leading to exudation of serum lipids and lipoproteins which results in DR changes and diabetic macular odema (DME) formation.
Methods: *A prospective study was carried on 205 eyes of 110 cases of DR*
Results: *Study showed the diagnostic potential and efficacy of OCT and FFA over ophthalmoscopic fundus examination in detection of DR. 95/205(46%) eyes of DME & DR showed increased in severity with abnormal biochemical parameters. Mean HbA1C for Severe NPDR and PDR is >8.4. Lipid profile (TG, LDL) also correlated with more DME and increase in severity of stage with level >150 of TG and >130 of LDL Level, however, no significant correlation was found between LFT, RFT and stages of DR.*
Conclusion: *OCT is rapid non invasive technique provides valuable information about retinal thickness and also helps in monitoring the response to treatment in DME (Laser or AntiVEGF).*
FFA is essential for assessment of foveal perfusion state and helps in diagnosis of Macular ischemia in eyes with unexplained vision loss.
We conclude that decreasing in HbA1c values and control of lipid alterations is required at least to postpone or prevent loss of vision from retinopathy.
Key Words: *OCT, FFA, Diabetic Retinopathy, HbA1C.*

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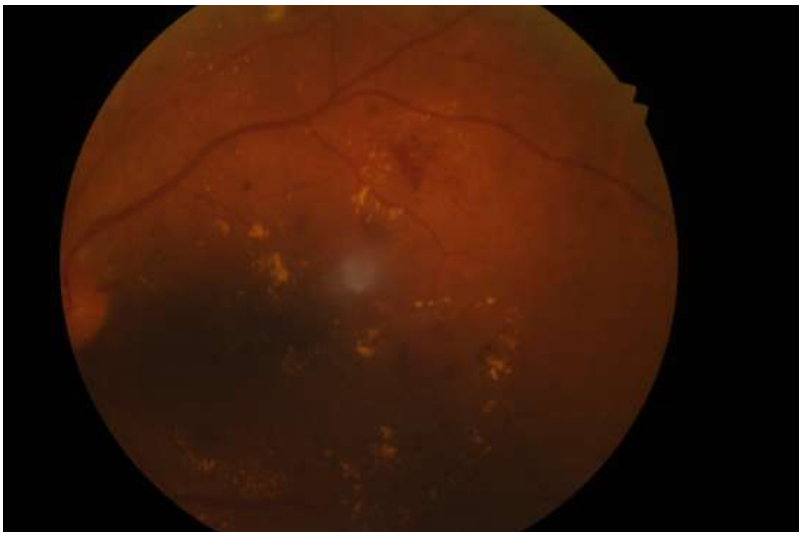

Fig 1A: Clinical fundus picture of left eye showing NPDR with CSME

I. Introduction

Diabetes Mellitus is a complex metabolic disease, primarily characterised by hyperglycemia, caused by variable interactions between hereditary and environmental factors.

They are classified on the basis of pathogenic processes that lead to hyperglycemia. Type 1 diabetes is the result of complete or near total insulin deficiency. Type 2 diabetes is heterogenous group of diseases characterized by variable degree of insulin resistance, impaired insulin secretion and decreased insulin production.

Diabetes is the major health problem in India. India with 180 Million population, 15 Million are known to be with Type 2 Diabetes mellitus (T2DM) [1]

According to WHO estimation for prevalence of T2DM, it is in the fifth position worldwide & by the year 2030, it is expected to occupy second place. T2DM comprises an array of metabolic dysfunctions associated with an increased incidence of microvascular and macrovascular complications[2], which are the major causes of morbidity and mortality. Hyperglycemia is the most important factor at the onset & if not controlled leads to various biochemical disorders such as hyperlipidemia and oxidative stress[3].The biochemical derangements in both T1DM & T2DM further leads to various vascular complications. To name a few, nephropathy, retinopathy, neuropathy and atherosclerosis

Diabetic retinopathy is a chronic progressive, potentially sight-threatening disease of the retinal microvasculature associated with the prolonged hyperglycaemia and other conditions linked to diabetes mellitus such as hypertension.

Approximately 382 million people across the world have been estimated to have DM in 2013 and if no action is taken this number will rise to 592 million by 2035[4] . WHO estimates that 19% of the world's diabetic population lives in India and 80 million people in India will have diabetes by the year 2030.

Diabetic retinopathy (DR), a very common complication of diabetes mellitus (DM), is the leading cause of visual deficits and blindness around the world .

It has been seen that patients having DR are 25 times more at risk of blindness than a non-diabetic individual. Timely diagnosis with the help of better screening and referral facilities, strict control of systemic parameters and timely intervention in the form of medical and surgical intervention can delay the sight threatening complication of DR.

It has been estimated that 30% of people with DM have DR worldwide[5] . A pooled analysis of 35 studies showed that the overall prevalence of DR of any severity is 34.6% and the prevalence of proliferative diabetic retinopathy (PDR) and diabetic macular edema (DME) is 6.96% and 6.81% respectively[5] . The presence of diabetic retinopathy is directly proportional to the duration of DM.

Risk Factors:-

- Duration of diabetes
- Poor Control of Diabetes
- Miscellaneous factors :
  - Pregnancy. (Hormonal changes)
  - systemic hypertension.
  - Renal disease .
  - Anaemia.(↓oxygen)
  - Elevated serum lipid.
  - carotid artery occlusive disease.
  - Alcohol.
  - Obesity.

Ocular Risk Factors-

- PVD
- High myopia
- Removal of cataract

Pathophysiology

Diabetic retinopathy is characterized by gradually progressive alterations in the retinal microvasculature, leading to areas of retinal nonperfusion, increased vasopermeability and the pathologic intraocular proliferation of retinal vessels. The complications associated with increased vasopermeability and uncontrolled neovascularization can result in severe and permanent visual loss.

The mechanisms include abnormal metabolic pathways, oxidative stress, and subclinical inflammation[6]Meanwhile, some therapeutic approaches targeting inflammation such as intravitreal injections of corticosteroids or anti-VEGF agents are effective for slowing down the development of DR Therefore, inflammation seems to be very important in the development of DR.

Several biochemical pathways have been proposed to link hyperglycemia and microvascular complications. These processes are thought to modulate the disease process through effects on cellular metabolism, signaling, and growth factors.

- Polyol accumulation
- AGEs (Advanced Glycation End-product)
- Oxidative damage-formation of reactive oxygen species(ROS)
- Growth factors:VEGF,IGF-I,TGF –β,PEDF

The VEGFs are a family of proteins that are mitogenic for vascular endothelial cells and increase vascular permeability. VEGF is important in fetal vascular development, with VEGF levels diminishing after birth. However, increased expression of VEGF has been demonstrated in diabetic retinopathy. In addition, VEGF has been shown to be upregulated by hypoxia, with increasing levels of VEGF in the vitreous associated with increasing retinal ischemia.

DR can be divided into two stages:

1) Non proliferative diabetic retinopathy (NPDR) :-

Typical changes seen in NPDR are micro-aneurysms, intra-retinal hemorrhages, cotton-wool spots, venous beading & loops, IntraretinalMicrovascularabnormalities(IRMA) and hard exudate. According to the severity of the lesions, NPDR can be subdivided into mild, moderate,severe and very severe stages.

2) Proliferative diabetic retinopathy (PDR):-

With the aggravation of the disease, NPDR enters into the PDR stage. In The PDR stage, lesions such as neovascularization of retina, disc, iris or angle, pre-retinal or vitreous hemorrhages, tractional retinal detachment can be seen

Diabetic macular oedema (DMO) is a thickening of the central part of the retina, the macula, that may affect people with diabetic retinopathy (DR). Diabetic retinopathy is a complication of diabetes in which the retina (a layer of tissue at the back of the eye) becomes progressively damaged.

Diabetic Macular Oedema-

The most frequent cause of visual impairment in DR is due to diabetic macular edema (DME), which occurs with leakage of plasma and lipid in the macula.

It has been estimated that 30% of people with DM have DR worldwide[5]. A pooled analysis of 35 studies showed that the overall prevalence of DR of any severity is 34.6% and the prevalence of proliferative diabetic retinopathy (PDR) and diabetic macular edema (DME) is 6.96% and 6.81% respectively[5]

DMO can be seen at any stage of DR, either nonproliferative or proliferative, with two types: focal oedema (FO) arising from micro aneurysm (MA) leakage, and diffuse oedema related to increased capillary permeability. **Focal macular oedema** has been defined as an area of retinal thickening less than two disc areas in diameter, not affecting the centre of the macula. **Diffuse macular oedema** has been defined as having two or more disc areas of retinal thickening with involvement of the macular centre.

The decision for treatment is based on the criteria of clinically significant macular oedema (CSMO) defined by the Early Treatment for Diabetic Retinopathy Study (ETDRS) in 1985 with clinical exam or colour fundus photographs. According to their definition, one of the following three criteria should be fulfilled:

1. Any retinal thickening within 500 μm of the macular centre.
2. Hard exudates within 500 μm of the macular centre with adjacent retinal thickening.
3. Retinal thickening at least one disc area in size, any part of which is within one disc diameter of the macular centre[7]

Diabetic Retinopathy (DR) is one of the common microvascular complications of T2DM, leading to impairment or total loss of vision.DR is estimated to account for nearly 5% of all global blindness[8]The duration of DM, hyperglycemia, hypertension &hyperlipidemia have shown to be the known and well established risk factors for DR, primarily the microvascular injury.

Bilirubin, a major intravascular product of haemcatabolism is traditionally considered as a toxic waste product.Previous studies have shown that elevated serum Bilirubin levels provide protection against cardiovascular disease, stroke & peripheral arterial disease .This created an interest in us to hypothesize in rural population that, whether high Serum Total Bilirubin levels within the physiological range has a decreased risk of development of retinal complications in T2DM.

Purine metabolites are strongly associated with the development of diabetic microvascular complications. **Uric acid**, an end product of the purine metabolism, acts as a pro-oxidant and it may thus be a marker of oxidative stress .

High **Serum lipid levels** have also been proposed as a risk factor for DR. High lipid levels are known to cause endothelial dysfunction due to a reduced bioavailability of nitric oxide and this endothelial dysfunction

was suggested to play a role in retinal exudate formation in DR . However large clinical studies showed a discrepancy about the association of serum lipids with the severity of DR or diabetic macular edema (DME). In ETDRS report, high total cholesterol and LDL levels were associated with retinal hard exudates; in the Chennai Urban Rural Epidemiology Study, serum lipids were higher in patients with DR than those without DR[9].

Diabetes is a disease of impaired carbohydrate metabolism characterized by hyperglycaemia and glycosuria, The onset of uncontrolled hyperglycaemia causes various microvascular complications such as damage of retina, nephron, neuron and cardiovascular tissues due to complex and multifunctional metabolic changes.

The most widely used clinical test in diabetes is the measurement of blood **glycosylated hemoglobin** (also called HbA1C), which is a form of haemoglobin used primairly to identify the average, plasma glucose concentration over prolonged periods of time. It is formed in a non-enzymatic pathway by hemoglobin's normal exposure to high plasma levels of glucose. Glycation of hemoglobin has been associated with cardiovascular disease, nephropathy and retinopathy in diabetes mellitus. It gives an assessment of long term glycemic control.

HbA1C has become the gold standard for the therapeutic management of diabetes mellitus in research and in the clinical setting.[10] The ADA recommends that the goal of glycemic control is an HbA1C level less than 7%.

Improving HbA1c measurement decreases development and progression of eye, kidney and nerve complication in both DM type 1 and DM type 2. Each 1% reduction in updated mean HbA1c was associated with reduction in risk of 21% for any end point related to diabetes and 37% for microvascular complications[11]

It determine the relationship between the glycemic control, manifested as HbA1C and the development of diabetic retinopathy.

Diabetic retinopathy (DR) is one of the most common microvascular complications of diabetes and ranks as a common cause of blindness worldwide Diabetic retinopathy could become a major threat to public health in the future due to the global prevalence of diabetes, which is projected to affect 438 million people by 2030[12]

India comprises a largest hub of diabetics, with 31.7 million cases of T2DM and a three- fold rise in disease prevalence in rural (2-6%) and urban (5-15%) areas[13]We need to describe and understand the clinical and biochemical profile of diabetes population, to facilitate early diagnosis and suggest lifestyle modifications to curb the onward progression of the disease

Ophthalmoscopy, fundus photography and fluorescein angiography are the common tools to diagnose diabetic retinopathy. In Diabetic retinopathy vision is decreased because of maculopathy or proliferative complications. It is essential to examine the **fundus** of every diabetic patient periodically at regular intervals to detect early changes. The complications mainly include intraocular haemorrhage and its sequel, tractional retinal detachment, vitreous haemorrhage, cystoid macular edema, optic neuritis etc. which are the causes for ocular and visual morbidity. Diabetic retinopathy remains the number one cause of loss of vision, because of delay in detection of Diabetic retinopathy.

However, there is an increasing demand for high resolution imaging of ocular tissues to improve the diagnosis and management of diabetic retinopathy. **Optical coherence tomography (OCT)** provides important additional information about the retinal thickness and extent of retinal edema in DME.

It also helps in monitoring the response to treatment in DME (Laser and/ or Intravitreal Triamcinolone Acetonide injection/Anti VEGF). The role of OCT in assessment and management of diabetic retinopathy has become significant in understanding the vitreo-retinal relationship and the internal architecture of the retina. In patients with refractory DME, taut posterior hyaloid membrane (TPHM) can be readily recognized by OCT scan. Also, the focal vitreo-retinal adhesions, subretinal fluid, and the axial distribution of fluid in an edematous macula which cannot be identified on clinical examination can be evident on OCT[14].

Fundus Fluorescein angiography (FFA) allows study of the circulation of the retina and choroid in normal and diseased states.

It is useful in demonstrating the leakage of fluid, consequent to the breakdown of the blood retinal barrier. Simple leakage on angiogram may not always be associated with retinal thickening in the macula. Reports suggest that actual macular thickness is better correlated with loss of visual acuity. It is in all probability more important in a case of a doubtful macular ischemia, when the foveal perfusion is in question. But how to diagnose a case of doubtful macular ischemia when the foveal perfusion in question is still not clear. FFA is useful in differentiating between cystoids macular edema and ischemic maculopathy and to determine whether laser therapy is indicated or not[15] Fluorescein Angiography (FA) can assess macular edema qualitatively, whereas OCT can provide a quantitative measurement of foveal thickness. Therefore, FA assess the pathophysiological aspect of DME and the anatomical features such as the extent of retinal thickening and the retinal layer involved can be assessed best usingOCT[16]

The purpose of this study is to identify the concentrations of HbA1c, Lipid profile (Cholesterol, Triglyceride, HDL, LDL, TC/HDL), bilirubin , uric acid , Blood urea and Serum creatinine in DM patients and

to clarify the related roles in DR patients. This was a prospective study conducted between January 2017 and June 2018 of Diabetic Retinopathy patients who were attended in the Ophthalmology Department of JLN Medical College & Hospital, Ajmer (Rajasthan), INDIA. A complete fundus examination was done to all patients by Ophthalmoscopy, OCT and FFA.

II. Materials And Methods

- It was a prospective study conducted between January2017 and June2018 of Diabetic Retinopathy patients who attended in the Ophthalmology Department of JLN Medical College& Hospital, Ajmer (Rajasthan), INDIA.
- 205 Eyes of 110 cases of Diabetic Retinopathy included in this study.

Methods:-

After taking informed consent, all the subjects underwent thorough systemic and ophthalmic examination.
It includes-

1. Assessment of visual acquity[Distant And Near vision].
2. Fundus examination were done by using Direct and Indirect ophthalmoscope (Using 20D lens).
3. Blood investigations(Blood sugar- Fasting,Post Prandial, HBA1C , Lipid Profile, Blood urea, S. Creatinine, S.Uric Acid) were done for changes in biochemical parameters.
4.Fundus Fluorescein Angiography-(Kowa 10 Xa, Japan)
5. OCT(Optical Coherence Tomography) was performed through a dilated pupil by 3D OCT – 1 maestro, Topcon).

FOLLOW UP:-

3 follow ups were done after 1 month, 3 months & 6 months.
Any therapeutic intervention in the form of Retinal laser , intravitreal Anti VEGf/Steroid injection, or V-R surgery if required were done according to the need of patient.
At every follow up Investigations done were-.

1. Biochemistry investigations
2. Fundus Examination
3. OCT
4. FFA[Fundus fluorosceine Angiography

III. Observations And Results

A Prospective study carried on 205 eyes of 110 cases(Males -74, Females-36) of DR. Ophthalmic Fundus examination,OCT, FFA and Biochemical Investigation were done in all the 100 eyes of 54 Patients.

In this study there were more of male patients compared to females which was in concordance with study conducted by Salil L.Gadkri et al.[17]though the cause of higher prevalance in males is still unknown

Table 1: Showing Distribution Of Patients with Different Grades Of Diabetic Retinopathy NPDR-122 Eyes{(Mild 6 eyes(2.9%), Moderate 51 eyes(24.9%), Severe 65 eyes(31.7%)} and PDR 72 eyes(35.1%)

Table 1: Stages of Diabetic retinopathy

Stages of DR	Frequency	Percentage
Mild NPDR	6	2.9%
Moderate NPDR	51	24.9%
Severe NPDR	65	31.7%
PDR	72	35.1%
Others	11	5.4%
Total	205	100

Table 2: Showing Distribution Of patients according to duration of diabetic period. This shows Severity of Diabetic Retinopathy increased as duration of diabetes increased. Number of Patients between Duration of 0 -5 yr is 76(37.1%) and for >5yr is 129(62.9%)

Table 2: Duration of diabetes

Duration of Diabetes	Frequency	Percentage
0-5 years	76	37.1%
6-10 years	68	33.2%
11-15 years	31	15.1%
16-20 years	21	10.2%
>20 years	9	4.4%
Total	205	100

In this study patients with longer duration of diabetes had more frequency of having diabetic macular edema compared with those with shorter duration of diabetes.Even study conducted by Rohit varma et al[18] had positive correlation between duration of diabetes and prevalence of diabetic macular oedema.

Age of the patients in the study ranged fron 36 to 84 years,with Mean age 56.59 (±9.50)yr for Males and 57.47 (±10.50)yr for Females. Prevalence of diabetes In age more than 40 years was found to be high which was in concordance with study conducted by salil L. Gadkri et al[17]

Table 3: showing Distribution of Oedema according to OCT Findings in DR Patients. According to datas showing Diffuse Oedema in 36eyes(17.6%), Cystoid Macular Oedema 68(33.3%),No Oedema in 79(38.5%), VMT in 4 eyes (2%),Atrophic Macula in 4(2%),and Media haze in 14 eyes (6.8).

Table 3: Distribution of patients according to OCT findings of Diabetic Macular Edema

OCT finding	Frequency	Percentage
Diffuse Oedema	36	17.6%
Cystoid Macular Oedema	68	33.3%
No Oedema	79	38.5%
VMT	4	2.0
Atrophic Macula	4	2.0
Media Hazy	14	6.8
Total	205	100

Fig 1B: showing Diffuse macular edema

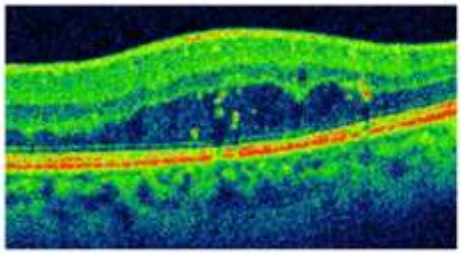

Fig 2: OCT showing Cystoid MacularEdema

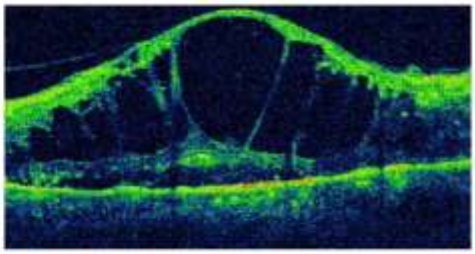

Fig 3: OCT showing Vitreo-macular Traction

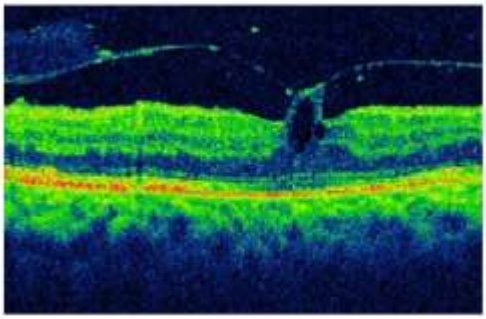

Fig 4: OCT showing Atrophic Macula

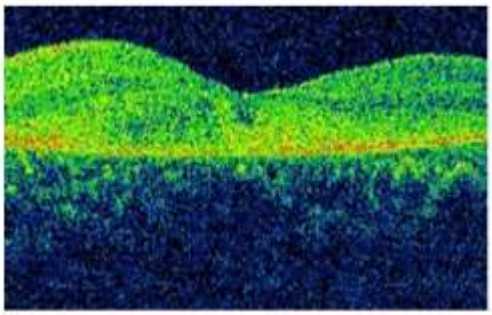

Table 4 showing Pattern Of leakage on FFA. Data Showing focal leak in 33 eyes(16.1%),Diffuse leak in 42 eyes(20.5%), Cystoid leak in 62 eyes(30.2%), Macular Ischemia in 9 eyes(4.4%), No leak in 52 eyes(25.4%).

Table 4: Distribution of patients according to pattern of leakage in FFA

FFA finding	Frequency	Percentage
Focal leak	33	16.1%
Diffuse leak	42	20.5%
Cystoid leak	62	30.2%
Macular ischemia	9	4.4%
No leak	52	25.4%
Media hazy	7	3.4%
Total	205	100

Fig 5: Pateloid pattern Leakage in FFA

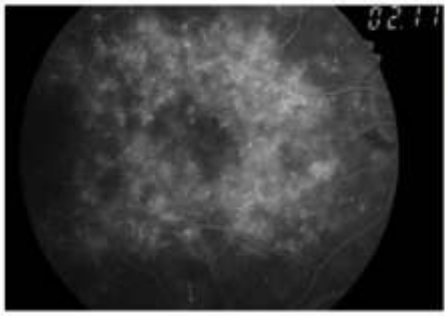

Fig 6 : FFA showing Macular Ischemia

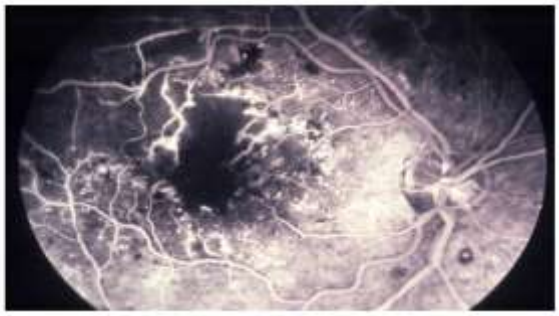

Fig 7: Focal Leakage into FAZ

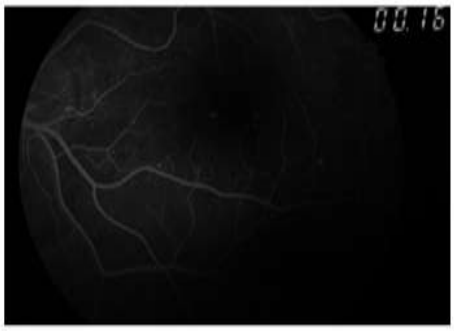

Fig 8 : FFA showing diffuse leakageinto FAZ

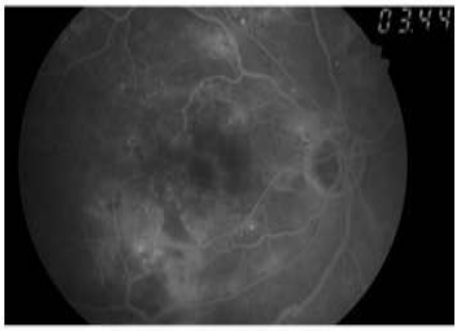

Table 5: Comparison of OCT and FFA findings

OCT finding	OCT	FFA
Diffuse Oedema/Diffuse leak	36	42
Petaloid/Cystoid Macular Oedema	68	62
Noleak/No Oedema	79	52
Focal leak	0	33
Macular ischemia/Atrophic Macula	4	9
Media Hazy	14	7

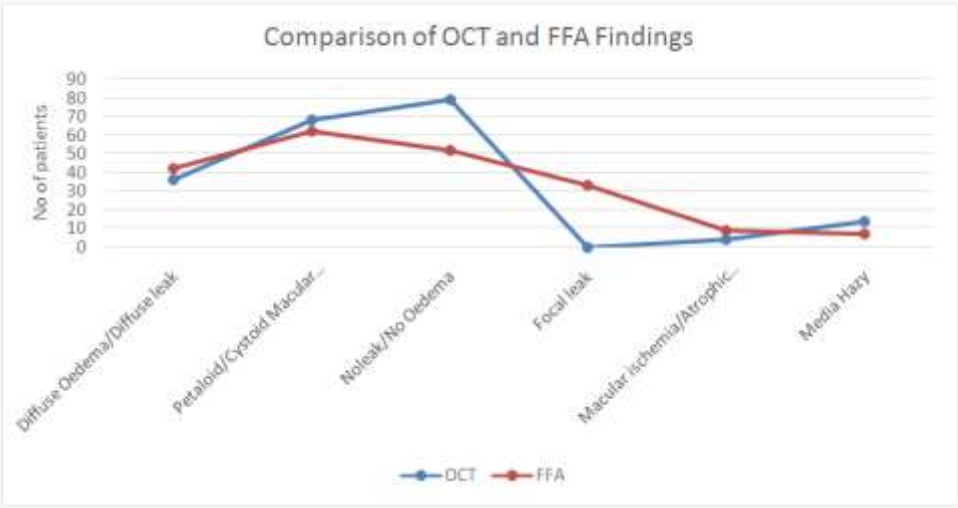

Fig: 9 Line Diagram showing pattern of DME on OCT compared with FFA

Table 6 Showing that as level of LDL increases there is more Macular oedema. With LDL level ≤130 i.e. normal number of cases of macular changes is 87 (45.5%) and with level >131 number of cases is 104(54.4%). This shows significant Correlation between OCT findings and LDL Level with
P value-=<0.001

Table 6: Association between LDL level and OCT findings

LDL	Cystoid Oedema	Diffuse Oedema	No Oedema	Atrophic macula	VMT	Media hazy
≤130	20	13	52	1	1	10
131-159	29	14	17	0	3	3
>159	19	9	10	3	0	1
Total	68	36	79	4	4	14

Chi-square test, p-value=<0.001

Table 7 Showing that With LDL level ≤130 number of cases of with macular changes are 87 (45.5%) and with level >131 number of cases are 104(54.4%). This shows significant Correlation between FFA findings and LDL Level with P value-=<0.001

Table 7: Association between LDL level and FFA findings

LDL	Focal leak	Cystoid leak	Diffuse leak	No leak	Macular ischemia	Media hazy
≤130	5	20	20	45	4	4
131-159	17	20	7	4	4	2
>159	11	22	15	3	3	1
Total	33	62	42	52	9	7

Chi-square test, p-value=<0.001

Table 8: showing Significant correlation with P-value=0.022.If TG(Triglyceride level) with in normal limit i.e.<150 macular changes present in 32 eyes (17.1%)and as value increases changes Present in 155 eyes(82.8%)

Table 8: Association between Triglyceride level and OCT findings

TG	Cystoid Oedema	Diffuse Oedema	No Oedema	Atrophic macula
<150	14	8	8	2
150-199	17	14	38	2
>199	37	14	33	0
Total	68	36	79	4

Chi-square test, p-value=0.022

Table 9: showing Significant correlation with P-value=<0.001.If TG(Triglyceride level) with in normal limit i.e.<150 macular changes present in 34 diabetic eyes(23.2%)and with increase increases in Triglyceride level i.e.>150 macular changes seen in 112 diabeticeyes(76.7%)

Table 9: Association between Triglyceride level and FFA findings

TG	Focal leak	Cystoid leak	Diffuse leak	No leak	Macular ischemia	Media hazy
<150	3	22	4	15	5	5
150-199	22	18	21	18	2	2
>199	8	22	17	18	2	0
Total	33	62	42	51	9	7

Chi-square test, p-value=<0.001

Table 10: Showing No Significant correlation(P-value=0.262) between HDL Level and OCT Findings in form of Macular Oedema and Atrophy.

Table 10: Association between HDL level and OCT findings

HDL	Cystoid Oedema	Diffuse Oedema	No Oedema	Atrophic macula	VMT	Media hazy
Low	36	27	53	3	2	8
Normal	32	9	26	1	2	6
Total	68	36	79	4	4	14

Chi-square test, p-value=0.262

Table 11: Showing No significant Correlation (P-value=0.114) between HDL Level and FFA findings in form of Leakage and Ischemia.

Table 11: Association between HDL level and FFA findings

HDL	Focal leak	Cystoid leak	Diffuse leak	No leak	Macular ischemia	Media hazy
Low	23	31	30	35	7	3
Normal	10	31	12	17	2	4
Total	33	62	42	52	9	7

Chi-square test, p-value=0.114

Table 12 showing significant correlation(p-value=0.040)between HbA1C and DME. As the level of HbA1C Increased from normal ,there are increase in number of DME in Different forms of OCT Findings. HbA1c up to 6.4% have 28 eyes(14.9%) ,HbA1c Level >6.4% have 159 eyes(85.02%)

Table 12: Association between HbA1c level and OCT findings

HbA1c level	Cystoid Oedema	Diffuse Oedema	No Oedema	Atrophic macula
Upto5.7	3	1	1	0
5.7-6.4	5	4	14	0
6.5-8.5	48	16	41	1
8.5-11.2	12	15	23	3
Total	68	36	79	4

Chi-square test, p-value=0.040

Table 13 HbA1c showing Significant correlation(P- value= 0.04)with FFA finding in form of different type of leakage.

Table 13: Association between HbA1c level and FFA findings

HbA1c level	Focal leak	Diffuse leak	Cystoid leak	Macular ischemia
Upto5.7	1	0	3	0
5.7-6.4	3	4	6	1
6.5-8.5	20	23	42	3
8.5-11.2	9	15	11	5
Total	33	42	62	9

Chi-square test, p-value=0.04

Table 14 showing Significant Correlation(P-value=0.032) between Post prandial blood sugar level and OCT findings

Table 14: Association between Post-prandial glucose level and OCT findings

PP (mg%)	Cystoid Oedema	Diffuse Oedema	No Oedema	Atrophic macula
Upto140	17	5	6	1
>140	51	31	73	3
Total	68	36	79	4

Chi-square test, p-value=0.032

Table 15: Association between Post-prandial glucose level and FFA findings

PP (mg%)	Focal leak	Diffuse leak	Cystoid leak	Macular ischemia
Upto140	10	5	5	2
>140	23	37	57	7
Total	33	42	62	9

Chi-square test, p-value=0.029

Table 16:showing No significant correlation(P-value=0.373) between Fasting blood glucose level and OCT Findings.

Table 16: Association between Fasting glucose level and OCT findings

Fasting glucose (mg%)	Cystoid Oedema	Diffuse Oedema	No Oedema	Atrophic macula
Upto 125	34	12	39	2
>125	34	24	40	2
Total	68	36	79	4

Chi-square test, p-value=0.373

Table 17: showing No Significant correlation between Fasting blood glucose level anf FFA findings

Table 17: Association between Fasting glucose level and FFA findings

Fasting glucose (mg%)	Focal leak	Diffuse leak	Cystoid leak	Macular ischemia	No leak	Hazy media
Upto125	14	11	33	4	28	1
>125	19	31	29	5	24	6
Total	33	42	62	9	52	7

Chi-square test, p-value=0.033

Table 18: shows that LDL cholesterol shows significant(P-value=<0.001) with severity of Diabetic Retinopathy stages(P=<0.001)

Table 18: Association of LDL with Diabetic retinopathy stages

LDL	Mild NPDR	Moderate NPDR	Severe NPDR	PDR	Others	Total
<130	6	30	30	19	6	91
131-159	0	17	22	25	4	68
>159	0	4	13	28	1	46
Total	6	51	65	72	11	205

Chi-square test, p-value=<0.001

Fig: 10 Association between LDL Level and Diabetic Retinopathy stages

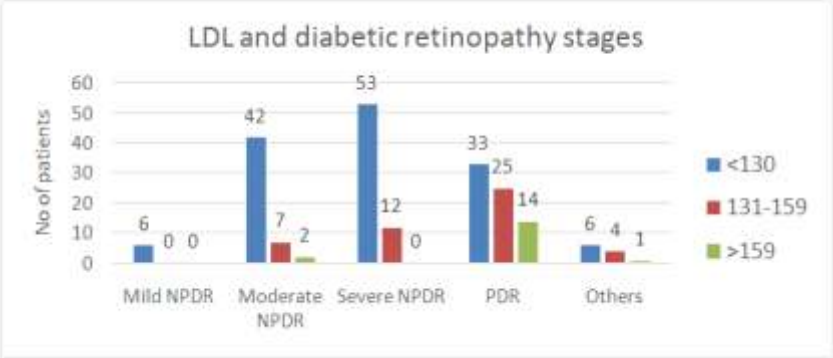

Table 19: showing that TG level showing significant correlation(p-value=0.001)with Severity of Diabetic Retinopathy stges.

Table 19: Association between Triglyceride level and Diabetic retinopathy stages

TG	Mild NPDR	Moderate NPDR	Severe NPDR	PDR	Others	Total
<150	4	21	27	12	8	72
150-199	2	14	26	40	1	83
>199	0	16	12	20	2	50
Total	6	51	65	72	11	205

Chi-square test, p-value=0.001

Fig: 11 Association between Triglyceride Level and Diabetic Retinopathy stages

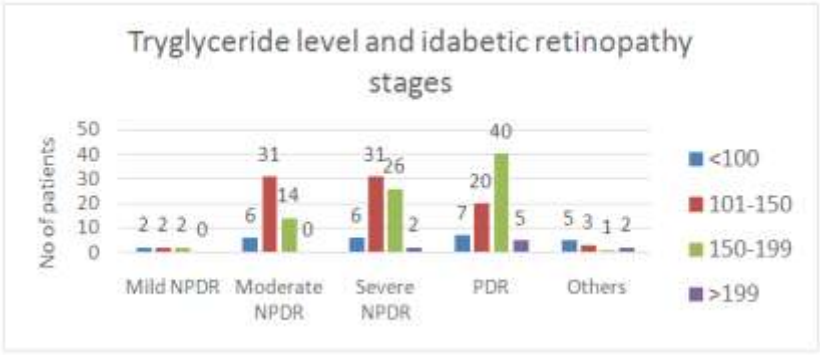

Table 20 showing no significant correlation(P-value=0.883) with HDL Level and stages OF Diabetic Retinopathy.

Table 20: Association of HDL with Diabetic retinopathy stages

HDL	Mild NPDR	Moderate NPDR	Severe NPDR	PDR	Others	Total
Low	4	30	41	48	6	129
Normal	2	21	24	24	5	76
Total	6	51	65	72	11	205

Chi-square test, p-value=0.883

Table 21: showing significant correlation with (P-value=<0.001)HbA1c level and Severity of Diabetic Retinopathy stages.

Table 21: Association between HbA1c level and Diabetic retinopathy stages

HbA1c level	Mild NPDR	Moderate NPDR	Severe NPDR	PDR	Others	Total
Upto 5.7	0	0	4	1	0	5
5.7-6.4	2	6	15	6	0	29
6.5-8.5	4	33	33	27	3	100
8.5-11.2	0	12	13	38	8	71
Total	6	51	65	72	11	205

Chi-square test, p-value=<0.001

Fig 12: Association between HbA1c level and Diabetic Retinopathy stages

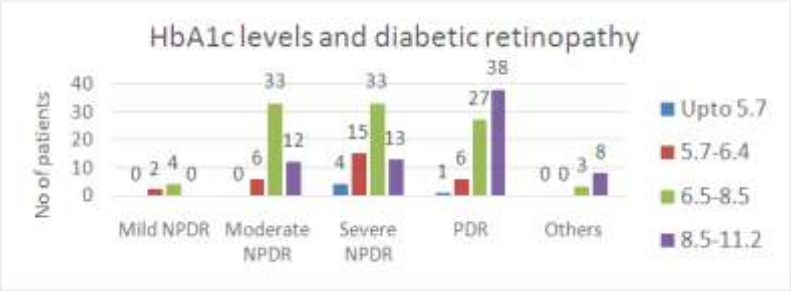

Table 22: showing significant correlation between Post Prandial blood glucose level and Severity of Diabetic Retinopathy stages.

Table 22: Association between Post-prandial glucose level and Diabetic retinopathy stages

PP (mg%)	Mild NPDR	Moderate NPDR	Severe NPDR	PDR	Others	Total
Upto 140	1	12	14	1	0	18
>140	5	39	51	71	11	187
Total	6	51	65	72	11	205

Chi-square test, p-value=0.002

Fig 13: Association between Post Prandial Blood glucose level and Diabetic Retinopathy stages

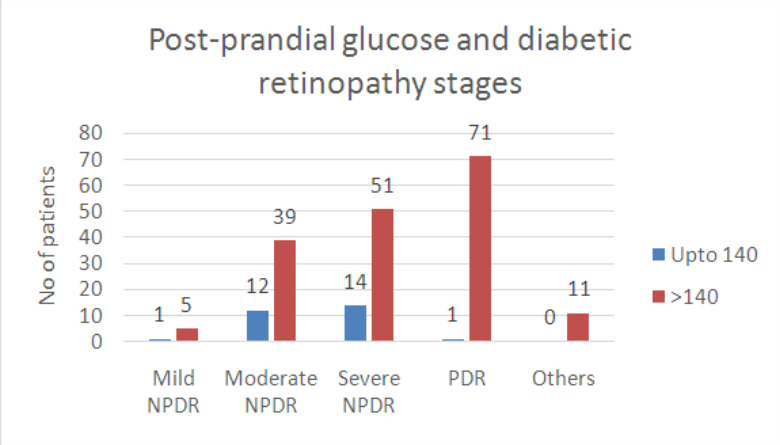

Table 23: showing No significant correlation(P-value=0.179) between Fasting blood Glucose level and Severity of Diabetic Retinopathy stages.

Table 23: Association between Fasting glucose level and Diabetic retinopathy stages

Fasting glucose (mg%)	Mild NPDR	Moderate NPDR	Severe NPDR	PDR	Others	Total
Upto 125	4	26	33	26	7	91
>125	2	25	32	46	4	114
Total	6	51	65	72	11	205

Chi-square test, p-value=0.179

Table 24: Comparison of various biochemical parameters among Diabetic retinopathy stages

Variable	N	Diabetic retinopathy stage	Mean	SD	P-value
FBS	6	Mild NPDR	112.37	3.02	<0.001
	51	Moderate NPDR	136.71	40.67	
	65	Severe NPDR	210.87	60.50	
	72	PDR	149.43	49.80	
	11	Others	139.94	46.47	
PPBS	6	Mild NPDR	191.48	35.28	<0.001
	51	Moderate NPDR	233.68	83.00	
	65	Severe NPDR	340.29	92.45	
	72	PDR	253.25	57.73	
	11	Others	244.09	76.48	
HbA1c	6	Mild NPDR	6.82	0.60	<0.001
	51	Moderate NPDR	7.62	1.01	
	65	Severe NPDR	8.86	1.27	
	72	PDR	8.43	1.41	
	11	Others	7.43	1.42	
LDL	6	Mild NPDR	89.85	43.88	<0.001
	51	Moderate NPDR	111.74	32.40	
	65	Severe NPDR	107.49	51.00	
	72	PDR	131.72	33.77	
	11	Others	111.18	25.67	
TG	6	Mild NPDR	120.13	49.35	0.002
	51	Moderate NPDR	132.28	27.66	
	65	Severe NPDR	124.08	59.20	
	72	PDR	157.58	48.48	
	11	Others	140.18	33.34	
S. Creatinine	6	Mild NPDR	0.82	0.24	0.026
	51	Moderate NPDR	1.02	0.26	
	65	Severe NPDR	1.02	0.23	
	72	PDR	1.18	0.46	
	11	Others	1.04	0.34	
Blood Urea	6	Mild NPDR	29.98	9.00	0.237
	51	Moderate NPDR	31.05	12.92	
	65	Severe NPDR	30.54	11.52	
	72	PDR	34.13	10.86	
	11	Others	29.97	9.40	
S. Uric acid	6	Mild NPDR	6.03	2.33	0.189
	51	Moderate NPDR	5.40	1.45	
	65	Severe NPDR	4.55	2.18	
	72	PDR	5.76	2.07	
	11	Others	5.20	1.91	

ANOVA test

According to ANOVA Test (Statistical Analysis) Blood Urea level, Serum Uric Acid Level not showing any significant correlation with Doiabetic Retinopathy stages.

IV. Discussion

As diabetic retinopathy is one of the major causes of visual disability, assessing the risk factors were added an immense value to the study.

The mean age in this study was 56.59±9.50years for Males and 57.47±10.50years for Females. These findings are relevant to previous studies done on Diabetic Retinopathy screening where most of participants were middle aged patients with median age of 58.1years and 54 years respectively.

In this study males with Diabetic Retinopathy were (67%) compared to females (33%).

In our study Number of Patients with Mild and Moderate NPDR are 27.8% and Severe NPDR and PDR are 66.8% and others are 5.4%. So, this shows that with increase in biochemical parameters, there is also increase in severity of Diabetic Retinopathy grade.

Duaration of Diabetes is also a Major risk factor. In our study its proved that with increase in duration of DM, number of patients of Diabetic Retinopathy also increased. Number of Patients with duration of diabetes 0-5 yr is 37.1% and with >5year number of Patients are 62.9%.

Otani et al[19] reported that OCT images showed three basic types of macular edema: sponge-like retinal swelling, CME and serous retinal detachment.

In the current study, we have found similar results in our study population which included even the patients with no ophthalmoscopic evidence of diabetic maculopathy.

In the current study cystoid macular edema with cystoids spaces in retinal layers was the most common tomographic pattern and was seen in 33.3% eyes. The Diffuse macular edema was detected in 17.6 %

of eyes. Vitreo- macular traction with macular edema was seen in 2% of eyes, Atrophic macula in 2% cases and OCT failed to detect any oedema in 6.8% due to media haze which were included in study because they are Patients with Diabetic Retinopathy. No Oedema was detected in 38.5% cases of Diabetic Retinopathy. The diagnostic asccuracy in differentiation of cystoid,Diffuse and Vitreo-macular traction of diabetic macular edema made by OCT, made this an essential diagnostic tool for diagnosis and management of DME.

Thinning of the retinal layers were found in 2% of eyes who underwent OCT evaluation which co-related to macular ischemia diagnosed with FA. The importance of fluorescein angiography is highlighted for detection of macular ischemia in the presence of Diabetic maculopathy.

In our study, most common pattern was cystoids leakage into FAZ which was seen in 30.2% of eyes followed by diffuse leakage in 20.5%. The Focal leakage was also seen 16.1%. FA was able to diagnose and confirm diagnosis in 4.4% of macular ischemia which cannot be diagnosed with other diagnostic methods.

Consistently high blood glucose levels can lead to macrovascular and microvascular complication that will eventually affect patients quality of life.The costs related to diabetes include increased use of health services, disability and productivity loss, which can be a considerable burden to the patient, families and society.

Proper glycemic control is the best strategy to prevent and delay the progression of diabetes complication and improve the quality of life

In our study, it has been observed that the Post Prandial glucose level shows significant correlation(P-value=0.032) with OCT findings in form of Diabetic Macular Oedema , with FFA Findings in form of leak(P-value=0.029) and with increase in severity of Diabetic Retinopathy stages (P- value=0.002)

Fasting Blood Glucose level showing No significant correlation with OCT findings(P-value=0.373) and FFA findings(P-value=0.033)and with severity of Diabetic Retinopathy stages(P-value=0.179)

In our study HbA1c shows significant correlation(P-value=0.040) with OCT findings. With HbA1c level with in Normal limit i.e. 6.4% number of Patients with DME are 32% and HbA1c >6.4% number of eyes with DME are 67.6% Similar significant Correlation also seen with FFA findings (P-value=0.04). With HbA1c 6.4% Findings in form of leak and Ischemia seen in 12% and if HbA1c >6.4% seen in 87.6% Diabetic eyes. We also found highly significant correlation(P=<0.001) between HbA1c level and Severity of Diabetic Retinopathy stages. With HbA1c level 6.4% number of Patients 17.5% and with HbA1c >6.4% number of patients seen are 82.4% .Mean HbA1C for Severe NPDR and PDR is >8.4%

In Rajiv Raman et al study, a strong association of HbA1c with sight threatening Diabetic retinopathy (P-value < 0.001) was found[20] .

Our study revealed that both FBS and PPBS are important to achieve optimal glycemic control, but PPBS has a closer association with HbA1c and better predictor for overall glycemic control compared to FBS, which is similar to the studies reported by Rosediani *et al.*, and Monnier *et al*.[21,22].

It has been postulated that an increase in blood viscosity and alterations in the fibrinolytic system, incorporation of triglycerides into the cell membrane and endothelial dysfunction occur in hyperlipidemia and lead to the formation of hard exudates, haemorrhage and odema in the retina[23]

Kern PA et al study have shown that diabetes is associated with dyslipidemia in the form of hypercholesterolemia and hypertriglyceridemia.[24]

The Wisconsin epidemiologic study of Diabetic Retinopathy, Klein et al. reported an association of Serum Cholesterol with severity of hard exudates in macula. Van Leiden et al, showed an association between Triglyceride levels and Diabetic Retinopathy in subjects with type 2 diabetes.[25] Haddad and Saad found that Plasma Total Cholesterol and Triglycerides were risk factors for Diabetic Retinopathy.[26]Reema et al. (2006) showed association of TG with DR and LDL with diabetic macular oedema in Chennai Urban Rural Epidemiology Study Eye study.[23] The Diabetes Control and Complications Trial found that the severity of Retinopathy was associated with increase in Triglycerides and inversely associated with HDL cholesterol.

However, Larson et al. and Hove et al. found no association between Triglycerides, Total Cholesterol, HDL Cholesterol with Diabetic Retinopathy [27]

In our study, it was found that LDL cholesterol shows significant correlation(p=<0.001) with OCT Findings in form of DME and with FFA Findings (P=<0.001) in form of leak and Ischemia and also with severity of Diabetic Retinopathy stages(P=<0.001)

Triglyceride (TG) Level also shows significant correlation (P-value=0.022) with OCT & FFA Findings(P=<0.001) and with severity of Diabetic Retinopathy stages(P-value=0.001).

However, In our study HDL Cholesterol shows No significant correlation with OCT Findings(P-value=0.262), FFA Findings (P-value=0.114) and with severity of Diabetic Retinopathy stages (P-value=0.883).

Lyons et al found that DR had a significant positive association with LDL-C and significant negative association with HDL.[28] van leiden et al study showed a significant association between plasma lipid profile.[25] Haddad and Saad found that plasma total cholesterol and triglyceride were risk factors for DR.[26]

In our study there we found significant correlation with Serum Creatinine and Diabetic Retinopathy stages (P-value=0.026) and no significant correlation with Blood urea(P-value=0.0237) and Serum Uric Acid (P-value=0.189). However, study conducted by Ossama Haddad etal., showed high levels of Urea, Creatinine, which were also associated with an increased risk for any grade of diabetic retinopathy [26].

Based on the findings of this study, it is recommended that stringent measures must be adopted to control modifiable risk factors associated with development and progression of DR in order to reduce the morbidity related with this disease.

Serum cholesterol, LDL-C and TG levels were significantly elevated and serum HDL-C level was decreased in patients with DR indicating a need to promptly address these modifiable risk factors in order to reduce the morbidity related to DR.

Our study revealed that both FBS and PPBS are important to achieve optimal glycemic control, but PPBS has a closer association with HbA1c and better predictor for overall glycemic control compared to FBS.

V. Conclusion

Following conclusion drawn from the Present study:-

- OCT is rapid non invasive technique provides valuable information about retinal thickness and also helps in monitoring the response to treatment in DME (Laser or AntiVEGF).
- FFA is essential for assessment of foveal perfusion state and helps in diagnosis of Macular ischemia in eyes with unexplained vision loss.
- Some of the diabetic structural changes in fovea such as serous foveal detachment, CME, and foveal traction can be detected early with OCT, which may not be evident in ophthalmoscopy or FA. These results indicate that OCT can facilitate deciding on the treatment protocol (surgical or medical) and follow‐ up of diabetic patients, especially in the early stages of diabetic maculopathy when the structural changes are not yet evident with slit‐ lamp biomicroscopy or angiographically.
- Serum cholesterol, LDL-C and TG levels were significantly elevated and serum HDL-C level was decreased in patients with DR indicating a need to promptly address these modifiable risk factors in order to reduce the morbidity related to DR.

We conclude that decreasing in HbA1c values, Blood sugar (Fasting & Post Prandial) and control of lipid alterations (LDL-C,HDL-C,TG etc.) is required at least to postpone or prevent loss of vision from retinopathy. However, no significant correlation was found between LFT, RFT and stages of DR.

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