““A STUDY ON THE ASSOCIATION BETWEEN TOTAL VITAMIN D LEVELS AND DIABETIC RETINOPATHY IN TYPE 2 DIABETIC MELLITUS”

By

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Dissertation submitted to BLDE (Deemed to be University), Vijayapura.

In partial fulfilment of the requirements for the award of the degree of

MASTER OF SURGERY

In

OPHTHALMOLOGY

Under the guidance of

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BLDE (DEEMED TO BE UNIVERSITY)

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2019

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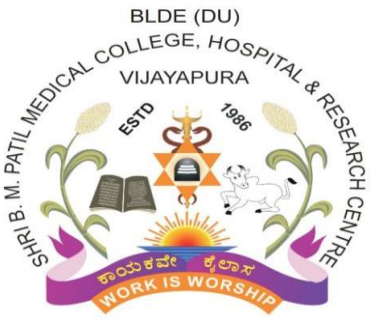
B.L.D.E (DEEMED TO BE UNIVERSITY), VIJAYAPURA, KARNATAKA



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LIST OF ABBREVIATIONS

DR	Diabetic Retinopathy
T2 DM	Type 2 diabetes mellitus
IOP	Intraocular pressure
HbA1c	Glycoselated haemoglobin
NPDR	Non proliferative diabetic retinopathy
PDR	Proliferative diabetic retinopathy
AGEs	Advanced glycosylation end products
OCT	Optical coherence tomography
B scan	Brightness Scan
RBS	Random Blood Sugar
FBS	Fasting Blood Sugar
PPBS	Post Prandial Blood Sugar
FFA	Fundus Fluorescein Angiography
ICG	Indocyanine Green Angiography
HRP	Horseradish Peroxidase
NVE	Neovascularization Elsewhere
NVD	Neovascularization Disc
FAZ	Foveal Avascular Zone

VDR	Vitamin D Receptors
GDM	Gestational Diabetes Mellitus
VEGF	Vascular Endothelial Growth Factor
GWAS	Genomic Wide Association Studies
DCCT	Diabetes Control and Complication Trial
UKPDS	United Kingdom Prospective Diabetes Study

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ABSTRACT

BACKGROUND

Diabetes mellitus (D.M.) is a significant public health problem where about more than 300 million people are affected, with severe morbidity and mortality. Its long-term complications can decrease the quality of life of patients.

Ocular manifestations of diabetes include anterior ischaemic neuropathy, glaucoma, cataract, retinal vascular occlusions, and retinopathy/ maculopathy.

Vitamin D plays a role in the pathogenesis of diabetic retinopathy through its effects on the immune system, angiogenesis and anti-inflammatory effects.

As the prevalence of Diabetes Mellitus is high in our area, this study is undertaken to estimate the prevalence of Vitamin D deficiency in Type 2 Diabetic Mellitus patients with diabetic retinopathy and correlate the Total Vitamin D levels with retinopathy changes.

AIM AND OBJECTIVES

This study aims to know the association between Total vitamin D levels and Diabetic Retinopathy in Type 2 Diabetic Mellitus.

MATERIALS AND METHODS

This is a cross-sectional and time-bound study carried out on patients attending the outpatient and inpatient departments of Ophthalmology, B.L.D.E. (D.U.).'s Shri B.M. Patil Medical College, Hospital and Research Centre, VIjayapura.

The study includes a total of 276 patients with Type 2 Diabetes Mellitus. They are grouped into two with those having diabetic retinopathy and those without diabetic retinopathy (138 patients per group)

They are screened for Diabetic Retinopathy by complete ophthalmic examination, including detailed History.

- Best-corrected visual acuity
- Slit-lamp examination
- Direct and Indirect Ophthalmoscopy
- Fundus Photography
- Relevant blood investigations like F.B.S., P.P.B.S., HBA1C, Vitamin D.
- Diabetic retinopathy is graded using E.T.D.R.S. (Early Treatment Diabetic Retinopathy Study).

RESULTS

A total of 168 patients were included in the study with majority belonging to the 6th and 7th decades of life. The relation of duration of diabetes to the severity of retinopathy showed positive correlation, with p value <0.001. Study demonstrated an inverse relationship between the severity of diabetic retinopathy and serum 25 hydroxy Vitamin D levels at baseline. Patients with mild NPDR and moderate NPDR had Vitamin D insufficiency which decreased to Vitamin D deficiency levels in severe NPDR and PDR.

CONCLUSION

A significant relation was found between diabetic retinopathy and serum Vitamin D levels. **Henceforth, it is important to** to study the association of serum 25 hydroxy Vitamin D with the level of Diabetic Retinopathy, its use as a predictor of the severity of Diabetic Retinopathy and as a tool to limit or prevent progression of retinopathy changes.

INTRODUCTION

Diabetes is the increasing status of a potential epidemic in India, with more than 62 million diabetic individuals diagnosed with the disease.[1]

According to Wild *et al*. the prevalence of diabetes is predicted to increase from 171 million in 2000 to 366 million in 2030, marking the highest in India. In 2000, India had a significant number of patients with Diabetes Mellitus. [2]

Diabetes mellitus is classified into two categories, depending upon the pathogenesis as Type 1 and Type 2 Diabetes Mellitus. Type 1 Diabetes Mellitus (insulin-dependent diabetes mellitus [IDDM]) is caused by autoimmune-mediated destruction of the beta cells of the pancreas and the cells where the insulin production takes place. Type 2 Diabetes Mellitus characterized by three main mechanisms such as insulin resistance, decreased insulin production, and increased glucose production. Even though it has been well proved that strict blood glucose control can lower the risk of microvascular complications from diabetes, the pathophysiology of retinopathy progression is still yet to be established. [3]

Studies have given evidence that poor glycemic control and longer duration of diabetes are risk factors of D.R. [4] Diabetes needs to be detected early as it has a devastating impact on the quality of life. Early detection of patients at risk for developing diabetic retinopathy is essential to reduce preventable blindness from this disease. Vitamin D is essential for a large number of physiologic processes such as musculoskeletal, immune , however, various studies have shown its role in diabetes mellitus. Vitamin D deficiency is an increasing health concern. Studies have shown widespread vitamin D deficiency, and insufficiency is seen in more than half of the world population.

Elevated risk of cardiovascular disease, cancer, and mortality is demonstrated with Vitamin D insufficiency [5]. Vitamin D deficiency has shown to be prevalent in individuals with Diabetes Mellitus (84.2%). Vitamin D, through its effects on the immune system, angiogenesis, and anti-inflammatory effects, play a role in diabetic retinopathy pathology. Additionally, it has been shown that in a mouse oxygen-induced ischemic retinopathy model, the calcitriol is an active metabolite of vitamin D and inhibits retinal neovascularization. [6-7]

NEED FOR THE STUDY

The association of vitamin D deficiency in type 2 Diabetic Mellitus patients with diabetic retinopathy has not yet been clearly established. Few studies state that the Vitamin D levels are unaffected in patients with Diabetic Retinopathy, while few studies state that there is an armed association between Vitamin d deficiency and Diabetic Retinopathy. Moreover, the studies on this subject in the Indian population are quite very few. As the prevalence of Diabetes Mellitus is high in our area, this study is undertaken with an aim to estimate the prevalence of Vitamin D deficiency in Type 2 Diabetic Mellitus patients with diabetic retinopathy and to correlate the Total Vitamin D levels with retinopathy changes.

AIM AND OBJECTIVE OF THE STUDY

The aim of this study is to study on the association between Total vitamin D levels and Diabetic Retinopathy in Type 2 Diabetic Mellitus.

REVIEW OF LITERATURE

I. HISTORY

Eduard Jaeger first observed retinal manifestations of diabetes in 1856. This was possible only after the development of the direct ophthalmoscope in 1855. Albrecht Von Graefe opposed Jaeger's findings and stated no causal relationship between diabetes and retinopathy.

In 1872, Edward Nettleship provided the first histopathological evidence of "Cystoid Degeneration of the Macula" in patients with diabetes in his publication. The proliferative changes occurring in Diabetic Retinopathy and the importance of tractional retinal detachments and vitreous hemorrhages were then described by Wilhelm Manz in 1876.

However, during the early 20th century, the controversy remained regarding whether macular changes were caused by diabetes or hypertension and arteriosclerosis. Arthur James Ballantyne in Glasgow, in the late 20th century, provided further evidence to support the fact that diabetes was the cause for the retinopathy observed in these patients.

II. DIABETES MELLITUS

Definition: Diabetes mellitus is known as a group of metabolic diseases characterized by hyperglycemia chronically resulting from both insulin secretion and insulin action.

Low levels of insulin, insulin resistance of tissues such as skeletal muscles, adipose tissue, and to a lesser extent, liver genes are responsible for these metabolic abnormalities. [8]

A. EPIDEMIOLOGY

In India: There is a worldwide rise in the incidence of diabetes mellitus reaching epidemic proportions in developing countries like India and China. India has about 77

million people affected with diabetes, which makes it the second most affected in the world, after China. One in six people is found to be in India. [9].

Global: According to the International Diabetes Federation (I.D.F.), in 2020, about 463 million people in the world have diabetes, and in Southeast Asia, 88 million people are affected.[10]

When surveyed for diabetic retinopathy, 16.9% of the population were of the age of up to 50 years. The reports state that in the 60-69 years age group, diabetic retinopathy was 18.6%, and 18.3% in the 70-79-years age group, it was 18.3%, with the lowest prevalence of 14.3%in the 50-59-years age group [11].

B. CLASSIFICATION OF DIABETES MELLITUS

Diabetes mellitus is classified into the following categories

1. Type 1 diabetes - β-cell destruction resulting in insulin deficiency.
2. Type 2 diabetes - Defect in insulin secretion & insulin resistance.
3. Gestational diabetes mellitus (G.D.M.) –Diagnosed in the second or third trimester of pregnancy.
4. Specific types of Diabetes – Ex: due to diseases of the exocrine pancreas, chemical-induced diabetes etc. [12].

C. TYPE 2 DIABETES AMERICAN DIABETES ASSOCIATION DIAGNOSTIC CRITERIA

The American Diabetes Association Expert Panel recommends a diagnosis of diabetes Mellitus when one of the following four criteria are met and confirmed with retesting on a subsequent day:

- HbA1c ≥6.5% (<5.7% = normal)
- plasma glucose level 2 hourly ≥200 mg/dL (11.1 mmol/L) with 75-g OGTT

- Random plasma glucose levels ≥200 mg/dl in a patient with symptoms of hyperglycemia, including polyphagia, polyuria, and polydipsia [13].

D. PREVENTION OF DIABETES

a) Indian Diabetes Prevention Program

The Indian Diabetes Prevention Program (I.D.P.P.) is a three-year randomized control trial that employed lifestyle modification and metformin to prevent type 2 diabetes in subjects with impaired glucose tolerance.

It concluded that lifestyle modification and metformin were cost-effective interventions for preventing diabetes among high-risk individuals in India and other developing countries [14].

b) National Diabetes Control Program

The National Diabetes Control Program (N.D.C.P.) was initiated in 1987 in Tamil Nadu, Jammu and Kashmir, and Karnataka. Its objectives included:

- Identify high-risk population
- Introduction of the health education for early measures
- Aim for early diagnosis and treatment.
- Reduction in mortality and morbidity among the high-risks.
- Prevention of ocular metabolic, renal, cardiovascular complications.
- Rehabilitation of the people disabled people due to the disease [15]

E. OCULAR MANIFESTATIONS OF HYPERGLYCEMIA

D.M. can lead to complications such as diabetic retinopathy, diabetic papillopathy, glaucoma, cataract, and ocular surface diseases [16]

a) Lids/Lashes

Individuals with diabetes are generally prone to acute infections of any kind, especially when there is uncontrolled diabetes. The eyelids are more susceptible to infection

and, hence, ulcerative blepharitis and styles are more commonly found in diabetes patients. Good control of diabetes with simultaneous treatment of blepharitis will bring about a quick recovery. Recurrent styes are sometimes the first indications of diabetes and hence should prompt the individual to undergo blood tests [17]. Staphylococcus epidermis was reported to be isolated from the lid margins of nearly all diabetic patients

b) Extraocular muscle abnormalities

The extraocular muscles around the eyeball that help in the eye's normal function are controlled by the 3rd, 4th, and 6th nerves, which can be affected due to high blood sugar leading to nerve palsy. Nerve palsies due to diabetes recover completely if blood sugar is normalized. However, the recovery period may vary from 3-6 months [18]

c) Conjunctiva

Diabetic patients are at the risk of developing conjunctival bacterial infections, including acute infectious conjunctivitis. Conjunctival pathological changes were noted in up to 86% of diabetic patients. These changes included squamous metaplasia and a reduced goblet cell density [19]

d) Cornea

D.M. can trigger acceleration of ocular surface abnormalities, which have been termed diabetic keratopathy. It includes various symptomatic corneal conditions, such as punctate keratopathy and persistent corneal epithelial defect [20]. Corneal abrasions in diabetic patients result in deeper damage t with some even leading to detachment of the basement membrane.

e) Iris

One of the most deleterious effects on the iris is neovascularization. It is often present around the pupillary margin, but in advanced cases, it may involve the angle of the anterior chamber and even the whole of the iris [21]. These changes result in neovascular glaucoma.

f) Pupil

Diabetic pupils tend to be more miotic [22]. Loss of nerve terminals from the dilator muscle was shown in histological studies [23]. Surgically induced miosis following phacoemulsification was found to be much more pronounced in diabetic patients.

g) Changes in Refraction

Duke-Elder had earlier reported a shift towards myopia or hyperopia in association with hyperglycemia or hypoglycemia, respectively [24]. Recent studies have reported that the change in diabetic patients was more commonly towards hyperopia, primarily upon initiation of treatment.

Wiemer *et al*. reported on the effect of diabetes on the refractive power of the posterior part of the cornea; since this change did not affect total corneal power, it remains most likely that the refractive changes seen in diabetic patients are due to lens changes [25].

In addition to refractive changes, recent onset diabetic patients also exhibit changes in accommodation. Waite and Beetham studied paralysis of accommodation in 21% of diabetic patients, most commonly in between 20 followed by 50 years of age group [26].

h) Changes in Lens

Cataracts are a known cause of visual impairment in diabetic patients. As reported by **Framingham Eye Study**[27] there is up to a twofold increase in patients over 65 years of age and fourfold increase in the prevalence of cataracts in diabetic patients younger than 65 years of age and **The Blue Mountains Eye Study** has shown that the impaired fasting glucose, in the absence of clinical diabetes, is also leads to the development of cortical cataracts[28] .Deposition of advanced glycation end products in the lens is one possible mechanism for diabetic cataracts. [29]

The following are the hypotheses that explain lens changes in diabetics

1. The first mechanism is increased flux mediated by aldose reductase.
2. The second mechanism is glucose-mediated activation of a specific isoform of protein kinase C that results in early-onset cataracts in diabetics.
3. The third mechanism is an increase in the production of advanced glycation end products (A.G.E.s), which are produced by the non-enzymatic reaction of aldehydes such as glucose [30].

i) Retina

Diabetic retinopathy is a microvascular complication in both types of Diabetes mellitus. The damage observed in diabetic retinopathy is through the formation of advanced glycosylation end products and increased metabolism through the sorbitol and hexosamine pathway leading to increased production of several growth factors such as vascular endothelial growth factor (VEGF), aggravating the disease process. The incidence of D.R. is related primarily to duration and control of diabetes and is related to hyperglycemia, increased blood pressure, lipid levels, pregnancy and renal pathology. [31].

Diabetic retinopathy (D.R.) is microangiopathy affecting all of the smaller retinal vessels and is characterized by increased vascular permeability, retinal hemorrhages, exudations, due to the formation of newer vessels on the posterior vitreous surface and the retina [32].

III. BASIC ANATOMY

The retina forms the inner coat of the eyeball, where the optical system of the eye forms the optical image.

The macula measures approximately 5.5 mm in diameter and is centered between the optic nerve head and the temporal vascular arcades.

The 1.5 mm of the macula centrally, the fovea is specialized for colour vision and high spatial acuity. At the center of the foveola, there is a depression known as unborn, measuring 150–200 μm in diameter.

A region devoid of retinal vessels within the fovea is known as the foveal avascular zone (F.A.Z.).

Surrounding the fovea is the parafovea is the thickest, 0.5 mm in width.

a) Optic Disc

It is about 1.5 mm in diameter. All the retinal layers except the nerve fiber layer end here. It is insensitive to light due to the absence of photoreceptors and is hence called the blind spot. The retina outside the macula, known as the extra-areal periphery, is commonly divided into a few concentric regions, starting with the near periphery, a 1.5-mm ring peripheral to the temporal major vascular arcades.

The equatorial retina is the retina around the equator, and the region anterior to the equatorial retina is called the peripheral retina. In the far periphery, the border between the retina and the pars plana is called the Ora Serrata.

b) Histology

The layers of the retina from the inner to the outer retina are listed here:

1. Internal limiting membrane (I.L.M.)
2. Nerve fiber layer
3. Ganglion cell layer
4. Inner plexiform layer (I.P.L.)
5. Inner nuclear layer (I.N.L.)
6. Middle limiting membrane (M.L.M.)
7. Outer plexiform layer (O.P.L.)
8. Henle fiber layer (HFL)
9. 9.Outer nuclear layer (O.N.L.; the nuclei of the photoreceptors)
10. 10.External limiting membrane (E.L.M.)
11. Rod and cone inner segments (I.S.)

12. Rod and cone outer segments (O.S.)

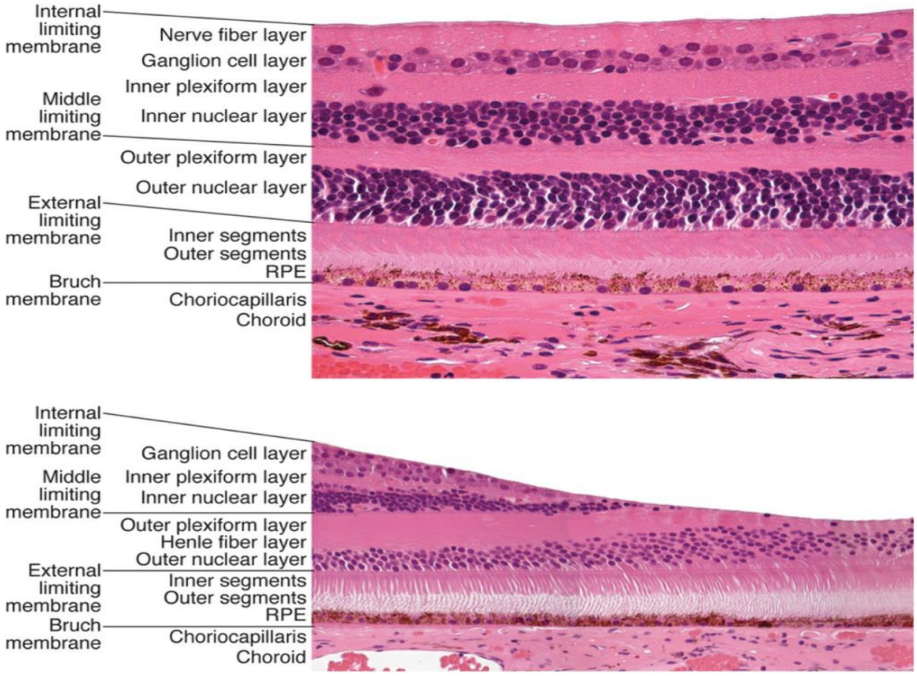


Figure 1. Schematic Cross-section of Retina Demonstrating Layers of Retina

c) Retinal Vasculature and Oxygen Supply

The vascular supply of the retina comes from the retinal circulation for the inner retina and indirectly from the choroidal circulation for the avascular outer retina. The central retinal artery enters the eye and divides into four branches, each supplying blood to a quadrant of the retina. Occasionally, a cilioretinal artery, derived from the ciliary circulation, will supply a portion of the inner retina.

On a tissue level, the retina is supplied by up to 4 layers of vessels:

I. Radial peripapillary capillary network located in the nerve fiber layer and around the optic nerve head,

II. Superficial vascular plexus in the retinal ganglion cell layer,

III. The deep capillary plexus with two capillary beds, one on either side of the I.N.L

The Outer Lamina consists of four layers: the pigment epithelium, the rods and cones, the external limiting membrane, and the outer nuclear layer supplied by the choriocapillaris.

The Inner Lamina comprises the remaining six layers, namely the outer plexiform layer, inner nuclear layer, ganglion cell layer, nerve fiber layer, and the internal limiting membrane supplied by the central retinal artery and veins.

The outer plexiform layer is supplied partially by the choriocapillaris and partially by the central retinal artery.

d) Retinal Pigment Epithelium

The Monolayer of pigmented cells is RPE, derived from the outer layer of the optic cup. This layer is continuous with the pigment epithelium of the ciliary body and iris.

Each RPE cell has an apex and base; the apical portion envelops the outer segments of the photoreceptor cells with villous processes.

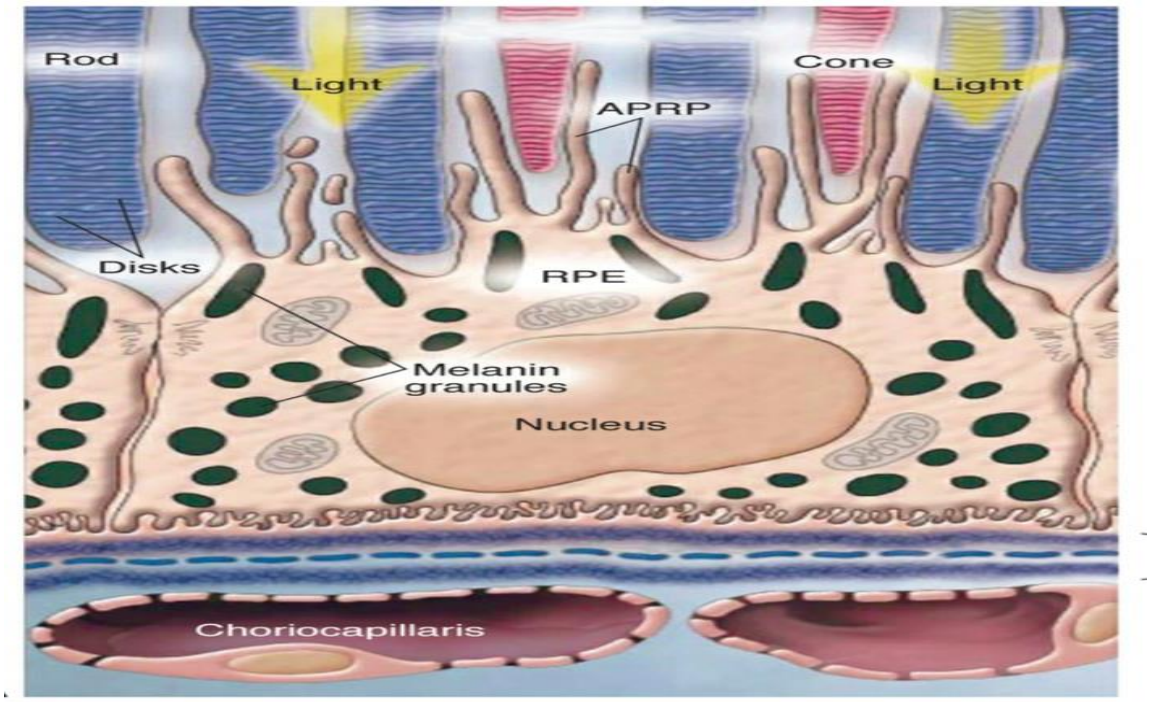


FIG 2. The RPE and its relationship to the photoreceptors and Bruch membrane.

The RPE contributes to retinal function in several ways; it:

- absorbs light
- phagocytoses rod and cone outer segments

- participates in the retinal and polyunsaturated fatty acid metabolism
- maintains the subretinal space
- heals and forms scar tissue
- regenerates and recycles visual pigment

e) Blood Retinal Barrier

The normal retinal capillaries are lined by endothelial cells bound together by intercellular junctions of the zonula occludens type. The free flow of solutes and fluids from the retinal vasculatures into the interstitium is prevented by these junctions, constituting the blood-retinal barrier.

In diabetes, this blood-retinal barrier is compromised, leading to the characteristic changes observed in diabetic retinopathy.

IV. DIABETIC RETINOPATHY

❖ RISK FACTORS OF DIABETIC RETINOPATHY

- **Non-modifiable**: Duration of Diabetes, Genetic Factors, Gender
- **Modifiable:** Glycaemia, Blood Pressure, and Lipid Levels.
- **Others:** Carotid arterial disease, pregnancy, renal impairment, and smoking.

a) **Non-Modifiable Factors**

- **Duration**

Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR) was the direct association of an increased prevalence of diabetic retinopathy with a longer duration of diabetes mellitus in patients with both type 1 and type 2 diabetes mellitus.

In the WESDR cohort, after 20 years of diabetes mellitus, nearly 99% of patients with type 1 and 60% with type 2 disease demonstrated some degree of diabetic retinopathy.

Proliferative diabetic retinopathy was found in 50% of type 1 patients who had 20 years' duration of disease and in 25% of type 2 patients who had 25 years' duration of disease [33].

- **Gender**

Men was observed with increased incidence of PDR with an earlier onset of diabetes than women in the WESDR study. But besides this, no difference in the prevalence or progression of retinopathy was observed between both genders in the WESDR study [33]. PDR was found in 33% and 50% of women and men, respectively, following a 20-year duration of diabetes.

- **Genetics**

Genetic factors may influence either the onset or the severity of DR. In fact, heritability estimates ranging from 25% to 50% have been reported for proliferative DR [34]. Patients with HLA DR 4 and DR 5 phenotypes have been found to have an increased risk of proliferative diabetic retinopathy.

Genome-wide association studies (GWAS) in various populations identified 70 loci associated with type 2 diabetes and revealed positive linkage of many mutations and SNPs that influence the expression and physiological impact of the related proteins and risk to develop type 2 diabetes [35].

b) **Modifiable Factors**

- **Glycemia**

The trial research group showed that for type 1 diabetic patients, a 10% reduction in the hemoglobin A1c (HbA1c) was associated with a diminution in the improvement of DR in the rigorous and traditional treatment group, respectively [36].

Diabetes Control and Complications Trial (DCCT) [37] and the **United Kingdom Prospective Diabetes Study (UKPDS)** have demonstrated the cost-effectiveness and efficacy of glycaemic control in reducing the incidence and progression of retinopathy. However, data from these and other studies have confirmed the difficulty to achieve and maintain good glycaemic control over a long period [38].

According to the Diabetic Control and Complications Trial (DCCT), a 10% decrease in HbA1c results in a decline in the incidence of diabetic retinopathy by 35% to 40%. The confirmation of the value of good glycaemic control in type 2 diabetes was obtained in the ACCORD Eye study where reduction of HbA1c from mean 58 to 46 mmol/mol was associated with reduced primary outcome (3-step increase on the ETDRS scale or development of proliferative retinopathy requiring photocoagulation or vitrectomy) from 10.2% to 6.5% and progression of retinopathy was reduced by 42% [39].

- **Blood Pressure**

In people with diabetes, increased blood pressure has been hypothesized as the effects of increased blood flow damage the retinal capillary endothelial cells [40].

The UKPDS showed that the increased incidence of retinopathy was associated with systolic blood pressure [41].

The UKPDS showed that a reduction of mean systolic blood pressure from 154 to 144 mmHg reduced microaneurysm count at 4.5 years follow up, reduced hard exudates and cotton-wool spots at 7.5 years, and was associated with less need for photocoagulation and less deterioration of 2-step or more on the ETDRS retinopathy scale [42]

- **Lipid Levels**

Consider statins in secondary prevention of macrovascular disease as well as in primary prevention, Ezetimibe for patients intolerant of statins adding fenofibrate to a statin for non-proliferative retinopathy in type 2 diabetes [43].

In the ETDRS, high levels of serum lipids at baseline were associated with an increased incidence of hard exudates at the macula and decreased visual acuity.

c) **Other Factors**

- **Pregnancy**

Pregnancy is a risk factor for the retinopathy progression and severity of retinopathy compared to non-pregnant diabetic women.

Human placental lactogen (HPL) has a very important role in the effect of pregnancy on DR due to its enormous production and growth hormone-like activity. Hyperdynamic circulatory state during pregnancy which potentially inflicts additional shear and stress and cause endothelial damage at the capillary level [44].

- **Smoking**

Smoking may be important in some patients with Type 1 diabetes, as smoking has been shown to be associated with microangiopathy when complications occur early in the course of type 1 diabetes [45]

❖ PATHOGENESIS OF DIABETIC RETINOPATHY

▪ Anatomical

a) Capillary basement membrane thickening

b) Electron microscopy has proved marked thickening of the basement membrane, with swiss-cheese-like vacuolization and deposition of fibrillar collagen, which stains positive for type III collagen.

c) Loss of microvascular intramural pericytes

d) In digest preparation, they have been noted as empty, balloon-like spaces bulging from the side of the capillary wall. This is probably related to the action of the sorbitol pathway.

e) C. Loss of endothelial cells and endothelial cell dysfunction

f) The endothelial cell junctions become loose, which could be related to the reduced expression of ZO-1 protein. Fenestrations appear in the endothelial cell cytoplasm.

- **Biochemical mechanisms in the pathogenesis of diabetic retinopathy**

Patients with DM develop microvascular abnormalities in the retinal vasculature, renal glomeruli, and vasa vasorum of the peripheral nerves.

Chronic hyperglycemia decreases the production of neuronal cell and endothelial trophic factors, leading to edema, ischemia, and hypoxia-driven neovascularization. (46)

In non-diabetic patients, endothelial dysfunction begins with atherosclerosis, whereas in diabetic patients, initiation seems to involve insulin resistance.

The mechanism of hyperglycemia-induced microvascular damage was studied by four hypotheses. These are:

a. Increase in polyol pathway flux

b. Advanced glycation end products accumulation (AGEs)

c. Activation of protein kinase C (PKC)

d. Increased hexosamine pathway flux

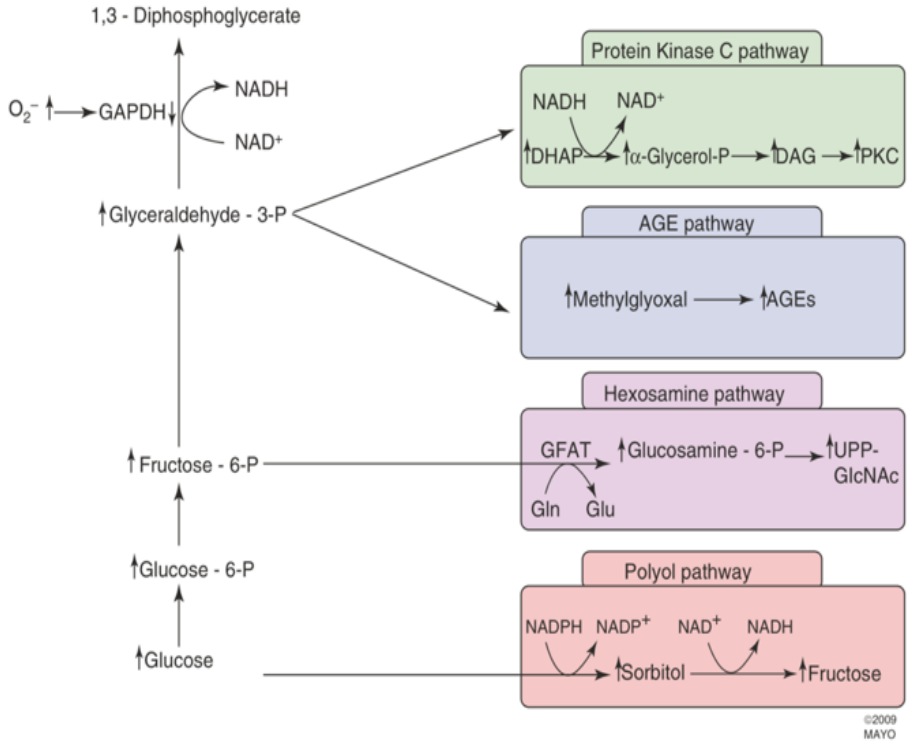


FIG 3. Hyperglycemia dysregulates four biochemical pathways.

a. Increased Polyol Pathway Flux

Aldose reductase during hyperglycemia glucose is converted to sorbitol with decreases in NADH. With reconstitution of NADH, sorbitol is subsequently oxidized to fructose. Sorbitol oxygenation inhibits glyceraldehyde-3-aldehyde dehydrogenase (GAPDH) activity thus increasing concentrations of triose phosphate, and the formation of methylglyoxal and diacylglycerol (DAG) [47].

Reduction of glucose to sorbitol consumes NADPH, worsening oxidative stress.

b. Advanced Glycation End Products (AGEs)

AGE formation is promoted by intracellular hyperglycemia, which is found in increased concentrations in glomeruli and diabetic retinal blood vessels [48].

AGE precursors modify critical proteins and alter their functions. These change extracellular matrix components and integrins, modifying plasma proteins that bind to AGE receptors.

Cross-linking induced by advanced glycation end product-expands the molecular packing of collagen type 1 and changes the composition of collagen type IV in basement membranes, thereby altering the function of blood vessels [(49)].

c. Activation of Protein Kinase C (PKC)

PKC isoforms are activated indirectly by hyperglycemia ligating AGE receptors [and increasing activity of the polyol pathway [(50)]. Activation of PKC-β isoforms decreases nitric oxide production and increases endothelin-1 activity to mediate blood flow abnormalities in the retina and kidney

A PKC-β-specific inhibitor reduces retinal activity, reverses the diabetes-induced increase in retinal mean circulation time [(51)].

d. Increased Hexosamine Pathway Flux

Excess flux induced through the hexosamine pathway leads to the activation of genes that lead to vascular endothelial dysfunction and several other changes that are seen in diabetic retinopathy.

Hyperglycemia-induced increase in gene transcription mediated by increased hexosamine pathway flux is unknown, but the covalent modification of the transcription factor Sp1 by N-acetylglucosamine (G1cNAc) explains the relation between the hexosamine pathway and hyperglycemia-induced changes in the transcription of the gene for PAI-1[(52)].

❖ PATHOGENESIS OF DIABETIC MACULAR EDEMA

A. Break down of blood retinal barrier

It may be due to either damage of the junctional complexes between RPE cells and capillary endothelial cells or changes in the cells' membrane state or pumping capacity.

Proposed mechanisms that cause leakage have included the development of fenestrations across the endothelial cell cytoplasm, increased transcellular transport via vesicles, and increased infolding of the RPE that promotes choroidal to subretinal space transudation[53] .

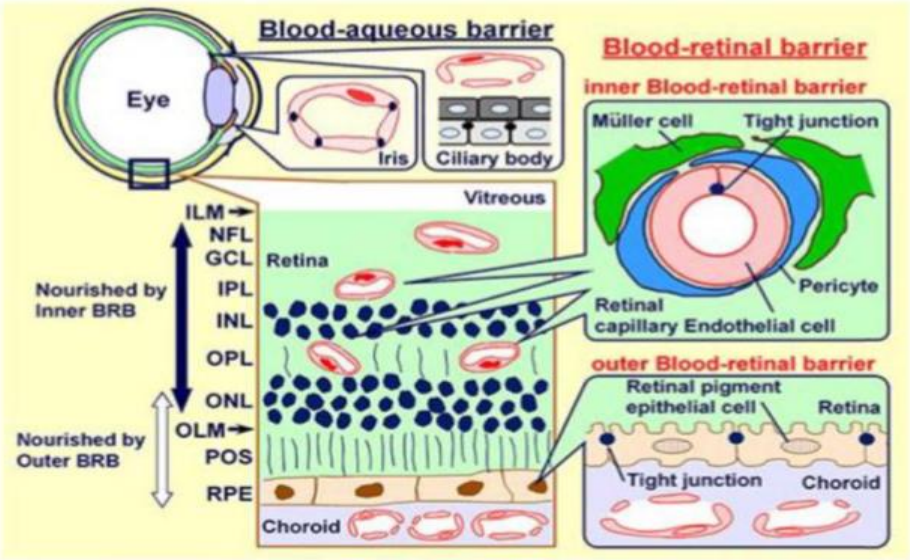


FIG 4. Breakdown of blood retinal barrier

B. Role of vasoactive factors

I. Vascular endothelial growth factor-A

II. Protein kinase C

III. Histamine

IV. Angiotensin II

V. Matrix metalloproteinases

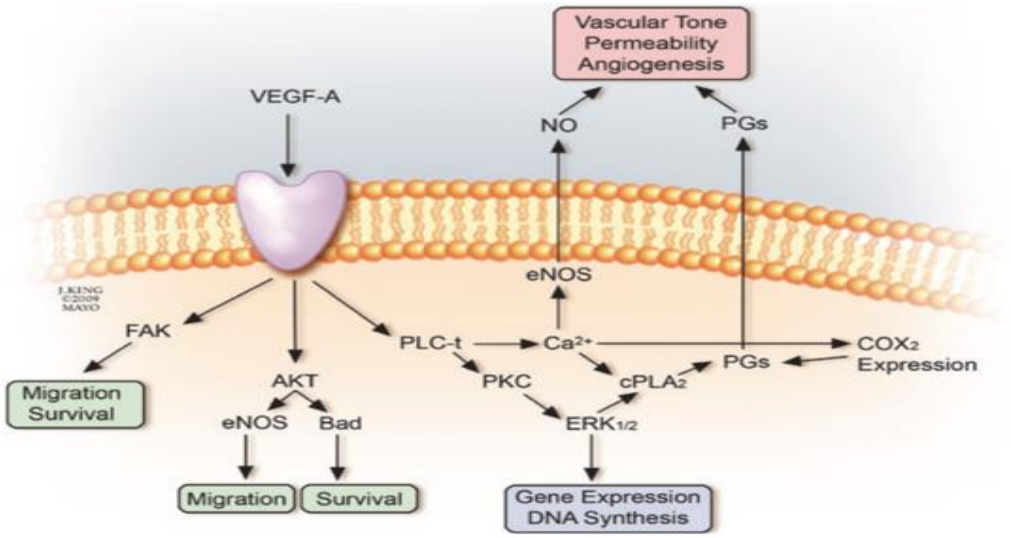
VI. Pigment epithelium-derived factor.

- VASCULAR ENDOTHELIAL GROWTH FACTOR

Vascular endothelial growth factor increases vascular permeability through several mechanisms (Fig.5)

First, it stimulates inositol triphosphate (IP3), which releases intracellular calcium and relaxes vascular smooth muscle.

Secondly, VEGF stimulates DAG production, which increases cellular permeability directly through DAG-sensitive Ca2+ channels. Thirdly, increased synthesis of DAG



activates PKC [54].

FIG 5. Vascular endothelial growth factor-A binds to transmembrane receptors.

- PROTEIN KINASE C

In the pathogenesis of diabetic BRB breakdown, Protein kinase C belonging to the family of serine/threonine protein kinases has been implicated through three ways:

Its effect is mediated via VEGF-A. In a transgenic mouse model, the regulation of VEGF-A gene expression has been shown to be controlled and enhanced by PKC-β.

Secondly, by oxidative stress through ROS produced by hyperglycemia or advanced glycation end-products (AGEs), PKC can be activated.

Thirdly, Phosphorylation of tight junction-associated proteins to induce BRB breakdown is triggered by PKC [55].

- HISTAMINE
  - Vascular endothelial cells of the retina are very sensitive to histamine.
  - Reduces the ZO1 protein expression.
- RENIN/ANGIOTENSIN SYSTEM

Angiotensin exerts significant effects on vascular smooth muscle cells, including growth, proliferation, and the deposition of extracellular matrix proteins.

These are mediated by factors such as TGF-β1, PDGF, VEGF, insulin-like growth factor, and connective tissue growth factor [56].

The pro-angiogenic effect of angiotensin II on mammalian retinas with oxygen-induced retinopathy is mediated by VEGF. Pharmacologic blockade of the RAS decreases angiogenesis by downregulating VEGF and VEGFR2[57].

Angiotensin II levels elevation correlate with vitreous VEGF concentrations in patients with diabetic macular edema. Evidence from studies suggests that this may be mediated through the AT1-R/NF-κB pathway, which creates new target sites for the prevention of diabetic retinopathy [58].

❖ CLINICAL FINDINGS OF DIABETIC RETINOPATHY

Vascular dysfunction and decreased perfusion remain the hallmarks of diabetic retinopathy, a growing body of evidence suggests that neuroretinal function is compromised, probably before overt vascular changes are seen.

- MICROANEURYSM

The earliest ophthalmoscopically visible signs of diabetic retinopathy are usually retinal capillary microaneurysms. These represent saccular dilations of the capillaries and appear as dark red or white fundus spots varying in diameter from 25 to 100 μm.

The mechanism for microaneurysm formation is unknown. Possible contributing factors may include alterations in the retinal microenvironment from metabolic effects on neurons, glial cells, and endothelial cells; endothelial cell injury secondary to leukostasis.

Fluorescein angiography reveals perfused microaneurysms as discrete hyperfluorescent spots with early pooling of dye followed by late leakage.

- RETINAL HAEMORRHAGES

Retinal hemorrhages can be either "flame-shaped," which generally occurs within the nerve fiber layer and arises from the superficial capillary plexus, or "dot and blot," which occurs within the spaces between the vertical-oriented axons the inner plexiform layer and arise from the deep capillary plexus. Hemorrhages usually indicate a more serious form of DR than do microaneurysms.

- HARD EXUDATES

Hard exudates are small white or yellowish-white deposits with sharp margins. In the OPL or Henle fiber layer, the exudates are seen pathologically as fat-filled (lipoidal) histiocytes. Massive exudation contains foamy histiocytes in the OPL. The concentration of exudates around diseased vessels causes a circular pattern called circinate retinopathy.

- SOFT EXUDATES

Cotton-wool spots occur in the nerve fiber layer and under the ILM. Cotton-wool spots are indicative of backup of axoplasmic flow. Histopathologically, the cotton-wool spots are cytoid bodies and are the swollen ends of ruptured axons in the nerve fiber layer in the infarcted area, just under the ILM

- INTRARETINAL MICROVASCULAR ANOMALIES (IRMA)

Intraretinal microvascular abnormalities (or IrMAs) are shunt vessels and appear as abnormal branching or dilation of existing blood vessels (capillaries) within the retina that act to supply areas of non-perfusion in diabetic retinopathy.

These vessels represent either new vessel growth within the retina or remodeling of pre-existing vessels through endothelial cell proliferation stimulated by hypoxia bordering areas of capillary nonperfusion.

The mechanism for the development of IRMA is a variant of collateral formation and may be seen in association with localized arteriolar occlusion and cotton wool spots. Cotton wool spots (CWS) and intraretinal microvascular abnormalities (IRMA) are usually associated with early retinal ischemia

- OPTIC DISC CHANGES

Swollen optic discs (diabetic papillopathy) is seen in diabetic patients with poor correlation to retinopathy levels.

Diabetic papillopathy need to be differentiated from ischaemic optic neuropathy and neovascularisation(NVD).

- RETINAL NEOVASCULARIZATION

Advanced retinal ischemia leads to the development of retinal neovascularization. New vessels sprout from pre-existing retinal (neovascularization elsewhere or NVE) or disc (neovascularization of the disc or NVD) vessels and grow along the scaffold provided by the posterior hyaloid surface.

The amount of blood vessel growth generally correlates with intraocular VEGF levels. New vessel growth defines proliferative diabetic retinopathy (PDR) though patients may also display all the characteristics of nonproliferative diabetic retinopathy, including diabetic macular edema.

- VITREO-RETINAL INTERFACE ANGIOGENESIS

New vessels grow between the posterior hyaloid face of the vitreous gel and the inner surface of the retina, which is most strongly adherent to the pars plana. They are usually asymptomatic. The symptoms arise from complications that occur because of the dynamic

interaction at the vitreoretinal interface. The interaction results in an inflammatory response and scar formation, elevating the new vessel off the retinal surface. Further contraction can cause vitreous hemorrhage, and it may lead to traction retinal detachment.

- RETINAL DETACHMENTS

Tractional retinal detachment may occur, the extent and location of which depends on vitreoretinal attachments.

❖ CLASSIFICATION OF DIABETIC RETINOPATHY

There are mainly two types of classification:

1. ETDRS CLASSIFICATION OF DIABETIC RETINOPATHY

"Disease severity level	**Findings observable upon dilated ophthalmoscopy**
MILD NPDR	At least one microaneurysm, and definition not met for Moderate NPDR. These patients have a 5 % risk of progressing to PDR within 1 year and a 15 % risk of progressing to high-risk PDR within 5 years
MODERATE NPDR	Hemorrhages and/or microaneurysms >/= standard photograph 2A; and/or soft exudates, venous beading, or intraretinal microvascular abnormalities definitely present; and definition not met for severe NPDR The risk of progression to PDR is 12-27 % within 1 year and 33 % within 5 years.
SEVERE NPDR	The 4-2-1 rule; one or more of: · Severe hemorrhages in all 4 quadrants · Significant venous beading in 2 or more quadrants · Moderate IRMA in 1 or more quadrants The risk of developing PDR is 52 % within 1 year and 60 % within 5 years.
VERY SEVERE NPDR	Two or more of the criteria for severe NPDR. The risk of developing PDR is 75 % within 1 year.
EARLY PDR	New vessels; and definition not met for high-risk PDR

HIGH RISK PDR	New vessels on or within one disc diameter of the optic disc (NVD)>/= standard photograph 10A with or without vitreous hemorrhage or pre retinal hemorrhage; or vitreous and/or preretinal hemorrhage accompanied by new vessels, either NVD<standard photograph 10A or new vessels elsewhere (NVE)>/= one quarter disc area"

Table 1. ETDRS Classification of Diabetic retinopathy

Clinically significant macular oedema (CSME) was defined in ETDRS as:

- Retinal thickening within 500 microns of the centre of the macula.
- Exudates within 500 microns of the centre of the macula, if associated with retinal thickening (which may be outside the 500 microns).
- Retinal thickening one disc area (1500 microns) or larger, any part of which is within one disc diameter of the centre of the macula.

2. MODIFIED AIRLIE HOUSE CLASSIFICATION

Seven standard photographic fields are shown for the right eye. Field 1 is centered on the disc, field 2 on the macula, and field 3 temporal to the macula so that its nasal edge passes through the center of the macula. Fields 4 to 7 are tangential to a vertical line passing through the center of the disc and to horizontal lines passing through its upper and lower poles.

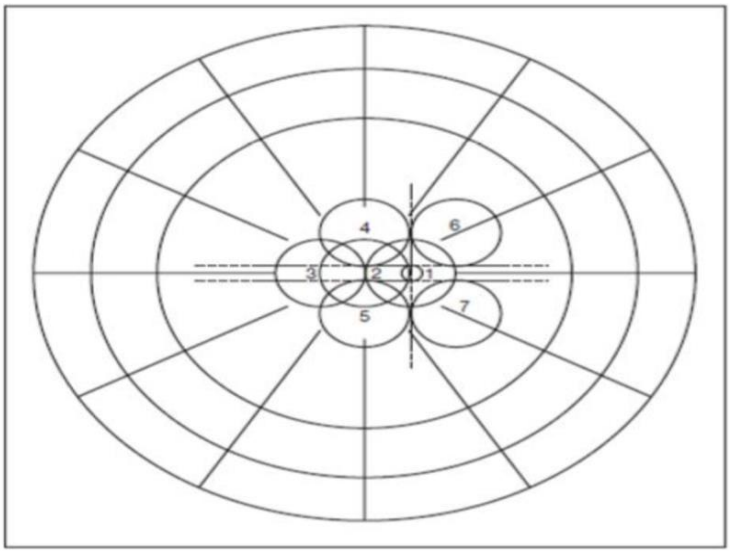


Fig6.: Modified Airlie House Classification

❖ **ETDRS RECOMMENDATION FOR FOLLOW-UP**

"CATEGORY	FOLLOW UP
No Diabetic Retinopathy	Review in 12 months
Mild NPDR	Review range of 6-12 months, depending stability, severity and associated systemic features
Moderate NPDR	Review in approximately 6 months
Severe NPDR	Review in 3 months
Very severe NPDR	Review in 2-3 months
Early PDR	Treatment considered according to stability, severity and associated systemic factors. If the patient is not treated, review in 2 months
High risk PDR	Treatment should be performed immediately if possible"

Table 2: ETDRS recommendation for followup in DR

❖ **DIAGNOSTIC TESTING**

(a) DIRECT OPHTHALMOSCOPE

In 1851, Helmholtz invented the first direct ophthalmoscope. The direct ophthalmoscope allows a highly magnified, monocular image of the retina and optic disk. The fundus is viewed through a tiny peephole located just above the illumination source of the instrument, producing an upright virtual image.

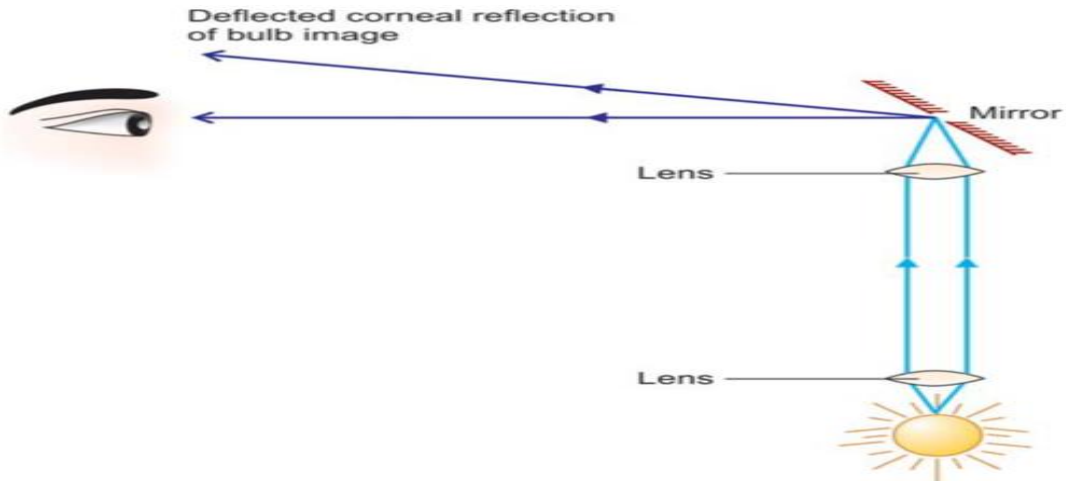


Fig 7. Ray diagram of the optics of the direct ophthalmoscope

(b) INDIRECT OPHTHALMOSCOPE

Introduced by Schepens, binocular indirect ophthalmoscopy offers an excellent resolution of fundus details. The binocular indirect ophthalmoscope provides a brightly illuminated, wide-angle, and stereoscopic view of the retina.

The power of the lens depends upon the magnification used and the refraction of the eye.

- 15D lens (magnifies four times and field is about 40°) is used
- for examination of the posterior pole.
- 20D lens (magnifies three times and field is about 45°) is most
- commonly used for the general overall examination of the
- fundus.
- 30D (magnifies 2.5 times and field is 60°) has a shorter
- working distance and is useful when examining the patient
- with small pupils.
- 40D lens (magnifies 1.5 times and field is about 65°) is
- used mainly to examine small children.
- Panretinal 2.2 lens magnifies three times, and the field observed is about 55°

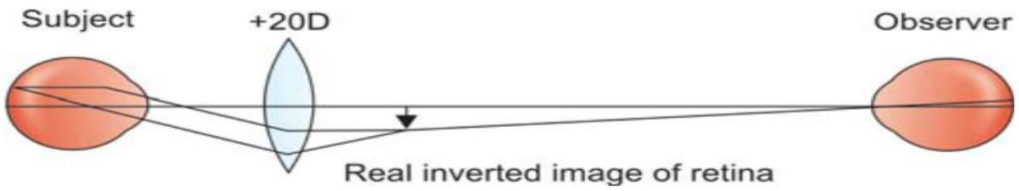


Fig.8. Ray diagram of the optics of the indirect ophthalmoscope

(c) FUNDUS PHOTOGRAPHY

The digital fundus camera is a low-power microscope specialized with a camera attached. The optical design of the camera is similar to the monocular indirect ophthalmoscope principle.

I. The fundus camera provides a magnified upright view of the fundus.

II. In color fundus photography, the retina is examined in full color and illuminated by white light.

III. Red colors are removed by filtration of imaged light, which improves the contrast of vessels and other structures in red-free photography. It shows small hemorrhages, microaneurysms, and hard exudates with more clarity than color fundus photos.

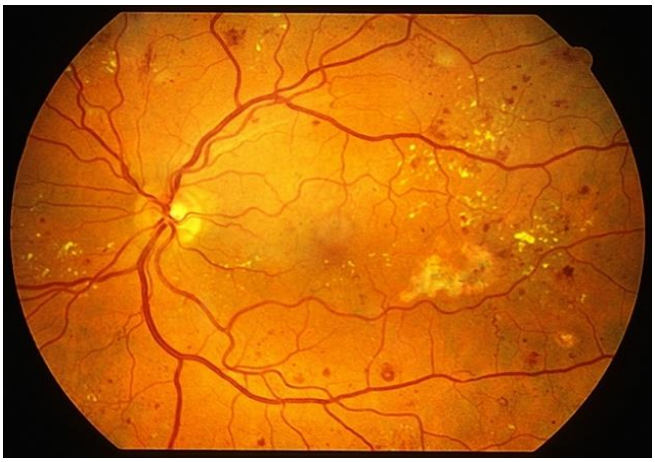


Fig 9. Fundus photography of Severe NPDR

(d) SEVEN STANDARD DIABETIC PHOTOGRAPHIC FIELDS

This is a technique of taking photos in a series using a digital fundus camera. A 35-degree field of view is utilized.

The fields are centered as follows:

The optic nerve is centered -Field 1.

The macula -Field 2;

Temporal to the macula -Field 3;

Superotemporally- Field 4, excluding the optic disc;

Inferotemporally- Field 5, excluding the optic disc;

Superonasally along the arcades- Filed 6, excluding the optic Inferonasally- Field 7, excluding the optic disc.

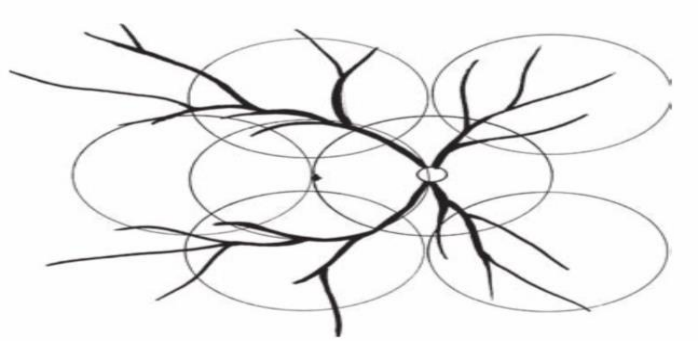


FIG 10. Diagram of seven standard photographic fields.

(e) FLUORESCEIN ANGIOGRAPHY

In FA, through intravenous injection of a fluorescent dye, the vessels are brought into high contrast. With an excitation color, the retina is illuminated, which fluoresces the light of another color.

By using a filter, the excitation color is excluded, and by passing the fluorescent stain, a higher contrast of the vessels is produced. Photos of the timed sequence show the dye's progression into the vessels reveals the flow dynamics and the different layers of the retina. Thus, different areas of the retinal architecture are delineated.

Clinical Applications of Fluorescein Angiography

Macular edema and non proliferative diabetic retinopathy and to evaluate areas of

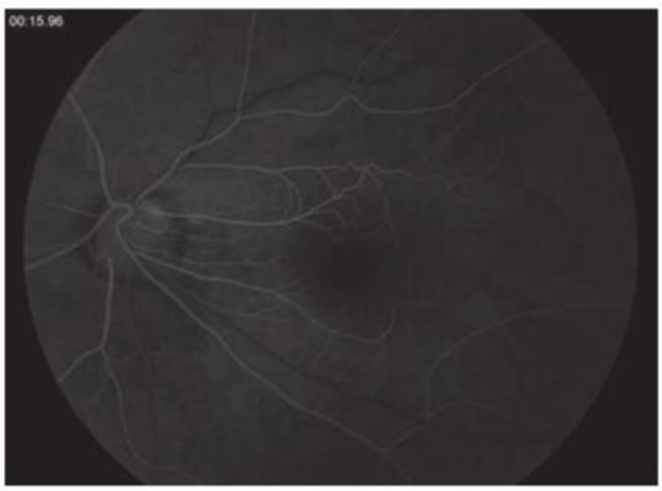


FIG 11 Fluorescein angiogram sequence, AVphase and progressing to midtransit.

capillary nonperfusion. Neovascularization of the retina elsewhere would also be identified. Fluorescein angiography is also useful to monitor macular edema post-laser.To evaluate the progression and resolution of residual macular edema, comparison photographs and angiographic frames from previous examinations can be used

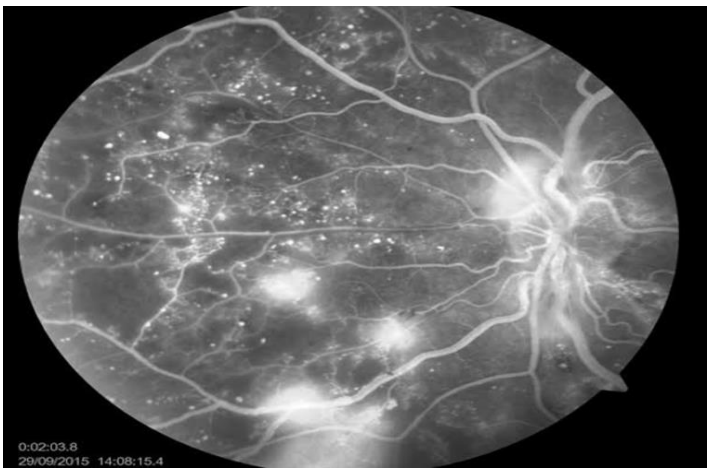


FIG 12. FFA IN PDR

(f) INDOCYANINE GREEN ANGIOGRAPHY

Indocyanine green dye angiography (ICG) is a method to capture the flow of the dye in the choroid. In approximately 15% of patients with nonproliferative diabetic retinopathy, ICG can reveal additional microvascular complications in diabetes not seen with conventional fluorescein angiography

Clinical Applications of Indocyanine Green Angiography

ICG is used to follow in patients with choroidal lesions or those patients with diabetes with an abnormal presentation of diabetic retinopathy.

(g) OPTICAL COHERENCE TOMOGRAPHY

OCT is based on white-light interferometry.

This ophthalmic imaging technique measures low-coherence interferometry.

It enables detection and quantification of macular edema and vitreomacular traction. The central macular thickness is used routinely to guide the decisions regarding the treatment modalities. The visual acuity may not correlate with OCT findings.

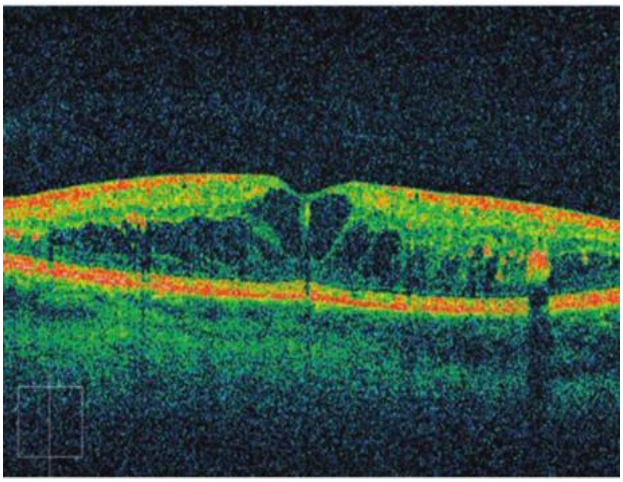


FIG 13. Oct scan of macular edema

(h) ULTRASOUND

Ultrasound is used for the examination of diabetic patients with opaque media. The anterior vitreous base in vitreous hemorrhages can be evaluated with ultrasound. Determining retinal detachment status or the retina integrity in a diabetic patient with a dense cataract or severe vitreous hemorrhage requires an ultrasound. Sometimes, the ultrasound can be deceiving in the cases of a dense vitreous hemorrhage and blood on the hyaloid face. The resulting ultrasound may mimic a retinal detachment. Thus, it is essential to change the decibel status by going higher on the decibel switch and having the patient look in the six cardinal positions to create a dynamic ultrasound picture of his posterior pole.

Ultrasounds can be used to follow diabetic patients with a vitreous hemorrhage if there is a worsening of vision or a new appearance of traction retinal detachment on successive B-scans

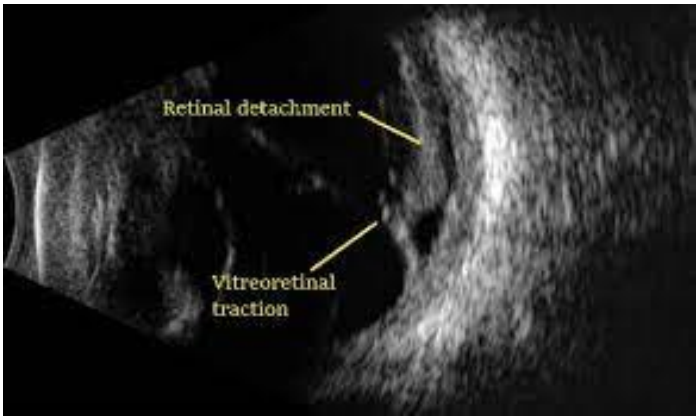


Fig 14. B scan image of Tractional RD

IV. VITAMIN D

Vitamin D is a fat-solute multifunctional metabolite required for humans' growth and development. There are two effective forms of vitamin D: vitamin D2, found in plants and better known as ergocalciferol (or calciferol), and vitamin D3, found in animal tissues and often referred to as cholecalciferol.

Vitamin D is essential for many physiologic processes, and vitamin D insufficiency is seen in more than half the world's population at risk and has reached pandemic proportions.

Compared to 1,25(OH)2D3 serum, 25(OH)D3 level is a better indicator of vitamin D status since the former has a slower clearance rate than the latter [(59)].

Vitamin D insufficiency has been related to the development of diabetes and also correlated with an elevated risk of cardiovascular disease, cancer, and mortality.

Vitamin D may play a role in the pathogenesis of diabetic retinopathy through its effects on the immune system and on angiogenesis which is discussed later.

a) CLINICAL APPLICATIONS

- **Skeleton**

Vitamin D deficiency may cause bone-deforming disease rickets during development, while in adults, it may cause osteomalacia and disturbed muscle metabolism owing to impairment in calcium balance.

These effects have also been observed in patients with type 2 diabetes, who may exhibit mineral and vitamin D metabolism abnormalities that can eventually produce osteopenia.

Xue *et al*. studied those humans and mice lacking a VDR (Vitamin D Receptor), or CYP27B1, develop rickets, which can be prevented by a diet high in calcium and lactose to increase calcium absorption by infusions of calcium and phosphate [(60)].

Vitamin D appears to have effects on bone remodeling and development directly and indirectly.

- **Parathyroid gland**

The inverse relationship between circulating 25OHD levels and parathyroid hormone levels is well established, and it is due to the ability of PTG to produce its own 1,25(OH)2D. Treatment of secondary hyperparathyroidism in CKD approves several 1,25(OH)2D and 1,25(OH)2D analogs.

PTH levels are a marker for vitamin D sufficiency. The maintenance of sufficient levels of 25OHD will reduce the risk for parathyroid gland hyperplasia and elevated PTH secretion with its potentially harmful effects on bone.

- **Skin**

Psoriasis is a disorder of hyperproliferation and decreased or abnormal differentiation driven by an abnormal immunologic component.

Bikle *et al*. proved the successful use of 1,25(OH)2D and its analogs is due to their ability of proliferation inhibition, stimulation of the differentiation, and suppression of the immune activity associated with this disease [(61)].

The 1,25(OH)2D analogs such as calcipotriol and maxacalcitol are used to treat hyperproliferative skin diseases such as psoriasis.

- **Cancer**

1,25(OH)2D and its analogs can prevent cancer development or retard its progress/metastasis once developed.

The mechanisms of tumor suppression by1,25(OH)2D can suppress tumor development, include inhibition of proliferation or interference with signaling by growth factors, induction of apoptosis, stimulation of DNA damage repair, inhibition of metastasis, prevention of tumor angiogenesis.

- **Cardiovascular**

Chen *et al*. found that VDR and CYP27B1 are expressed in the heart, both in the myocytes and fibroblasts [(62)].

Deleting the VDR specifically from the heart results in hypertrophy1,25(OH)2D, and its analogs suppress markers of cardiac hypertrophy.

Clinical trials have not been conducted to test the role of vitamin D and its analogs in the treatment/prevention of Congenital Vascular Disease.

b) **VITAMIN D ON B-CELL FUNCTION**

In both in vivo and in vitro models, it has been shown that vitamin D itself is essential for regular insulin release in response to glucose and maintenance of glucose tolerance.

25(OH) vitamin D is the primary form of vitamin D in the circulation is which is primarily metabolized in the kidneys by 1-alpha-hydroxylase to generate the active form of vitamin D 1,25(OH)2D [(63)].

Many studies have shown a beneficial role for vitamin D in pancreatic beta-cell function. In vivo studies in mice suffering from vitamin D deficiency have shown reduced insulin secretion from pancreatic islets. Vitamin D supplementation is shown to increase

insulin secretion. Evidence has also been presented indicating that vitamin D can protect beta cells from cytokine-induced apoptosis [64].

Wolden-Kirk *et al.* did not show any increase in insulin secretion following preincubation of mouse islets with vitamin D after stimulating with high levels of glucose [65].

Jeddi *et al.* reported that vitamin D combined with a high glucose concentration in the preincubation of rat islets stimulated insulin secretion [66].

c) VITAMIN D AND DIABETIC RETINOPATHY

Studies suggest that vitamin D, through its effects on the immune system, plays a significant role in the pathogenesis of diabetic retinopathy. Inflammatory cytokines are upregulated in patients with type 2 diabetes, and it has been shown that vitamin D reduces the production of several proinflammatory cytokines, such as IL-2, IL-6, IL-8, IL-12, and TNF-α [67].

Albert *et al.* and colleagues have shown that the calcitriol, is a potent inhibitor of retinal neovascularization. To assess the antiangiogenic activity of calcitriol, the mouse oxygen-induced ischemic retinopathy (OIR) model was used. The effects of calcitriol on retinal EC migration, proliferation, and capillary morphogenesis were assessed in vitro. Calcitriol-treated animals compared with control animals demonstrated a significant decrease in retinal neovascularization. This effect was dose-dependent, and retinal neovascularization was significantly inhibited in calcitriol-treated mice [68].

Zhigang *et al*. Studied that 1,25-$(OH)_2$ D_3 had a partially protective effect on diabetic rats of diabetic retinopathy. Researches have indicated that vitamin D prevents the development and progression of DR by inhibiting inflammation and neovascularization in retinal tissues. In this study, male Sprague-Dawley (SD) rats were divided into normal control group, 1,25-$(OH)_2$ D_3 group, and diabetes group. The rats in the 1,25-$(OH)_2$ D_3 group

and diabetes group were established to type 2 diabetes model with high-fat and high-sugar diet and streptozotocin (STZ), whereas the rats of 1,25-(OH) $_2$ D_3 group were treated with 1,25-$(OH)_2$ D_3. Morphological changes of retinal tissues were observed. VEGF and TGF-β_1 expressions in the retinal tissues were detected with immunohistochemistry staining after 13 weeks[(69)].

Bang-an Luo *et al*. Studied the Association between Vitamin D Deficiency in Type 2 Diabetes with Diabetic Retinopathy by a meta-analysis of Observational Studies that states that some genes were also associated with diabetic retinopathy development, such as Bsml, rs2228570, and TT [(70)]. Genetic studies have revealed that the human retina consists of vitamin D receptors (VDR), and the polymorphisms of VDR are related to the risk of retinopathy. Single nucleotide polymorphism of the Fok 1 vitamin D receptor gene has been associated with an increase in transcriptional activity of the VDR gene and less severe diabetic retinopathy, and Taq 1 polymorphism of the VDR gene is associated with decreased incidence of retinopathy [(71)].

Turkish study compared serum 25(OH.)D between 66 diabetic patients and 20 nondiabetics found it to be lower significantly in people with diabetes. This study found that the severity of retinopathy and serum 25(OH) D concentrations is inversely related to the lowest in patients with proliferative diabetic retinopathy (37). It also found that calcitriol inhibits retinal endothelial cell capillary morphogenesis in vitro. Furthermore, calcitriol downregulates hypoxia-inducible factor-1 (HIF-1) transcriptional activity and HIF-1 target genes, such as vascular endothelial growth factor (VEGF); thus, vitamin D could exert its positive effect via calcitriol mediated VEGF reduction [(73)].

Suzuki *et al*. studied Hypovitaminosis D in type 2 Diabetic Mellitus association with microvascular complications in 581 Japanese patients with diabetes mellitus type 2 and 51 patients without diabetes mellitus subjects. They analyzed the relation between serum 25-

hydroxyvitamin D(25-OHD) concentration and the clinical features of type 2 diabetes. Which found that levels of the 25-OHD were significantly lower in the population with apparent microvascular complications. Serum 25-OHD concentration in type 2 diabetes patients was 17.0 +/- 7.1 ng/ml, was not different statistically from normal population (17.5 +/- 3.6 ng/ml). The prevalence of hypovitaminosis D (<20 ng/ml) was 70.6%. Serum concentrations of 25-OHD were associated with HbA1c (P = 0.013), age (P = 0.070), and serum albumin (P < 0.001) but were not related to BMI or the duration of diabetes [74].

Dinesh R *et al*. in their study on Vitamin D and Diabetic Retinopathy in type 2 Diabetes Mellitus 412 Type 2 Diabetes Mellitus patients for their ophthalmic findings and relevant investigations for the evaluation of DM. All patients underwent complete ophthalmic examination required and relevant blood investigations including FPS and PPPS HbA1C, and Vitamin D estimation. In his study, it was found that a significant correlation is present between the severity of diabetic retinopathy and vitamin D deficiency, clearly establishing the role of Vitamin D in the pathology and severity of diabetic retinopathy [75].

R he *et al.* in China studied 1520 type 2 diabetics patients with retinopathy with low serum significant in those with retinopathy. This study found a increase in retinopathy among patients with serum 25(OH)D below 15.27ng/ml (Normal range 20-50 ng/ml). The patients with severe diabetic retinopathy had a higher prevalence of vitamin D deficiency and significantly lower serum 25-hydroxyvitamin D concentrations and (P < 0.05). With the increased stages of diabetic retinopathy, there was decrease in average 25-hydroxyvitamin D level (P < 0.01). The diabetic retinopathy prevalence in patients with vitamin D deficiency was also higher than control group (both P < 0.01) [76].

Mehrdad *et al.* studied levels of vitamin D in the serum of diabetic patients with and without diabetic retinopathy. He studied thirty patients with DR and thirty diabetic patients without retinopathy. Based on the ophthalmic examination, patients with DR were grouped

into having non-proliferative retinopathy (NPDR) and proliferative retinopathy (PDR). The study demonstrated that patients with DR had lower levels of serum vitamin D when comparimg with normal fundus [77].

Brownlee M *et al.* in his study on biochemistry and molecular cell biology in the evolution of diabetic retinopathy, reported that increased polyol pathway flux, increased advanced glycation end products (A.G.E.s), activation of the isoform of protein kinase C (PKC), and increased hexosamine pathway flux are the mechanisms responsible for diabetic retinopathy [78].

The E.T.D.R.S. group proposed usage of the modified Airlie House classification of diabetic retinopathy. It classified diabetic retinopathy into mild, moderate, severe, very severe, early P.D.R., and high-risk P.D.R. based upon the characteristic lesions observed [79].

MATERIALS AND METHODS

This study was done on patients attending the outpatient and inpatient departments of Ophthalmology, BLDE (DU.).'s Shri B.M. Patil Medical College, Hospital and Research Centre, Vijayapura.

STUDY DESIGN: - Cross-sectional comparative study

DURATION OF STUDY: October 2019-April 2021

SOURCE OF DATA

The study includes a total of 276 patients with Type 2 Diabetes Mellitus. They are grouped into two with those having diabetic retinopathy and those without diabetic retinopathy (138 patients per group)

They will be screened for Diabetic Retinopathy by complete ophthalmic examination, including detailed History.

1. **HISTORY**

All patients were screened with a detailed history including duration of symptom, its nature, duration of exposure to sunlight, diet history and history of tobacco chewing or alcohol consumption. History of treatment with oral hypoglycaemic agents, insulin, vitamin supplements and other drug intake, disorders known to influence Vitamin D levels and previous ophthalmic surgery/laser or other medical treatment history was also taken.

2. **OCULAR EXAMINATION**

Visual acuity was assessed by Snellen’s chart and refractive status was noted

- Anterior segment evaluation with slit lamp biomicroscopy was performed
- Intraocular pressure was measured using Goldmann Applanation tonometer
- Dilated fundus examination using 90D & indirect ophthalmoscopy
- Documentation of Fundus photographs
- ETDRS classification of diabetic retinopathy

3. INVESTIGATIONS

Relevant blood investigations like FBS, PPBS, HBA1C, Vitamin D were done.Fasting blood glucose levels (FBS), Post prandial blood glucose levels (PPBS),Random blood sugar levels (RBS), Glycolsated haemoglobin (HBA1c), serum 25 hydroxy Vitamin D were measured.

The patients were explained about the study, institutional clearance and patients' willful consent was taken. Details of the patients including history, clinical examination, investigations were recorded.

4. BIOCHEMICAL ESTIMATION OF VITAMIN D.

o VITROS IMMUNODIAGNOSTIC SYSTEM.

In our study a competitive immunoassay technique is used in which involves the release of the 25-OH Vitamin D in the sample from the binding protein using a low Ph denaturant and the subsequent competition of the free 25-OH Vitamin D with horseradish peroxidase (HRP) labeled 25-OH Vitamin D reagent for monoclonal anti-Vitamin D bound to well. Unbound materials are removed by washing.

- PRINCIPLE OF THE TEST

The bound HRP conjugate is measured by a luminescent reaction. A reagent containing luminogenic substrates (a lumina derivative and a peracid salt) and an electron transfer agent, is added to the wells. The HRP in the bound conjugate catalyzes the oxidation of the luminol derivative, producing light. The electron transfer agent (a substituted acetanilide) increases the level of light produced and prolongs its emission. The light signals are read by the system. The amount of HRP conjugate bound is indirectly proportional to the concentration of 25-OH vitamin D present.

- REAGENTS

- 100 Coated wells
- 6.9 mL conjugate reagent with horse serum and bovine gamma globulin
- 10mL dissociation reagent in the buffer.

- PREPARATION OF THE SAMPLES

- Samples should be thoroughly separated from all cellular material.
- Mix the sample and bring to 15-30℃ before use.

- REFERENCE VALUES

Deficiency:: <20 ng/ml

Insufficiency:: 20 – 30 ng/ml

Sufficiency:: 30 - 100 ng/ml

Toxicity:: >150 ng/ml

5. STATISTICAL TOOLS USED FOR DATA ANALYSIS AND RESULTS TABLES ARE EVOLVED THROUGH DATA ANALYSIS TOOL IN MS-EXCEL AS AN ADD ON TOOL

276 patients (138 per group) are required to have a 90% chance of detecting, as significant at the 5% level, a decrease in the incidence of Vit D deficiency from 17% in the NDR group to 5% in the DR group.

Calculation based on the formula:

$$n = f(\alpha/2, \beta) \times [p_1 \times (100 - p_1) + p_2 \times (100 - p_2)] / (p_2 - p_1)^2$$

where p_1 and p_2 are the percent 'success' in the control and experimental group respectively

6. THEORETICAL CONCEPTS AND EQUATIONS

concept of p –value: The p-value is calculated using the sampling distribution of test statistic under Null Hypothesis, the sample data, type of test being done.

WHAT IS P-VALUE?

In statistics, the p-value is the probability of obtaining results as extreme as the observed results of a statistical hypothesis test, assuming that the null hypothesis is correct. The p-value is used as an alternative to rejection points to provide the smallest level of significance at which the null hypothesis would be rejected. A smaller p-value means that there is stronger evidence in favour of the alternative hypothesis.

HOW IS P-VALUE CALCULATED?

P-values are calculated using p-value tables or spreadsheets/statistical software. Because different researchers use different levels of significance when examining a question, a reader may sometimes have difficulty comparing results from two different tests. P-values provide a solution to this problem.

To avoid this problem, the researchers could report the p-value of the hypothesis test and allow the reader to interpret the statistical significance themselves. This is called a p-value approach to hypothesis testing.

P Value	Conclusion	Level of Significance
0.001 to 0.010	Reject Null hypothesis at 1% level	Highly significant
0.011 to 0.050	Reject Null hypothesis at 5% level	Significant
0.051 to 1.00	Accept Null hypothesis at 5% level	Not Significant

Table 3: Concept of P value

Following tests are used in this study for statistical analysis:

Shapiro wilk test

The Shapiro–Wilk test tests the null hypothesis that a sample x_1, ..., xn came from a normally distributed population. The test statistic is

$$W = \frac{\left(\sum_{i=1}^{n} a_i x_{(i)}\right)^2}{\sum_{i=1}^{n} (x_i - \overline{x})^2},$$

Levene's test

Levene's test is equivalent to a 1-way between-groups analysis of variance (ANOVA) with the dependent variable being the absolute value of the difference between a score and the mean of the group to which the score belongs. The test statistic, W is equivalent to the F

$$W = \frac{(N-k)}{(k-1)} \cdot \frac{\sum_{i=1}^{k} N_i (Z_{i\cdot} - Z_{\cdot\cdot})^2}{\sum_{i=1}^{k} \sum_{j=1}^{N_i} (Z_{ij} - Z_{i\cdot})^2},$$

Mann–Whitney *U* test

In statistics, the **Mann–Whitney *U* test** (also called the **Mann Whitney Wilcoxon** (**MWW**), **Wilcoxon rank sum test**, or **Wilcoxon–Mann–Whitney test**) is a nonparametric test of the null hypothesis that, for randomly selected values *X* and *Y* from two populations, the probability of *X* being greater than *Y* is equal to the probability of *Y* being greater than *X*

Kruskal–Wallis test

The **Kruskal–Wallis test** by ranks, **Kruskal–Wallis *H* test** (named after William Kruskal and W. Allen Wallis), or **one-way ANOVA on ranks** is a non-parametric method for testing whether samples originate from the same distribution. It is used for comparing two or more independent samples of equal or different sample sizes. It extends the Mann–

Whitney *U* test, which is used for comparing only two groups. The parametric equivalent of the Kruskal–Wallis test is the one-way analysis of variance (ANOVA).

7. **INCLUSION CRITERIA:**

   All patients aged 30 years and above, with Type 2 Diabetes Mellitus are included in the study.

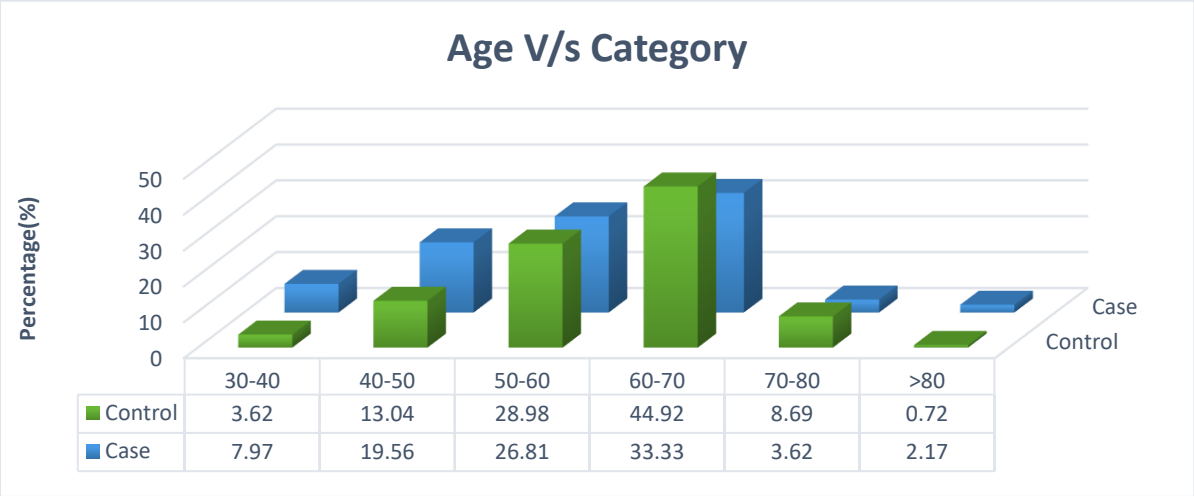
8. **EXCLUSION CRITERIA:**

- Any patient with a history of Vitamin D supplementation.
- Any patients with Low haemoglobin.
- Patients on drugs which affects retina such as quinolines, thiazide, latanoprost, tamoxifen, interferon.
- Subjects with disease such as tuberculosis, liver cirrhosis.
- Patients not willing for fundoscopy procedures.
- Pregnancy
- Hypertensive patient

RESULTS

276 patients were enrolled in this study. 138 patients had diabetic retinopathy changes in the fundus serving as case group whereas 138 had normal fundus findings (without diabetic retinopathy), serving as the control group.

1. AGE DISTRIBUTION

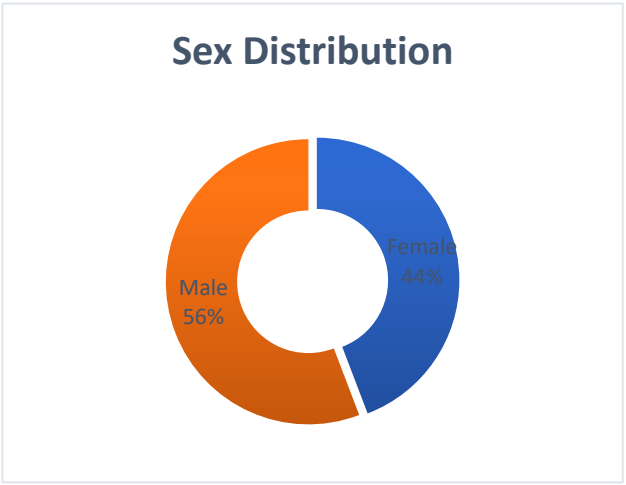


	30-40	40-50	50-60	60-70	70-80	>80
Control	3.62	13.04	28.98	44.92	8.69	0.72
Case	7.97	19.56	26.81	33.33	3.62	2.17

Graph 1. Graph showing Age vs category

In this study patients from the age group 30 years and above were included. Age group of 60 – 70 years were maximally affected (45%) among the case group (with retinopathy changes) and control group (without retinopathy changes). The least affected group in the study were those of above 80years in both groups

2. SEX DISTRIBUTION



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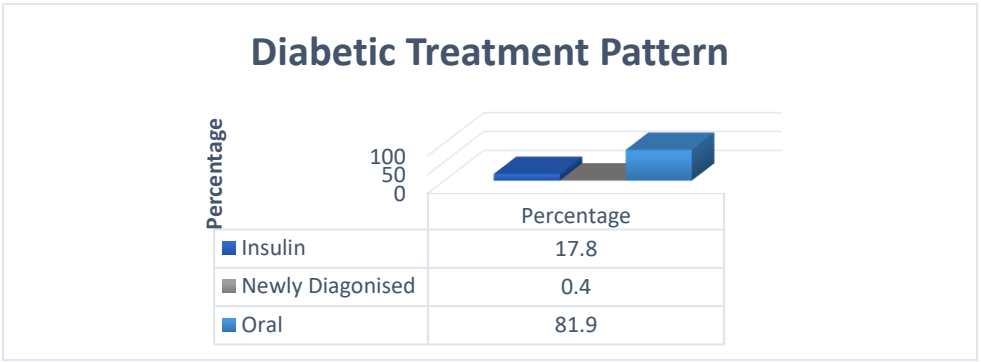
Graph 2. Pie chart showing Sex Distribution

In the study male were affected more (56%) when compared females (44%). Although an increased percentage of males were found to be affected, no significant male preponderance was observed.

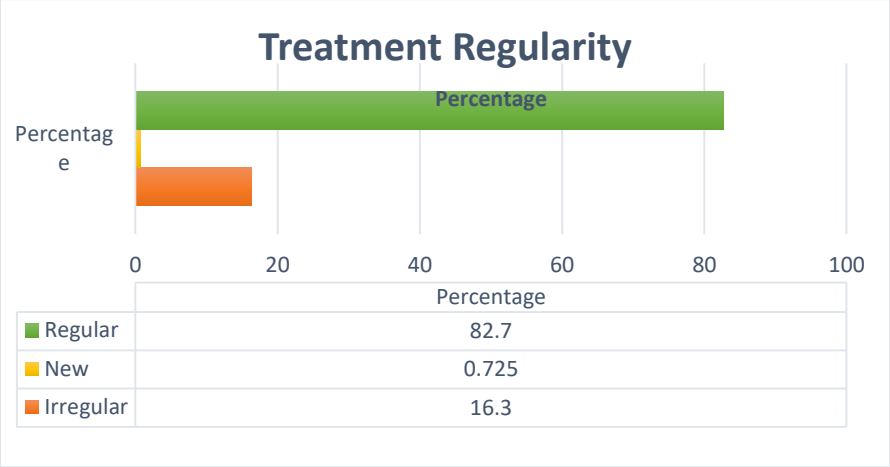
3. TREATMENT PATTERN OF THE PATIENTS



Graph 3. Graph showing Diabetic Treatment Pattern

In the study among the patients enrolled, most of the patients (82%) were under oral hyperglycaemic drugs, 18% of the patients were under insulin therapy while only 2 patients were newly diagnosed and was not under any treatment for hyperglycaemia.

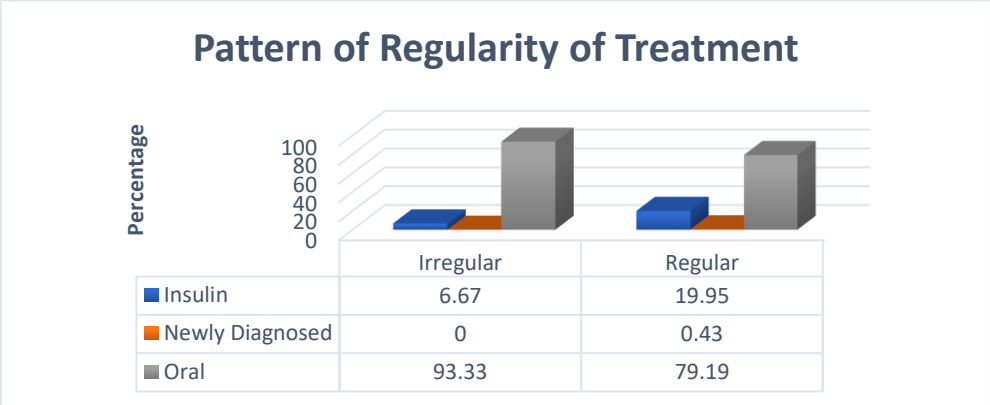
4. REGULARITY OF TREATMENT



Graph 4. Graph representing Treatment Regularity

Among the study group 83% were among those taking treatment regularly,16% takes treatment irregularly and remaining 0.7% were newly diagnosed.

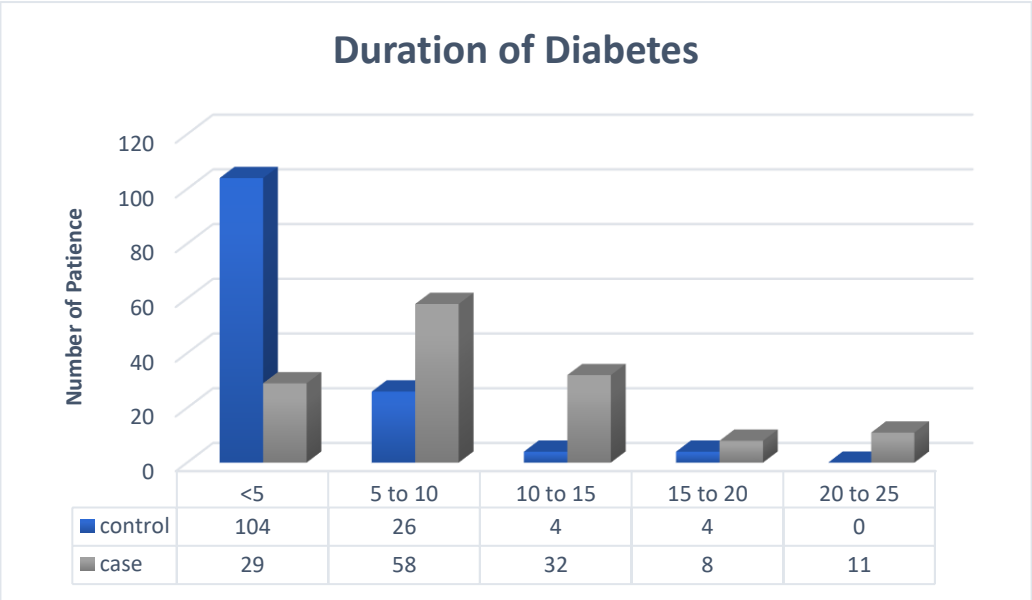
5. PATTERN OF REGULARITY IN TREATMENT



Graph 5. Graph showing Pattern of Regularity of Treatment

In the study on viewing the pattern of regularity in treatment, among the patients taking treatment irregularly and regularly majority of patients were under oral treatment 93% and 80% respectively.

6. **DURATION OF DIABETICS**

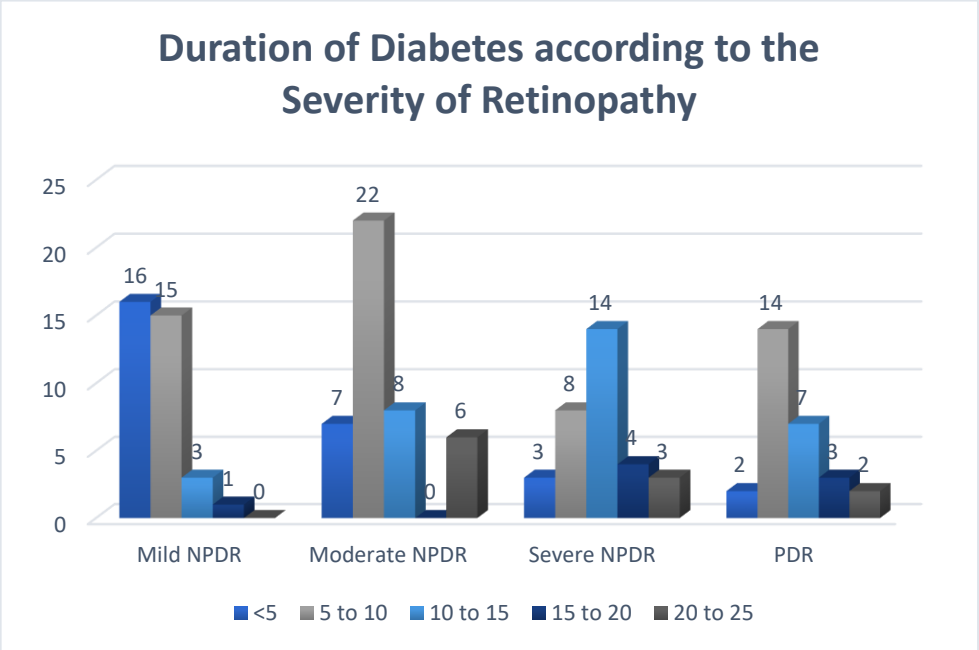


Graph 6. Graph representing Duration of Diabetes

The duration of diabetes was taken as the interval between the initial diagnosis of diabetes mellitus and the present study period. When considering the controls, a majority of patients (n=104) had duration of diabetes less than 5 years, followed by the duration between 5-10 and 15-20 years.

On the other hand, on considering the cases group, a majority of patients had the duration between 5 to 10 years (n=58) and about 11 patients had the duration of 20 to 25 years.

7. DURATION OF DIABETES ACCORDING TO THE SEVERITY OF RETINOPATHY

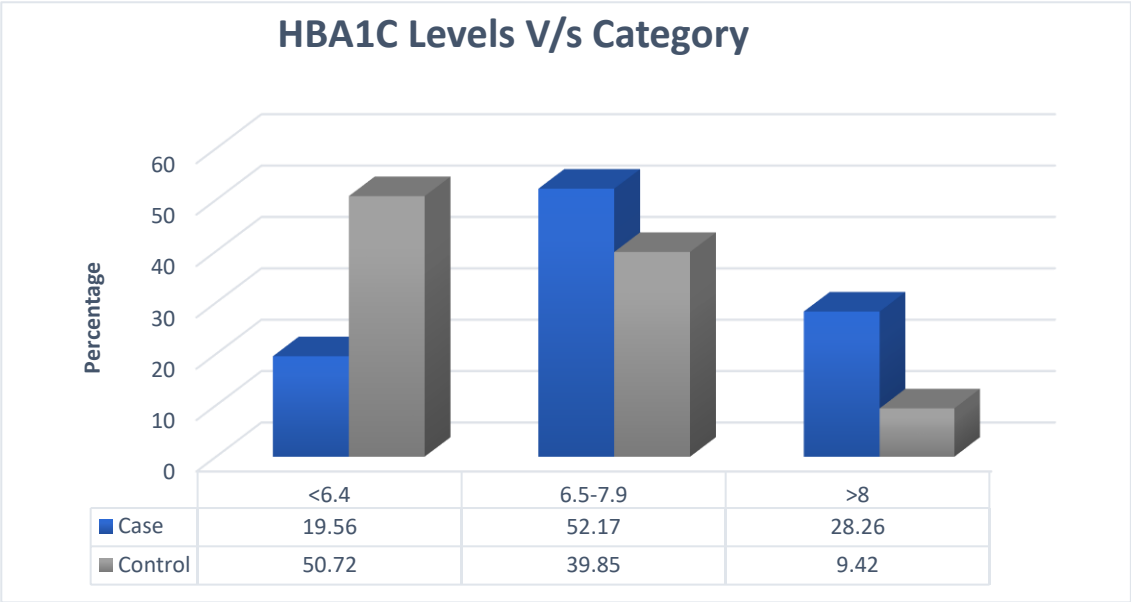


Graph 7. Graph showing correlation between duration of diabetes and grade of retinopathy

On reviewing the duration of diabetes according to the severity of retinopathy, among the patients with mild NPDR majority had the duration of less than 5 years(n=16), patients with moderate NPDR showed duration of 5 to 10years, while among the severe NPDR highest were included in the duration of 10 to 15 years.

On the other hand among the PDR cases, majority were included in 5 to 10 years but were among irregular treatment.

8. DISTRIBUTION OF HBA1C AMONG THE CASE AND CONTROL GROUP

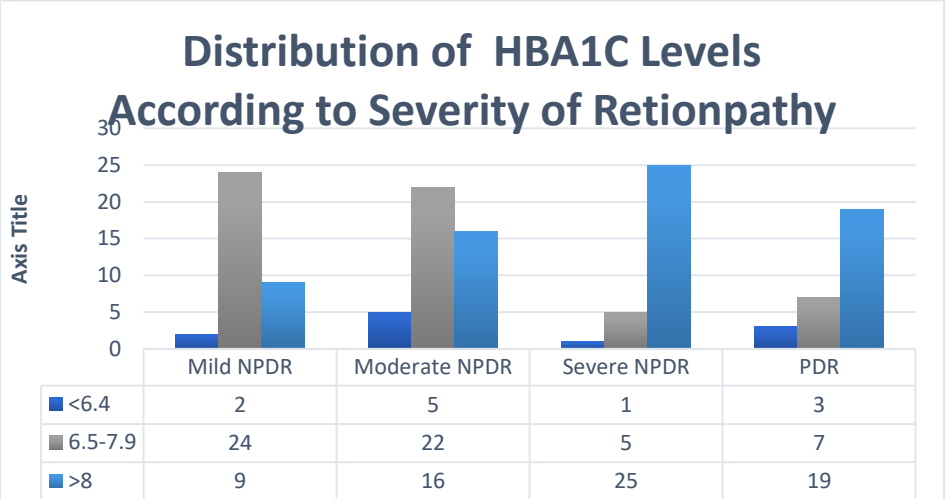


Graph 8. Graph representing HbA1c in control and case

The serum HbA1c levels were found to be statically significant among the case and control group.

Among the control group about 50.72% of the patients had serum HBA1c level below 6.4, while among the case group majority had serum HBA1c level between 6.5 to 7.9 (40%).

9. DISTRIBUTION OF HBA1C LEVELS ACCORDING TO SEVERITY OF RETIONPATHY

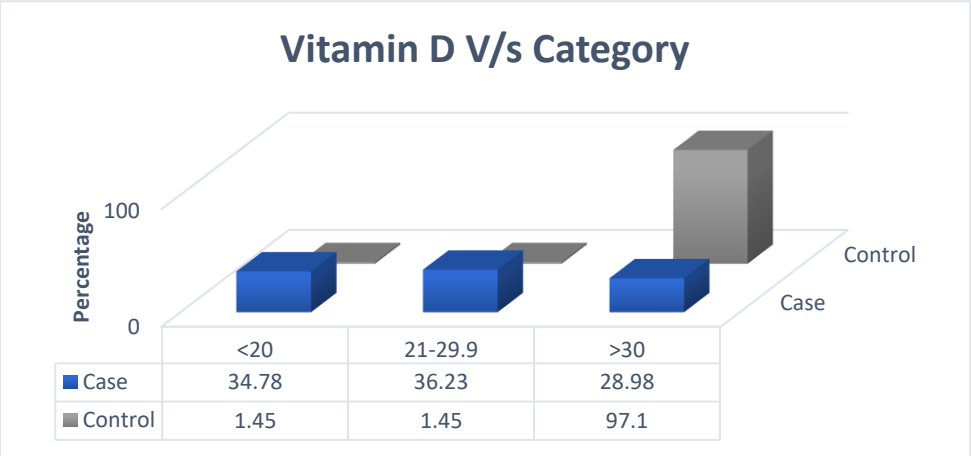


Graph 9 . Graph showing Distribution of HBA1C Levels According to Severity of Retinopathy

The levels of serum HbA1c were highest in patients with both severe NPDR and PDR which progressively decreased being lowest in patients with mild NPDR.

Of the patients enrolled in the study among the case group, a majority of the patients with severe NPDR and PDR demonstrated unsatisfactory control (serum HbA1c = 8.0%-10.0%), while fair gylcaemic control (serum HbA1c = 6.5%- 7.9%) was shown by the mild and moderate NPDR.

10. DISTRIBUTION OF VITAMIN D LEVELS AMONG THE CASE AND CONTROL GROUP

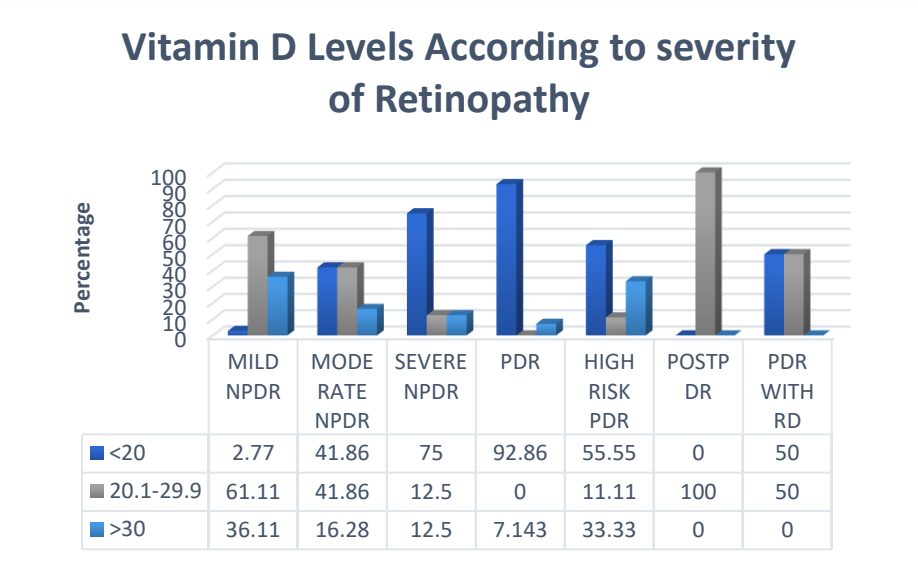


Graph 10. Graph showing relation between Vitamin D and Category

A total of 276 patients enrolled in the study, when considering the control group about (97%) were found to have Vitamin D sufficiently (Total vitamin D >30 ng/ml), (1.5 %) patients were found to have Vitamin D insufficiency and deficiency.

On the other hand on considering the case group about (35%) of the patients had Vitamin D deficiency (Total vitamin D< 20 ng/ml), while around (36%) of the patients had Vitamin D insufficiency (Total vitamin D between 21 - 29.9 ng/ml) and only (30%) of the cases had Vitamin D sufficiency (Total vitamin D> 30 ng/ml.

11. DISTRIBUTION OF VITAMIN D LEVELS ACCORDING TO RETINOPATHY



	MILD NPDR	MODERATE NPDR	SEVERE NPDR	PDR	HIGH RISK PDR	POSTPDR	PDR WITH RD
<20	2.77	41.86	75	92.86	55.55	0	50
20.1-29.9	61.11	41.86	12.5	0	11.11	100	50
>30	36.11	16.28	12.5	7.143	33.33	0	0

Graph 11. Graph showing Vitamin D Levels According to severity of Retinopathy

On considering the distribution of Vitamin D levels according to severity of retinopathy, 61% patients of mild NPDR had Vitamin D insufficiency and 3% had Vitamin D deficiency. While among the patients with Moderate NPDR and Severe NPDR, Vitamin D insufficiency and deficiency dominated than sufficiently.

P value of 0.000 shows significance which suggest there is relation between the grade of retinopathy and vitamin d levels.

High risk PDR cases had the lowest value of total vitamin D, 55.5 % were included in the deficiency group. None of the patients of post PDR and PDR with RD had Vitamin D sufficiency (total vitamin D> 30 ng/ml).

STATISTICAL TESTING PART

Assumption Checks by,

1. **TEST OF NORMALITY (SHAPIRO-WILK)**

		W	P
AGE	Abnormal	0.98	0.044
	Normal	0.987	0.232
DURATION	Abnormal	0.869	< .001
	Normal	0.8	< .001
RBS	Abnormal	0.92	< .001
	Normal	0.841	< .001
FBS	Abnormal	0.934	< .001
	Normal	0.764	< .001
PPBS	Abnormal	0.961	< .001
	Normal	0.86	< .001
HBA1C	Abnormal	0.929	< .001
	Normal	0.815	< .001
VITAMIN D	**Abnormal**	**0.953**	**<.001**
	Normal	**0.774**	**<.001**
Note. Significant results suggest a deviation from normality			

Table 4. Shapiro -Wilk Test

2. **TEST OF EQUALITY OF VARIANCES (LEVENE'S)**

	F	df	p
AGE	11.616	1	< .001
DURATION	23.178	1	< .001
RBS	10.64	1	0.001
FBS	35.196	1	< .001
PPBS	25.151	1	< .001
HBA1C	9.656	1	0.002
VITAMIN D	**1516.000**	**1**	**<.001**

Table 5. Levene's Test

As per test of normality (Shapiro Walk test) parameters such as duration, RBS, FBS, PPBS, HBAIC in both case and control groups shows deviation from normality.

VITAMIN D shows significant deviation from normality on considering the values in both normal (control group) and abnormal (case group). While on the other hand age doesn't show any significance among case and control groups.

Test of equality of Variances were used to further check for the significance of age among the case and control group.

3. **INDEPENDENT SAMPLES MANN-WHITNEY U TEST**

				95 % Cl for Hodges-Lehmann Estimate	
	W	**P Value**	**Hodges-Lehmann Estimate**	**Lower**	**Upper**
AGE	10308.5	0.235	2	-1	4
DURATION	15377	< .001	5	4	6
RBS	15752	< .001	77	62	89
FBS	16101	< .001	58	51	68
PPBS	15261	< .001	58	45	70
HBA1C	15153	< .001	1.6	1.4	2
VITAMIN D	**1516.000**	**<.001**	**-14.000**	**-16.130**	**-11.060**

Table 6. Mann-Whitney Test

On considering the Mann Whitney test, calculated P value <.001 is inferred that there is significant correlation with all parameters except of age where p value is 0.235

4. KRUSKAL - WALLIS H TEST

	TYPE OF TREATMENT	N	Mean Rank	Chi-Square Value	P-value
AGE	Insulin	49	148.87	3.395	0.183
	Oral	226	136.81		
	Newly diagnosed	1	13.5		
DURATION	Insulin	49	181.5	17.7777	0.000
	Oral	226	129.02		
	Newly diagnosed	1	174		
RBS	Insulin	49	178.58	15.985	0.000
	Oral	226	130.19		
	Newly diagnosed	1	52		
FBS	Insulin	49	179.82	18.239	0.000
	Oral	226	130.11		
	Newly diagnosed	1	10		
PPBS	Insulin	49	188.82	24.719	0.000
	Oral	226	128		
	Newly diagnosed	1	47		
HBA1C	Insulin	49	171.23	14.028	0.001
	Oral	226	128.48		
	Newly diagnosed	1	15.5		
VITAMIN D (MG/DL	**Insulin**	**49**	**83.28**	32.075	0.000
	Oral	**226**	**151.08**		
	Newly diagnosed	**1**	**1.00**		

Table 7. Kruskal Wallis Test

Kruskal Wallis test shows there is stastical significance between the type of treatment and the parameters such as duration, RBS, FBS, PPBS, HBA1C AND VITAMIN D.

DISCUSSION

Vitamin D deficiency (VDD) has been implicated in the development of diabetic complications, specifically diabetic retinopathy (DR). It has a number of metabolites the two most important of which are 1,25-dihydroxyvitamin D3 (1,25(OH)2D3) and 25 vitamin hydroxyapatites{25(OH)D}.

This cross-sectional study aimed to study on the association between Total vitamin D levels and Diabetic Retinopathy in Type 2 Diabetic Mellitus, on total 276 adult patients in the age group of above 30 years.

In our study about 45% of patients belonged to the 6th and 7th decades of life. This may be due to the prevalence of systemic diseases such as diabetes among the same age group and hence its resulting microvascular complications. These findings were similar to the study by **Daniel M. Taylor *et al***. who revealed similar age distribution. [80]

Wong *et al*. suggested that early onset age (<45 years) was an independent risk factor for DR however, disease duration, is known as an important risk factor to DR. [81] Supporting to the previous studies we have found that a majority of patient (n= 104) without retinopathy had duration of diabetes between less than 5 years, followed by 5 – 10 years. While considering the patients with retinopathy, majority of patients had duration of 5 – 10 years and 10 -15 years of which most of them were taking treatment irregularly. Thus, these values shows that in patients with a greater duration of diabetes, an increased severity of retinopathy was observed.

In our study, on considering the regularity and pattern of treatment, majority of the patients were under regular treatment 32.97%, and 16.30% were taking treatment irregularly and remaining 0.7% were newly diagnosed with diabetes. On further studying the pattern of treatment, majority of patients were taking oral hyperglycemic drugs in both regular and irregular groups 79.9% and 93.3% respectively and p value of 0.197.

In order to add to our findings, the ADVANCE trial reported a remarkable interaction between age at diagnosis and diabetes duration on the risk of microvascular events, and the highest risk of microvascular events was found in groups with the longest diabetes duration and the youngest age. [82]

Majority of patients enrolled in the control group had serum HbA1c levels of below 6.4% and while in the case group, serum HbA1c levels was between 6.4 and 7.9%. On further studying the relation between HbA1c and severity of diabetic retinopathy the levels of serum HbA1c were highest in patients with both severe NPDR and PDR (serum HbA1c = 8.0%-10.0%), and lowest in patients with mild NPDR. Thus, it signifies that serum HbA1c levels were found to be statically significant among the case and control group. The baseline mean serum HbA1c levels were 8.383 +/- 0.158% in cases and 6.575 +/- 0.132% in controls.

On performing the assumption checks with Shapiro -Wilk test, significant results suggest a deviation from normality with p value <0.001. On Kruskal-Wallis H Test Chi Square Value was 14.028.

Pragati et.al and Manaviat *et al*. have offered insights that patients having a good glycemic control (HbA1c < 7%) had lower prevalence of diabetic retinopathy as compared to those having poor control (HbA1c > 7%). To add on the previous studies we have also observed that only 1 (0.4%) patient having HbA1c levels < 7% had proliferative diabetic retinopathy as compared to (3.4%) of those having HbA1c level between 7.1-8.5% and (36%) of those having HbA1c level > 8.5%. [83-84]

In our study 97% of patients enrolled in the control group were found to have Vitamin D sufficiency (Total vitamin D: > 30 ng/ml), whereas in the case group (patients with retinopathy changes) 36.23% were found to have Vitamin D insufficiency (Total vitamin D: 20-30 ng/ml) ,34.7% were Vitamin D deficient (Total vitamin D <20 ng/ml) where as 28.9% were found to have normal Vitamin D levels.

The levels of Total Vitamin D measured in the 276 patients were found significantly at lower levels as the severity of retinopathy increased from moderate NPDR to PDR. The patients with mild NPDR 36 % had Total vitamin D of >30 ng/ml, while in patients of moderate NPDR 41.86% had Total vitamin D :20-30 ng/ml, severe NPDR and PDR cases demonstrated serum Total vitamin D of < 20 ng/ml. Hence our study here very well demonstrates an inverse relationship between the severity of diabetic retinopathy and Total Vitamin D levels, which were supported by other studies as well.

Thus, this strongly negative correlation between serum Vitamin D levels and severity of diabetic retinopathy was documented, suggesting that neovascularization in the retina may involve a decrease in vitamin D levels in patients with diabetic retinopathy and is supported by the study done by **John F. Payne *et.al*.** It was found that patients with type 2 diabetes, particularly those with PDR, had lower vitamin D levels than non-diabetes. Moreover, there was a higher percentage of subjects with vitamin D insufficiency in the diabetic retinopathy groups. [85]

CONCLUSION

Vitamin D contribute to diabetic retinopathy via angiogenesis mechanisms. Vitamin D decreases the expression of proinflammatory cytokines, a proliferation of immunocytes, and downregulate the vascular endothelial growth factor (VEGF). Vitamin D deficiency or insufficiency, both play significant role for the development and progression of diabetic retinopathy.

- The Study demonstrates an inverse relationship between the severity of diabetic retinopathy and serum Vitamin D levels at baseline.
- Majority of patients in the study with mild NPDR and moderate NPDR had Vitamin D insufficiency levels which decreased to Vitamin D deficiency levels in severe NPDR and PDR. On studying the statical tests, P Value of <.001 shows deviation from normality, thus showing that there is significant relation between the vitamin d levels and the grades of retinopathy.
- **Therefore, it is important to** to study the association of Total Vitamin D with the grades of Diabetic Retinopathy, and its use as a predictor of the severity of Diabetic Retinopathy.

SUMMARY.

In the study, majority of patients enrolled in both control and case group belonged to the 6th and 7th decades , 55.8% males and 44.2% females were affected with diabetic retinopathy in this study. Among the 138 patients studied with diabetic retinopathy, 36 patients had mild NPDR ,43 patients had moderate NPDR, 32 patients had severe NPDR, 14 had PDR, 8 had high risk PDR and 4 had PDR with RD.

On the other hand, among irregular treatment taking patient, majority were among the PDR cases with diabetic duration of 5 to 10 years.

The levels of serum HbA1c were highest in patients with both severe NPDR and PDR which progressively decreased being lowest in patients with mild NPDR.

Our study demonstrated an inverse relationship between the severity of diabetic retinopathy and serum Total Vitamin D levels at baseline. Patients with mild NPDR and moderate NPDR had majority in Vitamin D insufficiency levels which decreased to Vitamin D deficiency levels in severe NPDR and PDR. There is a statistically test significant deviation from normality. Parameters such as RBS, FBS, PPBS, HbA1c with p value<0.001 showed a positive correlation as well.

LIMITATIONS OF THE STUDY

- Limitations of our study were that the patients lacked the follow ups.
- Patients were not evaluated to study the benefit vitamin D supplementation in diabetic retinopathy.
- Longer follow up is necessary to document whether the beneficial effect of such supplementation is seen in diabetic retinopathy and also to re-evaluate the serum Vitamin D levels.

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ANNEXURES

ETHICAL CLEARANCE CERTIFICATES

22/11/2019

B.L.D.E. (DEEMED TO BE UNIVERSITY)

(Declared vide notification No. F.9-37/2007-U.3 (A) Dated. 29-2-2008 of the MHRD, Government of India under Section 3 of the UGC Act, 1956)

The Constituent College

SHRI. B. M. PATIL MEDICAL COLLEGE, HOSPITAL AND RESEARCH CENTRE

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The ethical committee of this college met on 13-11-2019 at 3-15 pm to scrutinize the synopsis of Postgraduate students of this college from Ethical Clearance point of view. After scrutiny the following original/corrected and revised version synopsis of the Thesis has been accorded Ethical Clearance

Title: A study on the association between total vitamin d levels and diabetic retinopathy in type 2 diabetic mellitus

Name of PG student: Dr Magna Mary Kuruvila ,Department of Ophthalmology

Name of Guide/Co-investigator: Dr. Sunil Biradar Prof & HOD, Department of Ophthalmology

DR RAGHVENDRA KULKARNI
CHAIRMAN

Institutional Ethical Committee
BLDEU's Shri B.M. Patil
Medical College,BIJAPUR-586103

Following documents were placed before Ethical Committee for Scrutinization:

1. Copy of Synopsis / Research project
2. Copy of informed consent form
3. Any other relevant documents.

STUDY SUBJECT CONSENT FORM

I confirm that Dr. Magna Mary Kuruvila has explained to me the purpose of research, the study procedure and the possible discomforts as well as benefits that I may experience in my own language. I have been explained all the above in detail in my own language and I understand the same. Therefore, I agree to give consent to participate as a subject in this research project.

_____ _____

(participant) (date)

_____ _____

(witness to signature) (date)

RISK AND DISCOMFORTS:

I understand that I may experience some pain and discomforts during the examination or during the treatment. The procedures of this study are not expected to exaggerate these feelings which are associated with the usual course of treatment.

BENEFITS:

I understand that my participation will help in the assessment of Vitamin D in diabetics.

I understand and accept the risks, benefits and costs involved. I willingly give consent to take part in the study.

CONFIDENTIALITY:

I understand that the medical information produced by this study will become a part of hospital records and will be subject to the confidentiality.

If the data are used for publication in the medical literature or for teaching purpose, no name will be used and other identifiers such as photographs will be used only with special written permission.

REQUEST FOR MORE INFORMATION:

I understand that I may ask for more questions about the study to Dr. Sunil G Biradar in the Department of Ophthalmology who will be available to answer my questions or concerns. I understand that I will be informed of any significant new findings discovered during the course of the study, which might influence my continued participation. A copy of this consent form will be given to me to keep for careful reading.

REFUSAL FOR WITHDRAWAL OF PARTICIPATION:

I understand that my participation is voluntary and that I may refuse to participate or may withdraw consent and discontinue participation in the study at any time without prejudice. I also understand that Dr. Magna Mary Kuruvila may terminate my participation in the study after she has explained the reasons for doing so.

INJURY STATEMENT:

I understand that in the unlikely event of injury to me resulting directly from my participation in the study, if such injury were reported promptly, the appropriate treatment would be available to me. But no further compensation would be provided by the hospital. I understand that by my agreements to participate in this study and not waiving any of my legal rights.

_____ _ _____

(participant) (date)

I have explained to _____the purpose of the research, the procedures required and the possible risks to the best of my ability.

_____ _____

Dr. Magna Mary Kuruvila Date

(Investigator)

1. PROFORMA FOR CASE TAKING

PROFORMA FOR CASE TAKING

DEPARTMENT OF OPHTHALMOLOGY

B.L.D.E UNIVERSITY'S SHRI B.M.PATIL MEDICAL COLLEGE HOSPITAL AND RESEARCH CENTRE, VIJAYAPURA-586103

CASE NO: OPD/IPD NO: DATE:

NAME: AGE: SEX:

OCCUPATION: ADDRESS:

KNOWN CASE OF TYPE 2 DM : YES / NO

DURATION OF TYPE 2 DM :

REGULAR FOLLOW-UPS : YES / NO

ON REGULAR MEDICATION : YES / NO

IF YES :ORAL / INSULIN

ANY OTHER RELATED COMPLICATIONS :

ANY OCULAR COMPLAINTS :

PERSONAL HISTORY,

FOOD HABITS

EXPOSURE TO SUNLIGHT :

PAST MEDICAL HISTORY:

PAST SURGICAL HISTORY:

FAMILY HISTORY:

Vitamin D level :

HBA1C level :

OPHTHALMIC EXAMINATION

	RIGHT EYE	LEFT EYE
External Appearance		
Ocular Motility		
Lids		
Conjunctiva		
Cornea		
Anterior Chamber		
Iris		
Pupil		
Lens		
Unaided		
Pinhole		
Near Vision		

Fundus Examination

	RIGHT EYE	LEFT EYE
Media		
Disc		
Blood vessels		
Background		
Macula		

COLOR PLATES

FigA. Oct in a patient with diabetic edema (high risk PDR)

Fig B. B SCAN Imaging

Fig C. Fundus photography in a patient with moderate NPDR

Case Photos

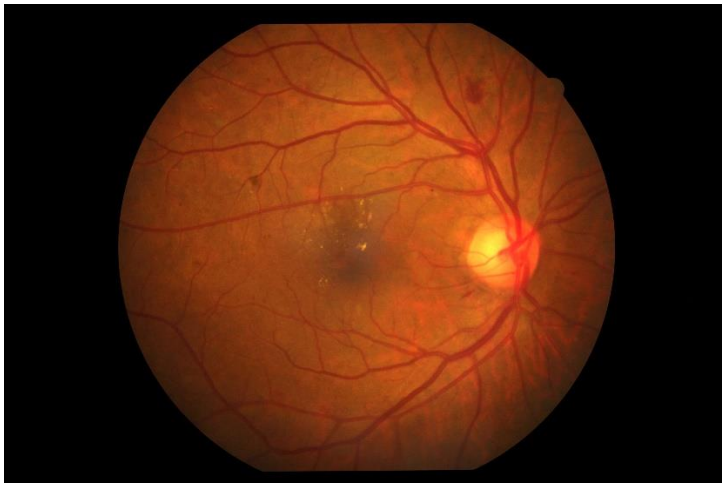

Fig D. Case No-4 Fundus photograph of a Moderate NPDR patient

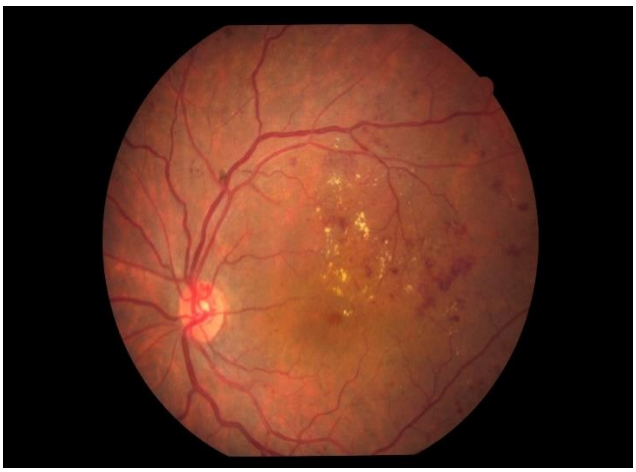

Fig E. Case No-6 Fundus photograph of a Severe NPDR patient

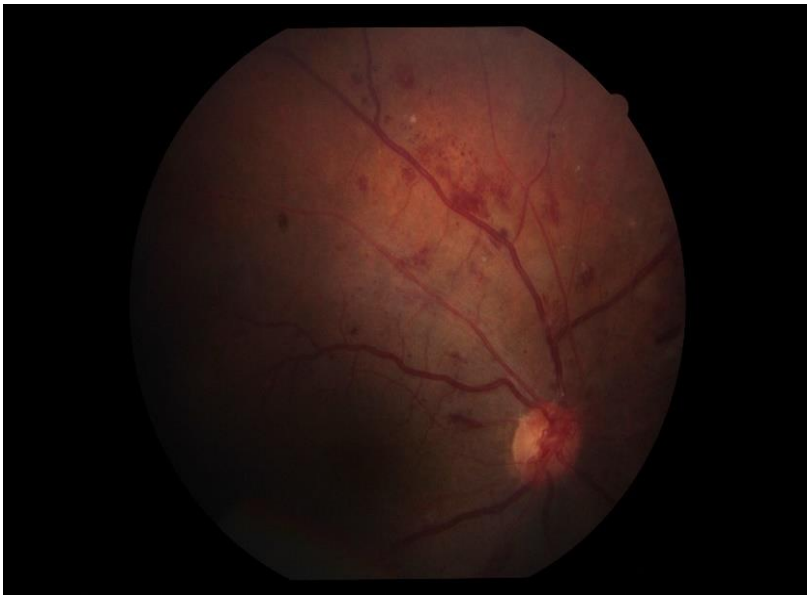

Fig F. Case No-18 Fundus photograph of a PDR patient

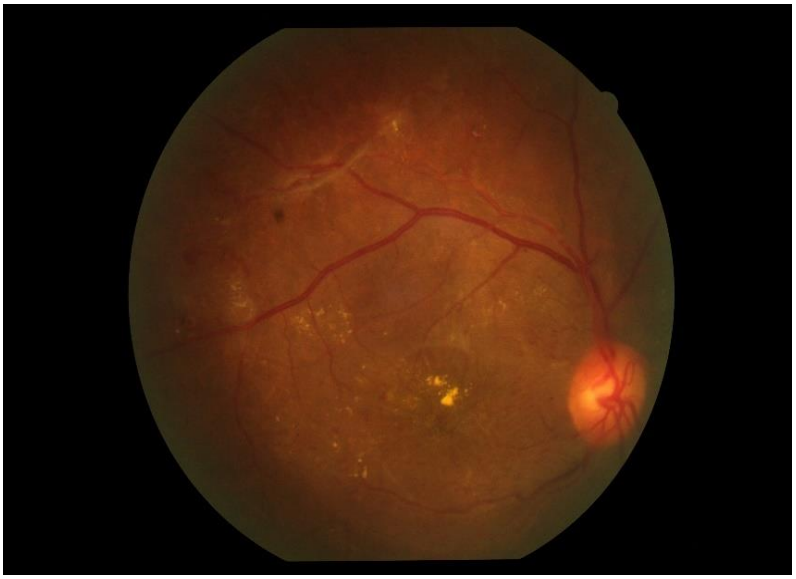

Fig G. Case No-69 Fundus photograph of a PDR with Tractional Band patient

2. KEY TO MASTER CHART

S. No – Serial Number

OP No. – Outpatient department number

IP No. – Inpatient department number

F – Female

M – Male

T2DM – Type 2 Diabetes Mellitus

RBS – Random Blood Sugar

FBS – Fasting Blood Sugar

PPBS – Post Prandial Blood Sugar

RE – Right Eye

LE – Left Eye

BE – Both eyes

CF – Counting fingers

HM – Hand movements

NI – No improvement

PL – Perception of light

NPDR – Non proliferative diabetic retinopathy

PDR – Proliferative diabetic retinopathy

RD _ Retinal Detachment

NORMAL FUNDUS

SL NO	NAME	SEX	AGE	IP/OP	VISION RIGHT	VISION LEFT	FUNDUS	DURATION	VITAMIN E D(MG/DL)	RBS	FBS	PPBS	HBA1C	TREATMENT	REGULAR/IRREGULAR
1	BHIMARAI	F	55	37464	RE:CF 3MTS, 6/36	LE :CF3MTS,6/60	NORMAL	0.1	35.4	156	91	171	5.9	ORAL	REGULAR
2	GANGAVVA	F	37	411420	RE:6/9 ,6/6	LE: 6/9,6/6	NORMAL	2	32	165	100	179	6.3	ORAL	REGULAR
3	MAHADEV	M	50	2367	RE:6/9 ,6/6	LE:6/6	NORMAL	7	44.3	**390**	**100**	**245**	**8.8**	INSULIN	REGULAR
4	SONABAI	F	60	2208	RE:6/18,6/9	LE: 6/9,6/6	NORMAL	5	43.8	145	91	180	5.8	ORAL	REGULAR
5	SHEKAR	M	65	2684	RE:6/9 ,6/6	LE: 6/9,6/6	NORMAL	2	32.3	123	98	176	6.5	Oral	Regular
6	SHIVANAD	M	63	474188	RE:6/18,6/9	LE:6/12 ,6/9	NORMAL	15	49.9	166	111	190	6	ORAL	REGULAR
7	RUDRABAR	M	65	474757	RE:6/9 ,6/6	LE: 6/9,6/6	NORMAL	10	53	125	92	168	5.5	Oral	Regular
8	PARVATI	F	65	474445	RE:6/6	LE: 6/9,6/6	NORMAL	4	32.2	158	90	157	6	Oral	Regular
9	JOGITA	F	43	455939	RE:6/9 ,6/6	LE:6/12 ,6/9	NORMAL	0	36.5	167	101	188	6.1	ORAL	REGULAR
10	SUSHILA	F	50	38934	RE:6/3 6,6/12	LE:6/36 ,6/12P	NORMAL	5	31.8	**294**	**258**	**307**	**9.9**	INSULIN	REGULAR
11	SHOBA	F	43	428665	RE:6/9 ,6/6	LE: 6/9,6/6	NORMAL	4	61.2	245	222	195	7	ORAL	IRREGULAR
12	SANGAMESH	M	65	447596	RE:6/18,6/9	LE:6/12 ,6/9	NORMAL	5	32.5	189	154	195	7	ORAL	Regular
13	MAYAWWA	F	65	39050	RE:6/3 6,6/12	LE:6/36 ,6/18	NORMAL	7	31.8	133	78	176	6.8	INSULIN	REGULAR
14	Gadigeppa	M	77	39246	RE:6/18,6/9	LE:6/12 ,6/9	NORMAL	10	39.6	193	191	145	6.7	Oral	Regular
15	Hanamanth	M	63	420155	RE:CF 3mts, 6/18	LE:6/60 ,6/36	NORMAL	15	47.3	156	98	188	6	ORAL	REGULAR
16	SHNATAMM	F	60	81476	RE:6/6 0,6/24	LE:6/60 ,6/36	NORMAL	2	34	86	123	145	4.5	ORAL	REGULAR
17	BHIMARAI	M	55	83523	RE:CF 3mts, 6/18	LE :CF3MTS,6/60	Normal	0	35.4	160	90	190	6.9	ORAL	REGULAR
18	SUBBAYYA	M	50	5075	RE: 6/9,6/6	LE: CF 3MTS,6/36	NORMAL	2	32.5	131	98	140	6.5	ORAL	Regular
19	IRAYYA	M	84	73592	RE:CF 3mts, 6/36	LE :CF3MTS,6/36P	NORMAL	0.5	33.3	146	98	178	6	ORAL	REGULAR
20	GANGAVVA	F	37	37522	RE:6/9 ,6/6	LE: 6/9,6/6	NORMAL	2	32	97	73	167	6.5	Oral	Regular
21	VIJAYKUMAR	M	44	474850	RE:6/18,6/9	LE:6/36 ,6/12P	NORMAL	3	31	126	122	98	6.7	ORAL	REGULAR
22	Ramappa	M	60	37427	RE:6/3 6,6/12	LE:6/36 ,6/12P	NORMAL	5	34	166	101	173	6.4	ORAL	IRREGULAR
23	NARASAPPA	M	65	42018	RE:6/6 0,6/24	LE :CF3MTS,6/36P	NORMAL	2	31	125	91	179	5.9	ORAL	REGULAR
24	Davalsab	M	57	27524	RE:6/18,6/9	LE:6/12 ,6/9	NORMAL	0	36	131	75	187	5	ORAL	REGULAR
25	BASALINGAPPA	M	60	42566	RE:6/9 ,6/6	LE: 6/9,6/6	NORMAL	0	34	94	90	167	5	ORAL	REGULAR
26	PARAGOND	M	57	5921	RE:6/9 ,6/6	LE:6/12 ,6/9	NORMAL	4	71.5	125	112	140	6	ORAL	REGULAR
27	SHEKAWWA	F	60	31825	RE: 6/24, 6/12	LE:6/36 ,6/12P	NORMAL	0	30	235	156	241	6.7	ORAL	RGULAR
28	REVANAWWA	F	69	27526	RE:6/6 0,6/36	LE:6/60 ,6/36	NORMAL	2	32	170	100	178	5.5	ORAL	REGULAR
29	PARAMESHWAR	F	57	27549	RE: 6/24, 6/12	LE: 6/9,6/6	NORMAL	4	32	169	100	180	5.5	ORAL	REGULAR
30	Kallapa	M	65	139467	RE: 6/24, 6/12	LE: 6/9,6/6	Normal	3	38.7	**313**	**200**	**333**	**9.8**	Oral	Irregular
31	Krinappa	M	64	14007	RE: CF 3MTS, NI	LE:6/60 ,6/36	Normal	1	38.1	170	128	180	12	Oral	Regular
32	Gangadhar	M	55	14013	RE:6/9 ,6/6	LE: 6/9,6/6	Normal	0.25	32	123	156	167	5	Oral	Regular

33	Suresh chavan	M	46	139660	RE:6/18,6/9	LE:6/12,6/9	normal	5	31	134	99	215	7	Oral	Regular
34	Kasturi	M	62	140155	RE:6/18,6/9	LE:6/36,6/12P	Normal	2	48.8	125	104	136	6	Oral	Regular
35	REVANAVVA	F	69	27526	RE:6/18,6/9	LE:6/18,6/9	NORMAL	1	31	75	90	123	4.5	ORAL	REGULAR
36	Sharnappa	M	45	13360	RE:6/18,6/9	LE:6/18,6/9	NORMAL	4	39.2	113	100	197	6.5	Oral	REGULAR
37	Mahantesh	M	30	14366	RE:6/9,6/6	LE:6/9,6/6	Normal	0	35.6	**423**	**159**	**278**	**10.6**	Oral	REGULAR
38	Ningappa	M	65	14530	RE:6/36,6/12	LE:6/36,6/12P	Normal	3	42.6	157	121	180	6.6	Oral	Regular
39	Noorjahan	F	49	37459	RE:6/24,6/12	LE:6/60,6/36	Normal	8	31	206	105	236	5.8	ORAL	REGULAR
40	Sharanagouda	M	69	15250	RE:6/24,6/12	LE:6/36,6/12P	Normal	2	34	137	89	174	6.1	Oral	REGULAR
41	Dilip	M	45	36514	RE:6/24,6/12	LE:6/24,6/12	NORMAL	0	32	123	109	212	5.9	Oral	Regular
42	Irraya	M	60	36503	RE:6/18,6/9	LE:6/18,6/9	NORMAL	4	31	125	98	198	5	Oral	Regular
43	Hasnabai	F	77	22039	RE:6/36,6/12	LE :CF3MTS,6/60	Normal	2	**29**	156	112	187	6.4	Oral	Regular
44	Suryakanth	M	60	22462	RE: CF 3MTS, NI	LE :CF3MTS,6/36P	normal	2	32.5	189	102	200	7	oral	regular
45	shankrema	F	35	21806	RE:6/18,6/9	LE:6/12,6/9	normal	1	34	109	90	128	6	oral	regular
46	suvarna	F	51	24874	RE:6/24,6/12	LE:6/24,6/12	Normal	0	32	116	100	167	6.4	Oral	Regular
47	Gurappa	M	80	25699	RE:6/9,6/6	LE:6/12,6/9	NORMAL	2	32.2	145	111	189	6.9	ORAL	REGULAR
48	veeresh	M	37	24770	RE:6/9,6/6	LE:6/9,6/6	NORMAL	1	31	154	121	178	6.9	ORAL	RREGULAR
49	Revanasidda	M	60	17536	RE:6/9,6/6	LE:6/9,6/6	normal	0	32.45	145	116	147	6.4	Oral regular	Regular
50	Mallappa	M	56	18068	RE:6/24,6/12	LE:6/24,6/12	Normal	0	46.3	156	97	190	6.5	Oral	Regular
51	Sharadabai	F	75	18391	RE:6/9,6/6	LE:6/9,6/6	Normal	1	35	139	100	168	6	Oral	Regular
52	Rachappa	M	80	19954	RE:6/60,6/24	LE:6/60,6/36	Normal	2	32	165	90	178	6.5	Oral	Regular
53	Kalappa	M	58	24375	RE:6/18,6/9	LE:6/12,6/9	Normal	2	30.1	158	120	165	7	Oral	Regular
54	Vijaya	F	53	11067	RE:6/24,6/12	LE:6/36,6/12P	Normal	0	35.4	160	90	176	6.5	Oral	Regular
55	Khemanabai	F	65	3486	RE:6/36,6/12	LE :CF3MTS,6/60	Normal	0	40.02	110	90	167	6.6	Oral	Regular
56	Subash	M	55	3499	RE: CF 1MTS, NI	LE:6/18,6/9	Normal	1	39	108	91	134	5.5	Oral	Regular
57	Rajendra	M	53	11807	RE:6/9,6/6	LE:6/9,6/6	Normal	5	31.2	170	100	189	6.5	Oral	Regular
58	Jyothi	F	34	11145	RE:6/9,6/6	LE:6/12,6/9	Normal	1	35	120	78	156	6	Oral	Regular
59	Sairabanu	F	45	12592	RE:6/18,6/9	LE:6/24,6/12	Normal	0	30.5	121	91	189	5	Oral	Regular
60	Shnatbai	M	52	8056	RE:6/24,6/12	LE :CF3MTS,6/60	Normal	6	30.6	145	98	168	6.5	Insulin	Regular
61	Devappa	M	57	7186	RE:6/9,6/6	LE:6/9,6/6	Normal	2	32	109	98	167	5.6	Oral	Regular
62	Narayan	M	75	7620	RE:6/60,6/24	LE:6/60,6/36	Normal	1	38.2	104	90	145	5.5	Oral	Regular
63	shantabai	M	38	6094	RE:6/9,6/6	LE:6/18,6/9	NORMAL	0	34.5	**224**	**154**	**301**	**9.5**	Oral	0
64	Vittal	M	60	8032	RE:6/60,6/24	LE:6/24,6/12	Normal	0	33.45	111	98	121	4.5	Oral	Rgular
65	Yallamma	F	68	18015	RE:6/24,6/12	LE:6/9,6/6	Normal	2	**<8.0**	156	120	187	4.5	Insulin	0
66	Hanumath	M	68	5527	RE: CF 3MTS, 6/24	LE :CF3MTS,6/60	Normal	2	34	86	79	145	4.5	Oral	Regular
67	Mahadevi	F	50	8123	RE:6/36,6/12	LE:6/18,6/9	Normal	7	30.5	**246**	**120**	**212**	**7**	Oral	Regular

68	Suresh r	M	52	17461	RE:6/60,6/24	LE:6/36,6/12P	NORMAL	4	57.4	145	111	180	6.6	Oral	Regular
69	Laxmi	F	65	17457	RE: 6/24, 6/12	LE:6/12,6/9	Normal	5	32	134	100	178	6.7	Oral	Regular
70	Jantabee	F	75	16540	RE:6/18,6/9	LE:6/12,6/9	Normal	0	32	109	90	124	6	Oral	Regular
71	BABNAGAR	M	58	21465	RE: 6/9,6/6	LE: 6/9,6/6	normal	1	43.2	109	90	128	6	oral	regular
72	SUGALA BAI	F	65	23145	RE: 6/9,6/6	LE: 6/9,6/6	NORMAL	5	28.63	156	112	187	6.8	Oral	Regular
73	GANGA DHAR	M	45	24517	RE: 6/24, 6/12	LE:6/18,6/9	NORMAL	1	35.4	156	90	140	7	ORAL	REGULAR
74	RAJABEE	F	56	56421	RE:6/18,6/9	LE :CF3MTS,6/60	NORMAL	2	32.5	**212**	**132**	**235**	**7.8**	ORAL	REGULAR
75	SAVITA	F	70	34442	RE: CF 3MTS, 6/24	LE:6/12,6/9	NORMAL	7	44.3	156	100	180	6.8	INSULIN	REGULAR
76	MAHADEV	M	50	56742	RE:6/18,6/6	LE:6/18,6/6	NORMAL	5	43.8	134	101	178	5.8	ORAL	REGULAR
77	RAMESH	M	67	24562	RE:6/9,6/6	LE: 6/9,6/6	NORMAL	2	32.3	123	98	176	6.8	Oral	Regular
78	MALLANGOUDA	M	54	67414	RE:6/12,6/9	LE:6/18,6/6	NORMAL	**15**	**49.9**	**256**	**167**	**321**	**7.8**	**ORAL**	**REGULAR**
79	SHAILAJA	F	79	67867	RE: 6/24, 6/12	LE: 6/9,6/6	NORMAL	10	53	125	89	211	5.5	Oral	Regular
80	REKHA	F	70	89755	RE:6/36,6/12	LE:6/24,6/12	NORMAL	4	32.2	190	90	245	6.8	Oral	Regular
81	M H BIRADAR	M	65	75467	RE:6/9,6/6	LE:6/60,6/36	NORMAL	0	36.5	167	121	210	7.1	ORAL	REGULAR
82	ARUNA	F	39	56797	RE:6/36,6/12	LE:6/18,6/6	NORMAL	5	**31.8**	**294**	**258**	**307**	**9.9**	**INSULIN**	**REGULAR**
83	RAJESHRI	F	46	56784	RE:6/9,6/6	LE: 6/9,6/6	NORMAL	4	**61.2**	**213**	**190**	**245**	**7.8**	**ORAL**	**REGULAR**
84	T K IJERI	M	67	75639	RE:6/18,6/9	LE:6/24,6/12	NORMAL	5	32.5	189	154	195	7	ORAL	Regular
85	VEENA	F	41	64843	RE: 6/9,6/6	LE:6/12,6/6	NORMAL	7	**31.8**	**245**	**170**	**376**	**12.7**	**INSULIN**	**REGULAR**
86	SURESH	M	60	68943	RE:6/18,6/9	LE:6/18,6/9	NORMAL	10	39.6	123	91	145	6.7	Oral	Regular
87	SOMASHARAN	M	77	47593	RE:CF 3mts, 6/18	LE:6/24,6/12	NORMAL	15	47.3	98	156	190	6.5	ORAL	REGULAR
88	GURUDUTT	M	68	57759	RE:6/60,6/24	LE:6/12,6/9	NORMAL	2	34	86	122	167	4.5	ORAL	REGULAR
89	MALLIKARJUN	M	54	65967	RE:CF 3mts, 6/18	LE:6/12,6/6	Normal	0	35.4	**179**	**110**	**190**	**7.9**	ORAL	REGULAR
90	SHEELA	F	45	89643	LE : 6/9.6/6	LE: 6/9,6/6	NORMAL	5	33.3	146	98	178	6	ORAL	REGULAR
91	MARAMMA	F	68	75843	RE:6/9,6/6	LE:6/24,6/12	NORMAL	2	32	145	73	167	6.5	Oral	Regular
92	BOURAVVA	F	89	74843	LE:,6/24,6/12	LE :CF3MTS,6/60	NORMAL	3	31	126	102	198	6.7	ORAL	REGULAR
93	GURUBAI	F	65	98433	RE:6/36,6/12	LE:6/24,6/12	NORMAL	5	34	**256**	**220**	**354**	**12.6**	ORAL	IRREGULAR
94	HEMANTH	M	63	85067	RE:6/60,6/24	LE:6/24,6/12	NORMAL	2	31	125	91	179	5.9	ORAL	REGULAR
95	SHEELAJI	M	45	63974	RE:6/18,6/9	LE:6/12,6/9	NORMAL	0	36	131	75	187	5	ORAL	REGULAR
96	BISMILLA	F	56	97593	RE:6/9,6/6	LE: 6/9,6/6	NORMAL	0	34	94	90	167	5	ORAL	REGULAR
97	RAMESH	M	76	78533	RE: 6/24, 6/12	LE:6/60,6/36	NORMAL	4	71.5	125	112	140	6	ORAL	REGULAR
98	ABDUL	M	87	87974	RE: 6/24, 6/12	LE:6/12,6/9	NORMAL	0	30	**189**	**156**	**241**	**8.7**	ORAL	RGULAR
99	GANGHADHAR	M	43	87973	RE:6/18,6/6	LE:6/18,6/6	NORMAL	2	32	170	100	178	5.5	ORAL	REGULAR
100	MOHAMMED	M	52	86643	RE: 6/24, 6/12	LE:6/12,6/9	NORMAL	4	32	169	100	180	5.5	ORAL	REGULAR
101	NANDINI	F	38	76483	RE: 6/9,6/6	LE: 6/9,6/6	Normal	3	38.7	313	180	227	7	Oral	Irregular
102	GIRIDHAR	M	67	79043	RE: CF 3MTS	LE :CF3MTS,6/60	Normal	1	38.1	**157**	**128**	**180**	**12**	Oral	Regular
103	REHABHI	F	65	79732	RE:6/18,6/9	LE:6/12,6/9	Normal	0.25	32	123	98	167	5	Oral	Regular

104	JANTABEE	F	45	98754	RE:6/18,6/9	LE:6/18,6/6	normal	5	31	134	102	170	7.2	Oral	Regular
105	MALLANGOUDA	M	51	76863	RE:6/18,6/9	LE: 6/9,6/6	Normal	2	48.8	125	90	136	6	Oral	Regular
106	M.K PATIL	M	66	88763	RE:6/18,6/9	LE:6/18,6/9	NORMAL	1	31	144	90	180	4.5	ORAL	REGULAR
107	SATISH	M	78	89653	RE:6/18,6/9	LE:6/60,6/36	NORMAL	4	39.2	190	133	297	7	Oral	REGULAR
108	ARAVIND BIARADAR	M	52	87683	RE:6/9,6/6	LE: 6/9,6/6	Normal	0	35.6	**312**	**258**	**300**	**10.6**	Oral	REGULAR
109	SUNANDA	F	54	78508	RE:6/36,6/12	LE:6/24,6/12	Normal	3	42.6	157	145	200	5.8	Oral	Regular
110	JYOTI	F	43	86543	RE: 6/24, 6/12	LE: 6/9,6/6	Normal	8	31	206	105	236	5.8	ORAL	REGULAR
111	PARVATI	F	41	88754	RE: 6/24, 6/12	LE:6/12,6/6	Normal	2	34	**234**	**158**	**225**	**7**	Oral	REGULAR
112	AKSHAY	M	31	79743	RE: 6/24, 6/12	LE:6/12,6/9	NORMAL	0	32	123	109	212	5.9	Oral	Regular
113	PRIYANKA	F	42	68686	RE: 6/9,6/6	LE:6/18,6/6	NORMAL	4	31	125	98	198	5	Oral	Regular
114	PARAPPA	M	65	586210	RE:6/36,6/12	LE:6/24,6/12	Normal	2	29	156	112	187	6.5	Oral	Regular
115	BASAPPA	M	54	281883	RE: CF 3MTS	LE:6/18,6/9	normal	2	32.5	189	102	200	5.5	oral	regular
116	NINGANNA	M	53	197432	RE:6/18,6/9	LE: 6/9,6/6	normal	1	34	109	90	128	6	oral	regular
117	RUSELBI	F	47	109732	RE: 6/24, 6/6	LE:6/12,6/6	Normal	0	32	116	100	167	6.4	Oral	Regular
118	NINGAVVA	F	43	87432	RE:6/9,6/6	LE: 6/9,6/6	NORMAL	2	32.2	145	111	189	7	ORAL	REGULAR
119	CHANDU	M	60	89765	RE:CF 3mts, 6/18	LE :CF3MTS,6/18	NORMAL	1	31	154	121	178	6.9	ORAL	RREGULAR
120	GIRISH	M	43	87974	RE:6/9,6/6	LE: 6/9,6/6	normal	0	32.45	145	116	147	6.4	Oral regular	Regular
121	CHANDEE	F	33	216860	RE: 6/18, 6/6	LE:6/18,6/6	Normal	0	46.3	168	131	190	6.5	Oral	Regular
122	MALLMA	M	60	109822	RE: 6/24, 6/12	LE:6/18,6/9	Normal	6	30.6	**200**	**166**	**338**	**7.7**	Insulin	Regular
123	HIRMENATH	F	57	124578	RE:6/9,6/6	LE: 6/9,6/6	Normal	2	32	109	98	167	5.6	Oral	Regular
124	RAMESHA	M	43	468932	RE: 6/18, 6/6	LE:6/18,6/6	Normal	1	38.2	104	90	145	5.5	Oral	Regular
125	GIRIJA	F	50	364211	RE:6/9,6/6	LE:6/12,6/9	NORMAL	0	34.5	**220**	**145**	**301**	**9.5**	Oral	0
126	ARUNA	F	57	272112	RE:6/60,6/24	LE:6/18,6/6	Normal	0	33.45	111	98	121	4.5	Oral	Rgular
127	RAJESHRI	F	44	584292	RE: 6/24, 6/12	LE:6/18,6/9	Normal	2	**<8.0**	156	120	187	4.5	Insulin	0
128	SANGAMSH	M	49	488432	RE:6/18,6/6	LE:6/12,6/6	Normal	2	34	86	79	145	4.5	Oral	Regular
129	B Y INAMDAR	M	68	747432	RE:6/36,6/12	LE:6/36,6/12	Normal	7	30.5	146	102	190	7	Oral	Regular
130	GIRISH	M	55	797933	RE:6/12,6/6	LE:6/12,6/6	NORMAL	4	57.4	**194**	**105**	**215**	**7.6**	Oral	Regular
131	KASTURI	F	43	778632	RE: 6/24, 6/9P	LE:6/12,6/6	Normal	5	32	**234**	**145**	**245**	**7.3**	Oral	Regular
132	KAVITA	F	55	687973	RE:6/18,6/9	LE:6/12,6/9	Normal	0	32	109	90	124	6	Oral	Regular
133	KALLAPA	M	67	773263	RE: 6/9P,6/9	LE:6/12,6/9	normal	1	43.2	109	90	128	6	oral	regular
134	MAHADEVI	F	55	786833	RE: 6/9,6/6	LE: 6/9,6/6	NORMAL	5	28.63	156	112	187	6.8	Oral	Regular
135	CHANDINI	F	44	868833	RE: 6/24, 6/12	LE:6/24,6/12	Normal	0	46.3	161	130	176	6.5	Oral	Regular
136	BHIMAVVA	F	65	646383	RE:6/9,6/6	LE: 6/9,6/6	normal	0	32.45	132	116	145	6.4	Oral	Regular
137	PARVATI	F	40	684843	RE:CF 3MTS, 6/36	LE :CF3MTS,6/60	NORMAL	0.1	35.4	132	91	155	5.9	ORAL	REGULAR
138	NINGAPPA	M	78	897332	RE:6/60,6/18	LE:6/24,6/12	NORMAL	2	32	165	100	179	6.3	ORAL	REGULAR

ABNORMAL FUNDUS

SLNO	NAME	S§EX	AGE	IP/OP	VISION RIGHT	VISION LIGHT	0	DURATION	VITAMIND (mg/dL)	RBS	FBS	PPBS	HBA1C	TREATMENT	REGULAR/ IRREGULAR	ADVICED
1	ANITA PATIL	F	52	409090	RE:6/36, 6/12	LE: 6/24,6/18	**MILD NPDR**	6	30.6	200	166	339		Insulin	Regular	Followup Advised
2	IRAYYA	M	84	37595	RE:CF 3mts, 6/18	LE: CF 3MTS, 6/9	**SEVERE PDR**	0.5	33.3	187	107	211	11.1	ORAL	IRREGUAR	PRP Adviced
3	SACHIN AND	M	58	53632	RE:6/36, 6/12	LE:,6/24,6/12	**SEVERE PDR**	8	**21.3**	205	275	384		ORAL	Irregular	PRP Advised
4	BASAMMA	F	59	2894	RE:6/9,6/6	Le: 6/12,6/9	**MODERATE NPDR**	4	**28.9**	245	267	145	11	ORAL	IRREGULAR	Followup Advised
5	MALLIKARJUN	M	49	474833	RE:6/18, 6/9	LE:6/18,6/9	**MILD NPDR**	2	32.2	261	156	234	7.5	ORAL	REGULAR	Followup Advised
6	S.L KADANI	M	79	32466	RE:CF 3mts, 6/36	LE: CF 3MTS, 6/36	**SEVERE NPDR**	9	**22.8**	239	129	225	8	INSULIN	REGULAR	Followup Advised
7	MAHADEV	M	70	56446	RE: 6/24, 6/12	LE:,6/24,6/12	**MODERATE NPDR**	5	30.5	246	215	287	9.7	ORAL	IRREGULAR	Followup Advised
8	SH§§ARANATH	M	61	474822	RE:6/36, 6/9	LE:6/18,6/9	**MODERATE NPDR**	6	43.9	225	147	234	7.8	Oral	Regular	Followup Advised
9	SIDAGOND	M	38	476546	RE:6/60, 6/36	LE: 6/60,6/36	**SEVERE PDR**	6	**5.04**	128	87	167	5	NEWLY DIAGNOSED		Followup Advised
10	BASAMMA	F	55	42017	RE:6/60, 6/24	LE: 6/24 ,6/18	**MODERATE NPDR**	2	**24.5**	180	181	242		ORAL	REGULAR	Followup Advised
11	KASTURIBAI	F	65	40992	RE:6/60, 6/24	LE 6/36,6/12	**MODERATE NPDR**	0	**19.1**	189	213	211		ORAL	REGULAR	Followup Advised
12	CHINTAMMA	F	60	39215	RE:6/12, 6/9	Le: 6/12,6/9	**Severe npdr**	4	**26.3**	297	345	411	14.5	INSULIN	REGULAR	Followup Advised
13	SULOCHANA	F	65	38876	RE: 6/24, 6/6	LE 6/36,6/6	**MILD NPDR**	7	**27.5**	245	265	318	11	ORAL	REGULAR	Followup Advised
14	SHREESHAIL	M	42	38234	RE: 6/60,6/18	LE 6/36,6/12	**SEVERE NPDR**	15	**29**	210	186	256	10	ORAL	IRREGULAR	Followup Advised
15	PRAMILA	F	60	45342	RE:6/18, 6/9	Le: 6/12,6/9	**MILD NPDR**	0	33.3	178	135	180		ORAL	REGULAR	Followup Advised
16	ANITA	F	52	34521	RE:6/9,6/6	Le: 6/12,6/9	**MILD NPDR**	4	30.6	210	166	339	7.1	INSULIN	REGULAR	Followup Advised
17	MALLIKARJUN	M	65	474833	RE:6/36, 6/12	Le: 6/12,6/9	**SEVERE NPDR**	10	**23**	261	158	256	8.9	ORAL	IRREGULAR	Followup Advised
18	CHANDABAI	F	70	8366	RE:CF 3mts, 6/18	LE: CF 3MTS, 6/18	**PDR**	10	**<8**	284	289	321	7.8	ORAL	IRREGULAR	PRP Advised
19	INDU	F	60	5878	RE:6/18, 6/9	Le: 6/12,6/9	**MODERATE NPDR**	5	**28.5**	198	111	157	5.5	INSULIN	REGULAR	Followup Advised
20	Mohammed	M	63	6438	RE: 6/24, 6/12	LE:6/18,6/9	**MILD NPDR**	5	**29**	160	120	145	7	Oral	Regular	Followup Advised
21	Vimala	F	57	70546	RE:6/60, 6/24	LE: 6/24	**PDR**	6	32.5	167	122	189	8	ORAL	REGULAR	PRP Advic

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22	SANGAVVA	F	60	42552	RE:6/36, 6/12	Le: 6/12,6/9	**MILD NPDR**	1	**29**	213	201	245	7.9	ORAL	REGULAR	Followup Advised
23	RAVI	M	43	413481	RE:6/9,6/6	LE:6/9, 6/6	**MODERATE NPDR**	5	**26.5**	252	222	289	7.8	ORAL	IRREGULAR	Followup Advised
24	BILU	M	50	42542	RE:6/18, 6/9	Le: 6/12,6/9	**MODERATE NPDR**	5	**25.9**	215	168	256	7.9	ORAL	REGULAR	Followup Advised
25	SABAWWA	F	55	6285	RE:6/36, 6/12	LE 6/36,6/12	**SEVERE PDR**	6	**<8**	96	96	148	6	ORAL	REGULAR	Followup Advised
26	Girimalla	F	60	12773	Re: HM+	LE: CF: 1MTS	**PDR WITH RD**	17	**28.6**	101	134	189	6.6	INSULIN/ORAL	REGULAR	PRP with Vitrectomy
27	Mashaque	M	65	12726	RE:CF 3mts, 6/36	LE CF 3 MTS	**SEVERE NPDR**	10	**9.82**	129	129	181	9.4	INSULIN	REGULAR	Followup Advised
28	MALLAPPA	M	72	12789	RE: CF 1MTS	LE:CF 3 MTS, NI	**PDR**	6	**16.6**	625	213	200	9.2	INSULIN	IRREGULAR	PRP Advised
29	SADASHIV	M	60	12816	Re: HM+	LE 6/36,6/12	**SEVERE NPDR**	5	**13.9**	300	213	245	10.6	INSULIN	REGULAR	Followup Advised
30	Guraling	M	60	13022	RE:6/60, 6/36	LE: 6/60,6/36	**SEVERE PDR**	1	**16.6**	198	61	150	6.8	Insulin	IRREGULAR	Followup Advised
31	Maibibasab	M	60	141573	RE:6/36, 6/12	LE: 6/24 ,6/18	**MODERATE NPDR**	6	**23**	198	130	202	7.5	Oral	Regular	Followup Advised
32	SHAJEET	M	62	13946	RE: 6/24, 6/12	LE 6/36,6/12	**MODERATE NPDR**	8	**27.1**	236	121	182	9	Insulin	Regular	Followup Advised
33	Sumangala	F	61	14485	RE:6/60, 6/24	LE: 6/60,6/36	**Mild npdr**	10	**48.8**	139	183	228	5.9	Oral	Regular	Followup Advised
34	Sudram	M	45	14497	RE: CF 1MTS	LE CF 3 MT	**PDR**	7	**13.2**	200	154	245	7.1	Insulin	Reguar	PRP Advised
35	Gangavva	M	60	14861	RE:6/60, 6/24	Le: 6/12,6/9	**MILD Npdr**	10	**34.9**	256	315	240	13.2	Oral	Irregular	Followup Advised
36	Shanmukappa	M	69	14995	RE:6/60, 6/24	LE 6/36,6/12	**MODERATE NPDR**	20	**23**	278	156	212	7.5	Oral	Regular	Followup Advised
37	Ramjan	M	38	15469	RE:6/9,6/6	LE : 6/9.6/6	**MILD NPDR**	6	**20.4**	328	153	159	12.2	Oral	Regular	Followup Advised
38	Rudragouda	M	65	15404	RE: CF 1MTS	Le: cf 3mts, 6/60	**SEVERE NPDR**	1	**9.7**	156	198	41	5.8	Oral	Regular	Followup Advised
39	Suvarna	F	49	15482	RE: 6/24, 6/12	LE: 6/24,6/18	**MODERATE NPDR**	8	21.4	206	105	236	10.4	Oral	REGULAR	Followup Advised
40	Nagesh	M	45	17003	RE: 6/24, 6/12	LE: 6/60,6/36	**MODERATE NPDR**	10	30.5	317	267	389	11.2	Oral	Irregular	Followup Advised
41	Parvati	F	50	17507	RE: CF 3MTS	Le: cf 3mts, 6/60	**SEVERE NPDR**	6	**8.25**	213	98	371	7.3	ORAL	REGULAR	Followup Advised
42	Nagesh	M	55	17923	RE: CF 3MTS	LE: CF 1 MTS, NI	**MODERATE NPDR**	12	**<8**	245	153	162	7.8	ORAL	REGULAR	Followup Advised
43	Katuribai	F	35	18724	RE: 6/24, 6/12	Le: cf 3mts, 6/60	**MODERATE NPDR**	7	**<8.0**	147	213	211	7.8	INSULIN	REGULAR	Followup Advised
44	Hanumanthappa	F	60	720	RE:6/36, 6/12	LE: 6/60,6/36	**MODERATE NPDR**	10	**24.6**	111	100	210	5.5	Oral	REGULAR	Followup Advic

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45	Mahadev	M	60	6033	RE:6/18, 6/9	LE 6/60,6/36	**MODERATE NPDR**	5	**13.3**	269	178	245	8	Oral	Regular	Followup Advised
46	Amnuddhin	M	54	8067	RE: 6/24, 6/12	LE 6/36,6/12	**MILD NPDR**	7	**25.52**	245	212	290	7.6	Oral	Regular	Followup Advised
47	Chandrashekar	M	58	18909	RE: CF 3MTS	LE CF 3 MTS	**MODERATE NPDR**	8	**<8.0**	254	289	190	11.2	Oral	Irregular	Followup Advised
48	Gangbai	F	55	18333	RE:6/18, 6/9	LE : 6/9.6/6	**SEVERE NPDR**	0	**<8**	213	278	212	7.6	Insulin	New	Followup Advised
49	Mahadevi	F	55	1464	RE: 6/24, 6/12	LE 6/36,6/12	**MODERATE NPDR**	0	**20.94**	215	205	288	9.3	Insulin	Regular	Followup Advised
50	Krishana	M	47	1560	RE:6/36, 6/12	Le: 6/12,6/9	**Mild npdr**	7	**31.42**	231	213	245	8.5	Oral	Irregular	Followup Advised
51	Najurabi	F	67	11174	RE:6/36, 6/12	Le: 6/12,6/9	**Mild npdr**	5	**26.85**	213	180	245	7.2	Oral	Regular	Followup Advised
52	ashok rathod	M	35	15496	RE: 6/24, 6/12	LE: 6/24,6/18	**MODERATE NPDR**	7	**15.67**	256	211	289	6.1	Oral	Regular	Followup Advised
53	Premadayand	F	62	3397	RE: 6/24, 6/12	LE 6/60,6/36	**Mild npdr**	2	**31.5**	245	203	231	7	Oral	Irregular	Followup Advised
54	Rudrayya	M	65	3492	RE: CF 3MTS	LE: CF 1 MTS, NI	**SEVERE NPDR**	10	**15.39**	213	200	245	8.4	Oral	Irregular	Followup Advised
55	Shankramma	F	65	16492	RE:6/36, 6/12	LE 6/60,6/36	**MODERATE NPDR**	0	**17.33**	256	206	352	7.9	Oral	Regular	Followup Advised
56	Prema	F	62	15489	RE: CF 3MTS	Le: CF 3MTS, 6/60	**SEVERE NPDR**	10	8.51	256	221	276	8.5	Insulin	Regular	Followup Advised
57	Bhimsee	M	60	6391	RE:6/36, 6/12	LE: 6/60,6/36	**Mild npdr**	2	**29**	210	139	281	11.3	Oral	Irregular	Followup Advised
58	Nanda	F	30	21116	RE: 6/24, 6/12	LE 6/36,6/12	**PDR**	5	**5.12**	321	214	278	8	Oral	Irregular	PRP Advised
59	Danamma	F	72	25887	RE: 6/24, 6/12	LE:6/36,6/12	**Moderate NPDR**	8	**12.09**	187	155	211	**7.9**	Oral	Regular	Followup Advised
60	Sujatha	F	42	24058	RE: 6/24, 6/6	LE : 6/9.6/6	**Mild NPDR**	5	**28**	121	98	154	7.6	ORAL	REGULAR	Followup Advised
61	PANDAPPA	M	79	21234	RE: 6/60,6/36	LE 6/60,6/36	**POST PRP**	30	**28**	134	94	225	7.5	INSULIN	REGULAR	REPEAT PRP
62	SR LESANNAWAR	M	57	212778	RE : CF 2 MTS	Le: cf 3mts, 6/60	**PDR**	21	**14.96**	256	211	280	8	ORAL	IRREGULAR	PRP Advised
63	SUVARNA	F	60	23315	RE: CF 3 MTS, NI	Le: CF 3MTS, 6/60	**SVERE NPDR**	12	**9.6**	245	153	190	7.8	ORAL	REGULAR	Followup Advised
64	SHAKUNTALA	F	60	26765	RE: CF 3 MTS	Le: cf 3mts, 6/60	**PDR**	15	**11.4**	249	167	191	8	ORAL	REGULAR	PRP Advised
65	RAMABAI	F	60	61295	RE: 6/60,6/36	LE 6/60,6/36	**MODERATE NPDR**	7	**27**	145	156	190	7.5	ORAL	REGULAR	Followup Advised
66	RAJU	F	60	62911	RE: 6/60,6/12	LE 6/36,6/12	**MODERATE NPDR**	10	**16.32**	149	150	189	7.5	ORAL	REGULAR	Followup Advised
67	SHIVAND	M	64	23152	RE : CF 2 MTS	LE: CF 1 MTS, NI	**SEVERE NPDR**	30	**20**	410	440	411	9	INSULIN	REGULAR	Followup Advised

68	S R RAJPUT	M	56	71202	CF3, NI	LE:: CF3 MTS,6/60	**PDR**	10	**14**	321	145	211	11	ORAL	IRREGULAR	PRP Advised
69	GEETA MORE	F	40	71234	CF : 3 MTS	LE:PL+	**PDR WITH RD**	11	**14.25**	422	211	218	11.5	ORAL	IRREGULAR	PRP with Vitrectomy
70	SHAMEELA	F	53	71123	CF4MTS	Le: CF 3MTS, 6/60	**SEVERE NPDR**	15	**18**	211	209	276	8	ORAL	IRREGULAR	Follo wup Advised
71	Rajappa	M	64	74567	Re:6/12, 6/9	LE : 6/9.6/6	**Mild npdr**	2	**31.5**	240	200	230	7	Oral	REGULAR	Follo wup Advised
72	Shabana	F	60	76909	RE: 6/36,6/12	LE:6/36,6/12	**MODERATE NPDR**	20	**23**	276	150	212	7	Oral	Regular	Follo wup Advised
73	Mahboobi	F	55	77190	RE: 6/60,6/9	Le: 6/12,6/9	**MODERATE NPDR**	10	**34**	170	100	210	5.5	Oral	REGULAR	Follo wup Advised
74	Somaling	M	72	79089	Re:6/12, 6/9	LE : 6/9.6/6	**MILD NPDR**	6	30.5	201	160	330		Insulin	Regular	Follo wup Advised
75	Sidappa	M	54	81001	RE: CF 3 MTS	Le: CF 3MTS, 6/60	**SEVERE NPDR**	30	**30.5**	411	329	419	9	INSULIN	REGULAR	Follo wup Advised
76	Rachappa	M	60	81060	RE: 6/36,NI	LE: 6/24,6/18	**MODERATE NPDR**	8	**<8.0**	254	270	180	11.2	Oral	Irregular	Follo wup Advised
77	MALLIKARJUN	M	69	81079	RE: 6/60,6/24	LE:6/60,6/36	**SEVERE NPDR**	10	8.51	230	221	276	8	Insulin	Regular	Follo wup Advised
78	SHANKAR	M	50	81652	RE: 6/9,6/6	LE:6/9, 6/6	**Mild npdr**	4	**26.85**	245	190	245	7.2	Oral	Regular	Follo wup Advised
79	MALLAMMA	F	68	81423	RE;6/12, 6,9	LE 6/60,6/36	**MODERATE NPDR**	10	**16.32**	149	150	189	7.5	ORAL	REGULAR	Follo wup Advised
80	SAROJINI	F	54	81622	RE: CF 3 MTS	Le: CF 3MTS, 6/60	**SEVERE NPDR**	20	**20.1**	311	345	367	9	INSULIN	REGULAR	Follo wup Advised
81	NAGAMMA	F	64	81232	RE: CF - CF	LE: CF 1 MTS, NI	**PDR**	10	**14**	321	145	211	11	ORAL	IRREGULAR	PRP Advised
82	ARJUN	M	45	82131	RE : CF 2 MTS	LE:HM+	**PDR**	11	**14.25**	422	345	389	11.5	ORAL	IRREGULAR	PRP Advised
83	Ramesh	M	40	83241	Re: cf 3 MTS,6/60	LE: CF 1 MTS, NI	**SEVERE NPDR**	9.5	**19**	216	209	258	8	ORAL	IRREGULAR	Follo wup Advised
84	BHIMBAI	F	59	84532	RE CF 1 MTS	LE:HM+	**PDR**	7	**13.2**	200	154	245	7.1	Insulin	Reguar	PRP Advised
85	RAJENDRA	M	60	79511	Re:6/12, 6/9	LE : 6/9.6/6	**MILD Npdr**	10	**25**	176	123	213	6.9	Oral	Irregular	Follo wup Advised
86	KATTAPPA	M	58	78900	RE: 6/60,6/36	LE 6/36,6/12	**MODERATE NPDR**	21	**31**	278	156	212	7.5	Oral	Regular	Follo wup Advised
87	NEELAMMA	F	70	86542	RE: 6/60,6/12	LE:6/36,6/12	**MODERATE NPDR**	6	**21**	321	149	269	8	Oral	Regular	Follo wup Advised
88	RAJESHAWRI	F	46	87241	RE CF 3 MTS	Le: CF 3MTS, 6/60	**SEVERE PDR**	6	**<8**	321	167	390	12.2	ORAL	REGULAR	Follo wup Advised
89	MAHESH	M	50	88094	RE: HM+	LE:HM+	**PDR WITH RD**	17	**28.6**	234	140	309	6	INSULIN/ORAL	REGULAR	Follo wup Advised
90	GANGAPPA	M	69	89743	RE CF 3 MTS	LE:: CF3 MTS,6/60	**SEVERE NPDR**	11	**9.82**	230	160	290	9.5	INSULIN	REGULAR	Follo wup Advised
91	SHANKARAPPA	M	58	84532	RE: CF 1MTS	LE: CF 1 MTS,	**PDR**	6	**17**	454	213	300	9	INSULIN	IRREGULAR	Follo wup

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92	RAMESH	M	64	853 13	RE: 6/60,6/3 6	Le: CF 3MTS, 6/60	**SEVER E NPDR**	5	**14**	31 1	21 3	34 5	10.6	INSULI N	REGUL AR	Follo wup Advic ed
93	B.N ANGADI	M	62	872 42	RE: CF3MT, 6/60	LE: CF 1 MTS, NI	**SEVER E NPDR**	15	**17**	21 8	16 0	29 0	8.8	ORAL	REGUL AR	Follo wup Advic ed
94	Basavaraj	M	60	340 8	Re: 6/24,6/1 8	Le: 6/12,6/ 9	**Mild npdr**	9	**28**	17 6	12 3	21 3	6.9	Oral	Regular	Follo wup Advic ed
95	Shankare mma	F	48	379 8	RE: 6/9,6/6	LE : 6/9.6/6	**Mild npdr**	**0**	29	16 8	14 0	21 1	7.5	Oral	New	Follo wup Advic ed
96	Gangaraj	M	60	357 56	RE: 6/9,6/6	Le: 6/12,6/ 9	**MILD NPDR**	6	26	20 0	14 0	29 0	7.8	Insulin	Regular	Follo wup Advic ed
97	Hanumant p	M	66	346 32	RE;6/12, 6,9	LE:6/9, 6/6	**MILD NPDR**	0.5	29	18 5	10 7	21 1	7	ORAL	IRREG UAR	Follo wup Advic ed
98	Jateppa	M	60	109 81	RE: 6/60,6/2 4	LE: 6/24,6/ 18	**MODE RATE NPDR**	5	**35**	25 2	19 0	28 9	7.8	ORAL	IRREG ULAR	Follo wup Advic ed
99	Basappa	M	56	356 74	RE CF 3 MTS	LE: CF 2 MTS, NI	**PDR**	6	16	30 8	23 1	39 0	12	ORAL	REGUL AR	Follo wup Advic ed
10 0	Hanamant ryya	M	45	345 62	Re:6/12, 6/9	LE : 6/9.6/6	**MILD NPDR**	1	**29**	13 4	90	24 5	7	ORAL	REGUL AR	Follo wup Advic ed
10 1	Nangouda	M	67	456 32	RE: 6/36,6/1 2	LE: 6/24,6/ 18	**MODE RATE NPDR**	5	**28.5**	16 0	12 0	19 7	5.5	INSULI N	REGUL AR	Follo wup Advic ed
10 2	Dastirgsa b	M	70	543 73	RE: 6/60,6/3 6	LE 6/60,6/ 36	**SEVER E NPDR**	10	**32**	26 1	15 8	35 6	8.9	ORAL	IRREG ULAR	Follo wup Advic ed
10 3	Gurappa	M	50	456 21	RE: 6/9,6/6	LE : 6/9.6/6	**MILD NPDR**	0	27	16 8	10 0	18 0	6.8	ORAL	REGUL AR	Follo wup Advic ed
10 4	Nandappa	M	65	568 43	Re:6/12, 6/9	Le: 6/12,6/ 9	**MILD NPDR**	4	30.6	20 0	14 6	22 3	7.1	INSULI N	REGUL AR	Follo wup Advic ed
10 5	Yamanaw wa	F	54	421 39	RE: 6/9,6/6	LE:6/9, 6/6	**MILD NPDR**	7	**27.5**	14 5	10 0	24 5	7.5	ORAL	REGUL AR	Follo wup Advic ed
10 6	Hulagam ma	F	60	452 78	RE: 6/60,6/9	LE: 6/24,6/ 18	**Mild npdr**	15	**29**	21 0	18 6	25 6	7	ORAL	IRREG ULAR	Follo wup Advic ed
10 7	Fakiramm a	F	54	651 89	RE: 6/60,6/2 4	LE:6/3 6,6/12	**MODE RATE NPDR**	2	**24.5**	28 0	18 1	34 2	8.5	ORAL	REGUL AR	Follo wup Advic ed
10 8	Gangabai	F	65	615 78	Re: 6/24,6/1 8	LE 6/60,6/ 36	**MODE RATE NPDR**	6	43.9	22 5	12 3	23 4	6.5	Oral	Regular	Follo wup Advic ed
10 9	Chingana d	M	40	652 14	RE;6/12, 6,9	Le: 6/12,6/ 9	**MILD NPDR**	6	28	18 9	16 6	21 3	6.5	Insulin	Regular	Follo wup Advic ed
11 0	Jelabai	F	55	542 78	RE : CF 2 MTS	LE: CF 2 MTS, NI	**SEVER E PDR**	8	**21.3**	20 5	27 5	38 4	10	ORAL	Irregula r	Follo wup Advic ed
11 1	Mahadevi	M	60	513 25	RE: 6/9,6/6	Le: 6/12,6/ 9	**MILD NPDR**	0.5	33.3	16 0	10 0	19 0	7	ORAL	IRREG UAR	Follo wup Advic ed
11 2	K Budi	M	68	457 89	Re:cf 3mts , 6/36	Le: CF 3MTS, 6/60	**SEVER E NPDR**	9	**32**	23 9	12 9	32 5	8	INSULI N	REGUL AR	Follo wup Advic ed
11 3	Annapurn a	F	63	346 71	Re: 6/60, NI	LE 6/60,6/ 36	**SEVER E PDR**	6	**<8**	26 8	19 6	39 0	11	ORAL	REGUL AR	Follo wup Advic ed

114	Devamma	F	69	65278	Re 6/60,6/36	LE:6/36,6/12	**MODERATE NPDR**	21	**22**	278	156	212	7.5	Oral	Regular	Followup Advised
115	Ratnabai	F	59	54786	Re ;6/36,6/24	LE 6/60,6/36	**SEVERE NPDR**	9.5	**19**	390	209	309	8	ORAL	IRREGULAR	Followup Advised
116	Mahanada	F	76	42256	Re : Cf 2MTS , NI	LE: CF 2 MTS, NI	**PDR**	10	**14**	299	254	356	11	ORAL	IRREGULAR	PRP Advised
117	Neelamma	F	54	45632	RE: 6/60,6/36	Le: CF 3MTS, 6/60	**MODERATE NPDR**	10	**16.32**	149	150	189	7.5	ORAL	REGULAR	Followup Advised
118	Davalsab	M	54	54789	Re:cf 3mts , 6/36	Le: CF 3MTS, 6/60	**SEVERE NPDR**	10	8.51	270	190	300	8	Insulin	Regular	Followup Advised
119	Laxmibai	F	45	54673	RE;6/12, 6,9	LE : 6/9.6/6	**MILD NPDR**	6	25	134	111	187	5.5	Insulin	Regular	Followup Advised
120	Ramanna	M	67	43122	RE : 6/9.6/6	LE : 6/9.6/6	**Mild npdr**	2	**31.5**	167	123	190	7	Oral	REGULAR	Followup Advised
121	Yallawa	F	53	47865	RE:HM+	LE:HM+	**PDR WITH RD**	11	**14.25**	422	212	300	11.5	ORAL	IRREGULAR	Followup Advised
122	Bhimaray	M	60	76325	RE: 6/60,6/24	LE: 6/24,6/18	**MODERATE NPDR**	10	**16.32**	168	156	170	7.5	ORAL	REGULAR	Followup Advised
123	Dundaww a	F	71	75187	RE:CF3 MTS,NI	LE: CF 2 MTS, NI	**SVERE NPDR**	12	**9.6**	245	153	190	7.8	ORAL	REGULAR	Followup Advised
124	Mahadev	M	68	52378	Re: 6/24,6/18	LE: 6/24,6/18	**MODERATE NPDR**	30	**28**	190	179	225	7.5	INSULIN	REGULAR	Followup Advised
125	S R badiger	M	65	64256	RE: 6/60,6/24	LE:6/36,6/12	**Moderate NPDR**	8	**12.09**	187	155	211	**7.9**	Oral	Regular	Followup Advised
126	Yamanappa	M	54	117180	RE: 6/9,6/6	Le: 6/12,6/9	**Mild npdr**	2	**29**	167	110	201	11.3	Oral	Irregular	Followup Advised
127	Rajkumar	M	45	142055	RE: CF3MTS,NI	Le: CF 3MTS, 6/60	**SEVERE NPDR**	10	**8.51**	276	234	290	8.5	Insulin	Regular	Followup Advised
128	Bheerappa	M	65	145619	RE: 6/60,6/36	LE 6/60,6/36	**MODERATE NPDR**	0	**20.94**	260	200	318	9.3	Insulin	Regular	Followup Advised
129	Anita	F	59	134221	RE: 6/60,6/24	Le: CF 3MTS, 6/60	**MODERATE NPDR**	8	**<8.0**	254	270	190	11.2	Oral	Irregular	Followup Advised
130	Laxmibai	F	49	145623	RE: 6/9,6/6	Le: 6/12,6/9	**MILD NPDR**	7	**25.52**	190	110	170	7.6	Oral	Regular	Followup Advised
131	Gourava	F	56	143855	CF 4MTS, 6/36	Le: CF 3MTS, 6/60	**SEVERE NPDR**	6	**8.25**	400	290	371	7.3	ORAL	REGULAR	Followup Advised
132	Mallmma	F	67	12384	RE:6/60, NI	LE:6/36,6/12	**MODERATE NPDR**	20	**23**	278	156	298	7.5	Oral	Regular	Followup Advised
133	Dheerappa	M	56	13432	Re: 6/24,6/18	LE: 6/24,6/18	**MODERATE NPDR**	6	**20.4**	280	153	299	12.4	Oral	Regular	Followup Advised
134	Kattappa	M	78	158642	RE: CF 3MTS , 6/60	LE:: CF3 MTS,6/60	**SEVERE NPDR**	10	**9.82**	290	156	312	9.5	INSULIN	REGULAR	Followup Advised
135	Subhas	M	69	148221	RE: 6/18,6/9	LE:6/9,6/6	**MILD NPDR**	0.5	28	187	170	211	6.5	ORAL	REGULAR	Followup Advised
136	Sarojini	F	54	142110	RE:CF 2MTS, CF3MTS	LE: CF 2 MTS, NI	**SEVERE NPDR**	15	**17**	370	215	290	8.8	ORAL	REGULAR	Followup Advised

137	Indubai	F	67	132890	RE: CF 3MTS , 6/60	Le: CF 3MTS, 6/60	**SEVERE NPDR**	11	**9.82**	289	234	299	9.5	INSULIN	REGULAR	Followup Adviced
138	Shivanad	M	51	123733	RE: CF 3MTS , 6/60	LE: CF3MTS, NI	**SEVERE NPDR**	9.5	**31**	352	278	311	8.5	ORAL	IRREGULAR	Followup Adviced