"PREVALENCE AND RISK FACTORS OF DIABETIC RETINOPATHY AMONG KNOWN DIABETIC PATIENTS OF RURAL POPULATION OF BELGAUM DISTRICT – A ONE YEAR CROSS SECTIONAL STUDY"

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LIST OF ABBREVIATIONS USED

AGEs	Advanced Glycation End products
BMI	Body Mass Index
CSME	Clinically Significant Macular Edema
CURES	Chennai Urban Rural Epidemiology Study
DCCT	Diabetes Control and Complications Trial
DM	Diabetes Mellitus
DME	Diabetic Macular Edema
DR	Diabetic Retinopathy
ETDRS	Early Treatment of Diabetic Retinopathy Study
iBRB	Inner Blood Retinal Barrier
IRMA	Intra Retinal Microvascular Abnormalities
NPDR	Non Proliferative Diabetic Retinopathy
NVD	Neovascularization on the Disc
NVE	Neovascularization Elsewhere
PDR	Proliferative Diabetic Retinopathy
RFT	Renal function test
SN-DREAMS	Sankara Nethralaya Diabetic Retinopathy Epidemiology and Molecular Genetics Study
UKPDS	United Kingdom Prospective Diabetes Study
VEGF	Vascular Endothelial Growth Factor
WESDR	Wisconsin Epidemiologic Study of Diabetic Retinopathy

ABSTRACT

Aim: To determine the prevalence of diabetic retinopathy and associated risk factors among known diabetics in the rural population of Belgaum district.

Design: A cross sectional population based study was carried out in the rural areas of Belgaum district, from January 2018- December 2018.

A total of 340 patients were screened . They underwent detailed ocular examination for diabetic retinopathy. Clinical grading of diabetic retinopathy was based on ETDRS guidelines. Random blood sugar, blood pressure, height, weight, haemoglobin , serum creatinine and HbA1C were measured, after taking informed consent.

Results: The prevalence of diabetic retinopathy was found to be 23.82 %. Of this, 19.11 % had NPDR and 3.53 % had PDR . 1.18 % had CSME. A statistically significant association was found between diabetic retinopathy and duration of diabetes, HbA1C, smoking and family history of diabetes.

Conclusion: The prevalence of diabetic retinopathy as per this study is quite significant in rural Belgaum. The awareness regarding retinopathy as a complication of diabetes and the need for regular follow up is low in the rural population. Therefore, there is the need for regular , structured screening camps as well as the availability of basic vitreo retinal facilities at the primary level.

KEYWORDS: Diabetic Retinopathy, Prevalence, Risk Factors

TABLE OF CONTENTS

LIST OF TABLES

LIST OF GRAPHS

LIST OF PHOTOGRAPHS

INTRODUCTION

Diabetes mellitus (DM) is a major pandemic with significant public health implications. Estimates point to 439 million of world population likely to be diabetic by the year 2030. This balance is tilted more to the side of developing countries as compared to the developed ones, putting a burden on the already strained limited health care facilities in these nations for the management of diabetic complications.[1]

Diabetic retinopathy can be defined as a chronic microangiopathy , secondary to prolonged hyperglycaemia, with a potential to impair vision.

The India Diabetes study conducted by the Indian Council of Medical Research has estimated the number of diabetics in India to be 62.4 million people. Over the next two decades, this can increase by more than 15 million , bringing the number of diabetic retinopathy patients to 22.4 million and 2 million diabetics with sight threatening diabetic retinopathy.[1]

In India, the prevalence of diabetic retinopathy is found to be around 13-18% in urban areas and 9-10% in rural areas.

A disturbing trend creeping in the economy is the younger age at which diabetes is presenting in Indians. Raman et al in their study has observed the prevalence of diabetic retinopathy(DR) in those who developed diabetes before the age of 40 , to be twice the number than those who developed it after the third decade.[2] This can cause a significant set back to the workforce.

Diabetic retinopathy is the 6^{th} leading cause of blindness in India. The awareness among diabetic patients as well as the diabetic care providers at the

primary level regarding diabetic retinopathy as a sight threatening complication of long standing diabetes is very low.

In a study conducted at Chennai, it was found that 45% of the rural and 50% of the urban diabetics who had sight threatening diabetic retinopathy, had never had a detailed fundus evaluation before.[3]

This lack of knowledge regarding retinopathy as a microvascular complication of diabetes , which can hamper vision , significantly necessitates mass awareness as well as screening programmes for better utilization of health care services as well as preventing blindness.

There is no definite protocol for diabetic retinopathy in India. Most of the camps are conducted on an ad hoc basis with the participation of the ophthalmologist, physician and support from the local community and other organisations. Outreach screening programmes screen diabetic patients for sight threatening diabetic retinopathy, who are then referred to higher centres for further management.

A novel method to do this has become possible via telemedicine. Fully equipped mobile vans with trained technicians or ophthalmologists reach remote areas with little access to advanced healthcare services .[4] Here digital retinal images of the patients are recorded along with detailed history. These are then sent via satellite to an expert at a centralized reading centre. These images are graded and a report is generated with a plan for further management, which is sent back to the mobile van, where the patient gets counselled. This method has been declared a cost effective one as per WHO guidelines.

In India, services for people with diabetes and blindness are provided by the public health system along with private sectors and non profit organisations. The government of India has also included support for laser treatment for DR in the 11th 5 year plan. A collaborated effort can help tackle this much preventable cause of blindness and help restore vision to the needy.

AIMS AND OBJECTIVES

PRIMARY OBJECTIVE: To assess the prevalence of diabetic retinopathy among already diagnosed diabetic patients in the rural population of Belgaum district.

SECONDARY OBJECTIVE: To analyze the risk factors associated with diabetic retinopathy.

REVIEW OF LITERATURE

I. HISTORY OF DIABETES

The term 'diabetes' was conceived by Araetus of Cappodocia , from a Greek word meaning to flow through . The word 'mellitus' has a Latin origin, meaning honey, an addition made by Thomas Willis.[5]

In 1869, Paul Langerhans identified the Islets of Langerhans.

In the 1920s, Frederick Banting and Charles Best invented insulin, which was later purified by James Collip.

In 1955, Carbutamide, the first oral hypoglycemic agent was developed.

In the 1970s, Dean Kamen invented the insulin pump and HbA1c testing was introduced in 1977.

Other inventions include Humulin, the first biosynthetic human insulin and Novopen, the first insulin pen delivery system, by Novo Nordisk in 1985.[6]

II. CLASSIFICATION AND DIAGNOSIS OF DIABETES MELLITUS

Definition

It is a metabolic disorder, characterized by chronic hyperglycemia, and associated disturbances of carbohydrate, protein and fat metabolism, secondary to the deficiency of insulin production, impaired insulin action or both.[7]

Classification

Diabetes can be classified as

1. Type 1 - autoimmune beta cell damage, resulting in total deficiency of insulin.

2. Type 2 - gradual loss of insulin secretion, mostly with resistance to insulin.
3. Gestational - diabetes newly diagnosed in the later trimesters of gestation.
4. Other monogenetic syndromes

Diagnosis

Can be made by

1. A fasting plasma glucose ≥ 126 mg/dl .
2. 2 hours plasma glucose ≥200 mg/dl
3. HbA1C ≥6.5%
4. A random plasma glucose ≥200 mg/dl in a patient with specific features of hyperglycemia

III. EPIDEMIOLOGY OF DIABETES

The diabetic population will hit 438 million over the next 10 years, 54 % more than the predicted figures for 2010. The most affected will be rapidly growing developing nations like India and China.[7]

India is considered to be the world capital of diabetes. The number of diabetics in the nation is reaching an alarming number of 69.9 million by the year 2025 and around 80 million by 2030, amounting to an increase of over 266%.

Recent statistics shows that prevalence of diabetes is more in urban areas (28% of people living in urban areas are affected), as compared to rural areas(where around 5% of the population are affected)[8].Although genetic predisposition partly determines individual susceptibility to diabetes mellitus, other factors like lack of physical activity and convenience food are major reasons for this global epidemic.

IV. LONG TERM COMPLICATIONS OF DIABETES

The micro and macrovascular complications started to get noticed, only post insulin therapy when diabetes stopped being considered as a 100% mortality disease.[9]

Microvascular complications

1. **Diabetic retinopathy**

   It is considered to be the most common microvascular complication . It depends on the inadequacy of glycemic control as well as the duration of diabetes.

2. **Diabetic nephropathy**

   It is a urinary protein excretion of over 0.5 gram in a day.

   Without adequate intervention, diabetic patients with microalbuminuria (30-299 mg of albumin excretion in a day) , mostly develop nephropathy.

   The pathologic changes in the kidney comprise of increased basement membrane thickness in the glomerulus , microaneurysms, and Kimmelstein-Wilson bodies in the mesangium and other changes.

   There is evidence to correlate poor glycemic control and development of diabetic nephropathy. Treatment should be aimed at achieving the lowest safe blood glucose level that can either prevent or retard the development of diabetic nephropathy.

   Patients also obtain benefit from antihypertensive medications,which have renoprotective effects which are independent of their antihypertensive effects. They decrease the progression of microalbuminuria to macroalbuminuria in around 60- 70% patients.

3. Diabetic neuropathy

It is a diagnosis of exclusion. It is defined as symptoms and/or signs of peripheral nerve dysfunction in diabetic patients, not attributed to any other cause.

The risk is directly related to the poor glycemic control as well as duration of diabetes. The mechanisms by which chronic hyperglycemia can cause peripheral neuropathy include accumulation of polyol like sorbitol, Advanced glycation end products(AGEs) and oxidative stress.

It can manifest as sensory, focal/ multifocal as well as autonomic .

Chronic sensorimotor distal symmetric polyneuropathy is the most commontype of neuropathy.

Macrovascular complications

Cardiovascular disease is the major cause of death in diabetic patients.

Diabetes is also a risk factor for the development of cerebrovascular disease and stroke(around 150-400% increased risk)[10]

Both of these can be attributed to the hypercoagulability and excessive platelet adherence.

V. HISTORY OF DIABETIC RETINOPATHY

In **1846,** the French ophthalmologist , Appolinaire Bouchardat, observed poor vision in diabetic patients who did not have any cataractous changes in the lens. This was partially reversible and improved with good glycemic control.[11]

Diabetic maculopathy

In 1855, Eduard Jaeger reported round or oval yellowish spots along with full and partial thickness excavasations in the macula of a diabetic patient.[12]

Later ,in 1877, Nettleship along with Sir Steven Mackenzie published an article where they described in full detail the abnormal changes in retina of diabetic patients.[13]

Proliferative diabetic retinopathy

In **1876**, detailed diagrammatic representations of the fibrovascular degeneration of the optic nerve head and vitreoretinal traction were documented by Wilhelm Manz in his paper 'Retinitis Proliferans'. [14]

The term retinitis , suggesting an inflammatory etiology, although a misnomer continued to be used for several years.

The evolution of therapeutic modalities for diabetic retinopathy

In 1950,the German ophthalmologist Gerhard Meyer- Scwickerath , reported the management of retinal disorders with photocoagulation after seeing the effects of a solar eclipse on the retina in a student.[15]

The Diabetic Retinopathy Study Research Group,in 1979 proved the significant reduction of visual impairment by both xenon arc and argon laser panretinal photocoagulation.[16]

The Early Treatment Diabetic Retinopathy Study (ETDRS) also proved that argon laser photocoagulation aids in management of macular oedema.[17]

Robert Macherer advocated pars plana vitrectomy for management of the vitreous haemorrhages in proliferative diabetic retinopathy.[18]

VI. EPIDEMIOLOGY OF DIABETIC RETINOPATHY

GLOBAL

Prevalence of DR

Metanalytical studies have observed the global prevalence of DR to be 35.4%.[19]

WHO estimates DR to account for 4.8% of cases of blindness all around the globe.[20]

In general, Western countries have a higher prevalence as compared to their Asian counterparts.

Fast growing nations like India and China show an urban rural divide in the prevalence of DR.[21]

Prevalence of Diabetic Macular Edema(DME)

Population based studies have shown the prevalence of DME to range from 4.2 to 7.9% in type 1 diabetics and 1.4 to 12.8% in type 2 diabetics.

INDIA

The Sankara Nethralaya Diabetic Retinopathy Epidemiology and Molecular Genetics Study Report 2(SN-DREAMS 2) , found a higher prevalence of DR in urban areas (18.0 %) [22]compared to rural areas (10.8 %).[23]This can , to an extent be attributed to the increasing wealth along with dietary changes in urban areas, and also more likelihood of mortality as a result of diabetes related complications , owing to lesser access to healthcare facilities in rural areas.

VII. PATHOGENESIS OF DIABETIC RETINOPATHY

The main mechanisms involved in the pathogenesis of diabetic retinopathy include hyperglycemia and microangiopathy, inflammation, neuronal degeneration in retina and oxidative stress.

BIOCHEMICAL MECHANISMS

1. **The Aldose reductase theory**

   Glucose is reduced to its alcohol form sorbitol by the enzyme aldose reductase. This is further oxidized to fructose by sorbitol dehydrogenase. But, this is a slow reaction and can lead to sorbitol accumulation intracellularly. In a euglycemic environment, the aldose reductase pathway is redundant and glucose is not an ideal substrate , owing to it's high binding constant. But, under a hyperglycemic condition, this pathway comes into play as other metabolic pathways get saturated.[24]

   This will cause a decrease in intracellular NADPH , altering the redox balance at a cellular level, leading to a decreased levels of nitric oxide. This can also increase the NADH/NAD+ ratio, leading to cellular oxidative stress and damage[25].

2. **Advanced glycation endproduct (AGE) Theory**

   AGEs are proteins, lipids and nucleic acids which are irreversibly transformed by either reducing sugars or their products.

   AGEs can directly cause cell damage by impairing the function of both extracellular (eg: collagen)[26] and intracellular proteins.

3. **Photoreceptor metabolism theory**

Pseudohypoxia of the retina, as a result of hyperglycemia, along with anoxia of inner retina in a dark adapted state(rods consume high oxygen levels during dark adaptation, leading to reduced pO2 in the retina), lead to an increase in the production of VEGF. [27]

4. **Reactive oxygen intermediates (ROI) theory**

The production of free radicals like superoxide anion, which are the byproducts of oxidative phosphorylation,is increased with high glucose[28] levels. These disrupt the mitochondrial DNA as well as the cellular proteins. Increased oxidative stress also decreases the levels of nitric oxide, promotes leucocyte adhesion and also reduces endothelial barrier action.

5. **Protein Kinase C(PKC) theory**

Oxidative stress can also activate protein kinase C through greater synthesis of diacylglycerol (DAG)

This leads to greater vascular permeability[29], impairment of Nitric oxide (NO) balance,increased adhesion of leucocytes to vasculature and alteration of blood flow dynamics. PKC activation also leads to increased expression of VEGF.

Hyperglycemia and microangiopathy

The primary manifestations of retinal vasculature as a result of chronic hyperglycemia are blood vessel dilatation and haemodynamics, which is an autoregulatory mechanism to improve retinal metabolism .[31] Studies have also shown that hyperglycemia can trigger the apoptosis of pericytes[32], which provide structural support to the capillaries. This leads to capillary wall outpouchings and microaneurysm formation. This , and apoptosis of endothelial cells, thickening of

basement membrane result in impairment of inner blood retinal barrier(iBRB) and capillary occlusion and ischaemia.

This leads to the upregulation of Vascular endothelial growth factor (VEGF) via Hypoxia inducible factor 1(HIF-1), [33] which , through the phosphorylation of tight junction proteins leads to improved permeability of the retinal microvasculature. It also supports endothelial cell proliferation via mitogen activated protein(MAP) activation.

Other pro angiogenic factors implicated include angiopoetins 1 and 2.

Inflammation

Increased adhesion of leucocytes and upregulation of expression of leukocyte b2 integrins as CD11a, CD11b and CD18 can lead to occlusion of retinal microvasculature as well as endothelial cell loss and the breakdown of BRB through Fas (CD95)/Fas-ligand pathway.

There is also increased expression of endothelial cell adhesion molecules as intercellular adhesion molecule-1(ICAM-1), vascular cell adhesion molecule-1 (VCAM-1) and selectins as E-selectin. [35] Chemokines like monocyte chemotactic protein 1(MCP-1) , macrophage inflammatory protein -1 alpha(MIP-1alpha) and MIP-1 beta are also elevated in diabetic patients. Deficiency of MCP-1 has been shown to reduce vascular leakage in diabetic mice[36]. Others such as tumour necrosis factor alpha (TNF alpha), interleukin 6(IL-6) , IL-8 and IL-1 beta are also elevated..

Retinal neurodegeneration

Retinal neurons of diabetic animals and subjects show upregulation of proapoptotic molecules as cleaved caspase- 3, Bax and Fas.[37] The retinal neurodegeneration can also be due to mitochondrial dysfunction, due to pro apoptotic mitochondrial proteins as cytochrome c and apoptosis inducing factor(AIF).

Pathogenesis of diabetic macular oedema

Increase in vascular of permeability due to compromised iBRB leads to the development of macular oedema.

The tight junctions are made up by complexes consisting of occludins, claudins and junctional adhesion molecues (JAMS) and the membrane associated guanylate kinase homologs (MAGUKS) - Zonula occludens (ZO-1). The upregulation of VEGF-A leads to the loss of tight junction integrity at the level of endothelial cells and also aids in the transport of substances across these cells.[38]

Another mechanism is the increase in hydrostatic pressure of retinal capillaries in long standing cases of diabetes, owing to vasodilatation .

Genetic mechanisms in the pathogenesis of diabetic retinopathy

A DCCT research group report observed familial clustering of cases of diabetic retinopathy especially, the more severe forms in families with large number of diabetic members.[40]

The most well studied gene in the pathogenesis of diabetic retinopathy is the VEGF gene. Studies on the role (beneficial/risk) of single nucleotide polymorphisms (SNPs) in VEGF gene have not yielded any conclusive results as the associations derived are of conflicting values in different populations.

VIII. CLASSIFICATION OF DIABETIC RETINOPATHY

A. MODIFIED AIRLIE HOUSE CLASSIFICATION

This classifies diabetic retinopathy into 85 levels ranging from level 10 (no retinopathy) to level 85 (severe vitreous haemorrhage or macula involving retinal detachment).[41]

An **abbreviated ETDRS classification** of diabetic retinopathy is given below [42]

Diabetic retinopathy can be classified into non proliferative, proliferative and advanced diabetic eye disease

I. Non proliferative

1. Very mild- when there are only microaneurysms.
2. Mild - microaneurysms, retinal haemorrhages and cotton wool spots can be present, but not more than in moderate NPDR. Intraretinal microvascular abnormalities (IRMA) and beading should not be present.
3. Moderate –
   (i) 20 medium to large haemorrhages per quadrant in 1-3 quadrants or mild IRMA
   (ii) Significant venous beading, but only in a single quadrant
   (iii)Cotton wool spots
4. Severe – one or more of
   (i) severe haemorrhages in all quadrants
   (ii) significant venous beading in 2 or more quadrants
   (iii)moderate IRMA in one or more quadrants
5. Very severe - two or more of the above mentioned criteria.

II. Proliferative

1. Mild to moderate- when there are new vessels on the disc(NVD) or elsewhere (NVE), but less than high risk criteria
2. High risk –

   (i) NVD upto 1/3 disc area

   (ii) Any NVD with vitreous haemorrhage

   (iii)NVE of more than half disc area, with vitreous haemorrhage

III. **Advanced diabetic eye disease** includes

- Retro or intrahyaloid haemorrhage
- Tractional rd
- Rubeosis iridis

Management

Mild and moderate NPDR are advised annual and biannual review.

Severe and very severe NPDR are asked to review in 2- 4 months.

The risk of developing PDR increases with increasing severity of NPDR.

Low risk PDR can be advised photocoagulation or anti-VEGF. High risk PDR usually requires vitrectomy.

The ETDRS defines **clinically significant macular edema(CSME)** as

- "Thickening of the retina at or within 500 µm of the centre of the macula" or
- "Hard exudate at or within 500µm of the centre of the macula associated with thickening of adjacent retina" or

- "A zone of retinal thickening 1 disc area or larger , any part of which is within 1 disc diameter of the centre of the macula".[41]

  Diabetic Macular Edema(DME) can also be focal and diffuse.[43]

  Focal DME is edema due to the focal leakage from microaneurysms. Microaneurysm clusters are usually surrounded by a circinate pattern of hard exudates.

  Diffuse DME is due to iBRB. This involves microaneurysms, capillaries as well as arterioles. Hard exudates are usually not seen.

  Based on microaneurysmal fluorescein leakage in angiography , ETDRS classified diabetic macular edema as

  1.Focal-≥67 % of leakage originating from the microaneurysms

  2.Intermediate-microaneurysmal leakage between 33 to 66%.

  3. Diffuse- ≤33 %microaneurysmal origin leakage. [17]

The International Clinical Disease Severity Scale classifies DR into mild, moderate and severe NPDR and PDR.

IX. NATURAL COURSE OF NON PROLIFERATIVE DIABETIC RETINOPATHY

Diabetes mellitus without retinopathy

In early years of diabetes, studies have shown that the retinal parenchymal cells exhibit certain changes as glial cell reactivity , glutamate metabolism alterations and death of neurons. Minimal alterations in perception of colour and contrast sensitivity have also been observed .

Microaneurysms

These are saccular extensions of the capillary wall, seen as red dots with a diameter of 10-25 µm. Their lumen can get obliterated by agglutinated RBCs or thrombus ,and can even turn acellular .Most of them are fleeting and only a few remain stable. [24] The chance of increase in severity of diabetic retinopathy increases with more microaneurysms .

Retinal vascular hyperpermeability

Higher VEGF levels cause dysfunction of the tight junctions at the BRB, leading to increased vascular permeability and resultant leakage . This may be accompanied by focal zones of thickening of the retina.

Extravascular deposits of lipid rich material known as hard exudates are also observed. Intraretinal hemorrhages begin to crop up, especially in the posterior pole and periphery.

Diabetic macular edema

Leakage from microaneurysms or more diffuse leakage from the capillaries with increased permeability account for DME in areas of vascular incompetence.

In areas of capillary non perfusion, retinal thickening can exist without associated vascular leakage.

Macular oedema may or may not have associated cyst formation and subretinal fluid.

The natural history of DME is quite variable ranging from persistence for years to spontaneous resolution over time.

Capillary closure, microvascular remodeling and retinal ischaemia

In advanced diabetic retinopathy, trypsin digest retinal vascular mounts show areas known as ghost vessels , where capillaries have lost their lining endothelial cells and pericytes.

Increasing count and conjoining of these can lead to occlusion of the end arterioles which are responsible for their perfusion.

Increasing capillary closure and the resultant ischaemia in the retina are usually accompanied by intraretinal microvascular abnormalities, intraretinal haemorrhages and venous beading. In certain cases of extensive non perfusion ,the retina occasionally assumes a featureless appearance, with very few visible vessels, haemorrhages or microvascular abnormalities.[24]

Alterations in the vitreous and vitreoretinal interface

Epiretinal membrane formation , which occurs due to vitreous gel liquefaction along with resultant effects at vitreoretinal interface tends to be more common in diabetic patients.

Posterior cortical vitreous shows an increased adherence to the retina.

Biochemical changes in the vitreous of diabetic patients include greater cross linking of collagen, AGEs which enhance vitreoretinal adhesion and promote glial cell reactivity and also change in concentration of different soluble proteins.[24]

X. NATURAL COURSE OF PROLIFERATIVE DIABETIC RETINOPATHY

i. **Development and proliferation of new vessels-**arise mostly on the disc. They can cross both arterioles and veins. Initially, they might be associated with thickening of the optic nerve head as well as adjacent retina. Later, these vessels will develop surrounding fibrous tissue.

ii. **Contraction of the vitreous and fibrovascular proliferation-** with resultant posterior vitreous detachment and vitreous haemorrhage.

iii. **Distortion of retina and tractional detachment**-the contracted vitreous along with proliferated fibrovascular tissue leads to tractional retinal detachment, which may or may not involve the macula.

iv. **Involutional or Quiescent Proliferative Retinopathy**

In this stage, the vitreous contraction is completed and vitreous detachment has occurred at all areas, except where vitreoretinal adhesions prevent it.

The frequency and severity of vitreous haemorrhages decrease, and over a few months, the haemorrhage clears up.

If the detachment involves the macula, visual acuity will be impaired.

Both arterioles and veins become narrower with fewer visible branches. Occasionally haemorrhages and microaneurysms may be present. Fibrous tissues become thinner and more transparent, allowing better visualization of the retina.

XI. RISK FACTORS ASSOCIATED WITH THE DEVLOPMENT AND PROGRESSION OF DIABETIC RETINOPATHY

Race and ethinicity

In general, western countries have a higher prevalence of DR in diabetes type 2 patients as compared to their Asian counterparts.

Apart from the east-west divide, rapidly developing nations like India and China show an urban rural divide in the prevalence of DR.[21]

Genetic factors

The familial clustering of cases of diabetic retinopathy particularly, as evidenced in the DCCT study point to a probable genetic factor in the development of diabetic retinopathy .[40]

Studies on the role of SNPs in VEGF gene have not yielded any conclusive results as the associations derived are of conflicting values in different populations.

Ramprasad et al in 2007 found significant association in the the role of around 20 SNPs in the gene for AGEs i.e RAGE with proliferative retinopathy. [44]

Gender

Most studies have shown a higher prevalence of diabetic retinopathy in men than in women, but no gender predilection has been observed in the prevalence of sight threatening retinopathy or progression of retinopathy.

In women, among type 1 diabetics, menarchal status at baseline had a higher prevalence and severity of retinopathy over a follow up period. This may be attributed to the action of the sex hormones.[45]

Pregnancy, a high estrogen level state, is associated with significant progression of preexisting retinopathy.

Use of oral contraceptive pills and hormone replacement therapy[46] doesn't affect the progression of retinopathy.

Age at diagnosis

In type 1 diabetics, the WESDR study showed that the prevalence of diabetic retinopathy increased with increasing age. It was least common in children less than 13 years.[47]

In type 2 diabetics on insulin,the 4 year incidence and progression of retinopathy showed a decreasing trend with a higher age at baseline.[48]

Duration of diabetes

In the WESDR study, in the younger age group, the prevalence of retinopathy 3-4 years following diagnosis of type 1 diabetes was 14 % in men and 24% in women. Among those who had a duration of diabetes for 19-20 years , 50 % of men and 33 % of women had proliferative retinopathy.[47]

Glycemic control

The DCCT showed a statistically significant reduction in the progression of diabetic retinopathy in the intensive glycemic control group as compared to the conventional control group.

Incidence of CSME was also less in these patients, but it was statistically insignificant.[24]

The UKPDS study[49] also showed a reduction in progression of diabetic retinopathy and requirement of laser photocoagulation in the patients with intensive glycemic control .

These findings were also corroborated by the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial[50].

Exogenous insulin

As insulin began to be more widely used for blood sugar control, multiple trials observed a paradoxical worsening of diabetic retinopathy in the initial 3-12 months following initiation of intensive insulin treatment. Majority of these patients who had only mild and moderate NPDR before treatment, developed cotton wool spots and/or IRMA .This was mostly mild and short lived.

But, a few cases with poor glycemic control and severe retinopathy at baseline, developed PDR and /or macular edema amounting to a significant reduction in visual acuity.

Higher initial levels of HbA1C and greater reduction in it's level after intensive insulin therapy are considered to be the most significant risk factors implicated in early worsening. This may be explained by alterationsin retinal haemodynamics, reduced microvasculature autoregulation , short lived ischemia as a result of reduced availability of the substrate, and altered homeostasis , induced by insulin ,which can lead to upregulation of angiogenic factors as VEGF.

The Sankara Nethralaya –Diabetic Retinopathy Epidemiology and Molecular Genetics Study (SN-DREAMS, Report number 35) observed a significant association between longer duration(> 5 years) before commencing insulin therapy overall with presence of DR. This can be explained by the damaging effects of long term hyperglycemia as a result of longer insulin free duration , in patients with poor glycemic control.[51]

Blood pressure

The UKPDS study showed that for each 10 mm Hg decrease in mean systolic blood pressure there was a 13% reduction in microvascular complications. [52]

The WESDR study showed a similar higher risk of developing macular edema in diabetics with associated hypertension ,especially elevated diastolic blood pressure.[53]

The ACCORD study observed that the progression rate of diabetic retinopathy was slightly more in subjects on intensive anti hypertensive medication than in those on regular control. [50]

The ADVANCE study showed no beneficial effect of intensive blood pressure control on diabetic retinopathy.[54]

Anemia

A study conducted in south India by Rani et al,showed that in type 2 diabetics with anemia there was risk of developing retinopathy than those without anemia[55]

Quing Quio et al also reported a similar odds for presence of retinopathy in anemic patients.[56]

In the ETDRS study, David et al observed that anemic patients had a higher risk of development of proliferative retinopathy and resultant vision loss.

Conway et al reported the haemoglobin level to be a predictive factor in the development of proliferative retinopathy in diabetic patients.[57]

Anemia induced hypoxia results in the excessive release of vaso proliferative factors (X factor) , leading to progression of DR[56]. Another explanation is the decreased flexibility of RBCs in diabetic patients causing microangiopathy[58]

Smoking

Due to it's effect of vasoconstriction of microvasculature [59] and enhancing the platelet aggregation and adhesiveness[60], smoking is expected to have a deleterious effect on retinopathy. But most epidemiologic data like the WESDR have not found any association between smoking and retinopathy in diabetics.[61]

Proteinuria and diabetic nephropathy

The type 1 diabetics in the WESDR with gross proteinuria at baseline had more risk of development of proliferative retinopathy over 4 years, as compared to those who did not have gross proteinuria.

In a similar study in a Pittsburgh cohort study of type 1 diabetics, more subjects with microalbuminuria or overt nephropathy at baseline , progressed to proliferative retinopathy over 2 years as compared to those who did not have

nephropathy. But, the nephropathy at baseline was not found to be associated with the increase in severity of retinopathy over time.

Serum lipids and lipid lowering

The WESDR showed an association between higher prevalence of retinal hard exudates and greater levels of total serum cholesterol in both younger and older age onset groups on insulin, but not in the type 2 diabetics on oral agents.

A follow up study showed a mild protective association between higher levels of high density lipoprotein and diabetic retinopathy. The ETDRS showed an increase in the risk of developing macular edema and resultant decreased visual acuity in patients with elevated levels of serum triglycerides, low and very low density lipoproteins at baseline.

The ACCORD Lipid study, showed a lesser progression in those on fenofibrate as compared to those on placebo .

Progression of diabetic retinopathy following cataract surgery

NPDR can rapidly progress to severe diffuse macular edema in a few months following uncomplicated cataract extraction.

Jaffe and Burton [62]and also Schatz et al observed that the progression of retinopathy was at a faster pace in operated eyes as compared to the fellow phakic eyes, in patients who had not received pre-op photocoagulation.

Pollack [63]et al and Cunliffe et al demonstrated that , despite previous photocoagulation, macular edema and neovascularization may worsen following cataract extraction. Pollack et also also observed that 81% of eyes with pre existing

background retinopathy developed cystoid macular edema following an uneventful cataract extraction in comparison to 32% in eyes without any pre existing retinopathy.

This can be due to increased disruption of the BRB or the greater inflammation seen in diabetics following cataract surgery.

Despite a smaller incision and shorter duration of surgery in phacoemulsification, which should result in lesser chances of breakdown of BRB and lesser inflammation post op, Antcliff [64]et al showed no difference between ECCE and phacoemulsification in case of progression of retinopathy.

Wagner[65] et al showed no progression of retinopathy in eyes following cataract surgery when compared to the fellow phakic eyes.

In both these studies, the patients did not have any diabetic retinopathy preoperatively.

In a study by Borillo [66]et al, which studied progression of retinopathy in patients with pre existing retinopathy, following phacoemulsification, it was found that using phaoemulsification did not aid in decreasing the rate of progression of retinopathy. This study also showed that the progression was more in surgeries performed by residents as compared to attendings, probably because of increased surgical duration and more chances of posterior capsular rupture , leading to higher chances of post operative inflammation.

Hong et al in a cohort study also observed similar findings of more chances of diabetic retinopathy incidence and progression in diabetic patients following cataract surgery.[67]

Body mass index

The association between Body Mass Index (BMI) and diabetic retinopathy is inconsistent.

In the WESDR study, type 2 diabetics, not dependent on insulin, with older age of onset, who were underweight had a 3 fold more likelihood to develop retinopathy .[68]

This may be because these underweight, older age onset diabetics may already be in a more severe state of their diabetes.

Also patients who were obese at baseline had more chance for progression of retinopathy when compared to those who had a normal BMI at baseline.

MATERIALS AND METHODS

Study design:

Population based cross sectional study

Study Population

The source of data was already diagnosed diabetic patients, attending diabetic retinopathy screening camps organized in rural areas of Belgaum district.

Study duration:

One year: 1st January 2018-31st December 2018.

Sample size:

Calculated using the following equation

$N=(Za)^2[p \times q]/d^2$

p = 21.2% [69]

q =100-p=78.8

d=20% 0f p=4.24

where, p is the percentage of prevalence and d is the percentage likely difference in the prevalence.

Zα is associated with the level of significance. For a 5% level of the significance zα = 1.96.

With P=21.2% and d=20% of P, the sample size was 357

Sampling method:

Purposive sampling

Method of Collection of Data

Selection criteria:

Inclusion criteria:

1. All patients between 40-85 years of age , who are known diabetics [Type II] (duration - more than 6 months), visiting screening camps in rural Belgaum .

Exclusion criteria:

1. Ophthalmic diseases preventing view of posterior segment

– Senile mature cataract

– corneal opacity

2. Individuals with shallow anterior chamber

3. Acute ocular inflammation.

PR0CEDURE

After the approval from the institutional review board and ensuring that all the study procedures adhere to the tenets of The Declaration of Helsinki, the study was carried out.

Screening camps for detecting diabetic retinopathy were organised by the Department of Ophthalmology, KLES Dr. Prabhakar Kore Hospital and MRC in the rural areas of Belgaum district.

A single observer study was carried out and patients who satisfy the above mentioned criteria were enrolled in the study as subjects.

All the subjects were explained to ,in detail the aims of the study and the procedures to be undergone. Written and informed consent were obtained from the study subjects.

A thorough history of the patient, including patient particulars, ocular complaints, diabetic status and treatment and co morbidities was duly noted .

Visual acuity was checked using Snellen's visual acuity chart. Detailed anterior and posterior segment examination were done by both direct and indirect ophthalmoscopy. The patients were graded as per the abbreviated ETDRS classification of diabetic retinopathy.

Blood pressure was recorded. The BMI of the patient was calculated according to height and weight records.

The following blood investigations were recorded at the respective PHCs.

1. 1.Haemoglobin
2. Random blood sugar

Mini RFT and HbA1C were done at KLEs Dr. Prabhakar Kore Hospital and MRC.

All these data were used to assess the risk factors of diabetic retinopathy. The patients with no diabetic retinopathy and very mild NPDR were asked for regular annual checkup. Mild NPDR patients were to review after 6-12 months. Moderate to

severe NPDR patients were asked to review in 6 months. Very severe NPDR patients were advised 3 monthly follow up PDR patients were referred to base hospital for further management.

STATISTICAL MEASURES

The chi square test was used to assess the association between the above mentioned variables and the presence or absence of diabetic retinopathy.

OBSERVATION AND RESULTS

350 subjects were included in the study. 10 had to be excluded because 4 subjects refused blood testing, 3 refused dilated fundus examination and 3 blood samples could not be analysed.

A total of 340 subjects were studied, who met all the inclusion criteria.

All variables were categorized into different levels. The frequency table of these variables is tabulated below.

Table 1: Frequency table of variables

Factor	Sub-category	Number of Subjects	Percentage (%)
Gender	**Male**	138	40.59
	Female	202	59.41
Hypertension	**Yes**	198	58.24
	No	142	41.76
BMI (kg/m^2)	**Underweight (< 18.5)**	19	5.59
	Normal (18.5-22.9)	82	24.12
	Overweight (23-24.9)	83	24.41
	Pre-obese (25-29.9)	104	30.59
	Obese (≥ 30)	52	15.29
HbA1c (%)	**< 6.5**	43	12.65
	6.5-9.5	191	56.18
	9.6-12.5	95	27.94
	> 12.5	11	3.24
Hemoglobin (gm/dl)	**Normal (> 11)**	178	52.35
	Mild Anemia (10-11)	83	24.41
	Moderate Anemia (7-10)	79	23.24
	Severe Anemia (4-7)	0	-
	Very severe Anemia (< 4)	0	-
Creatinine (mg/dL)	**< 1.2**	255	75
	≥ 1.2	85	25
Insulin	**No**	316	92.94
	Yes	24	7.05
Smoking	**Yes**	66	19.41
	No	274	80.58
Posterior Segment	**No diabetic retinopathy**	259	76.18
	Very mild NPDR	7	2.06
	Mild NPDR	32	9.41
	Moderate NPDR	23	6.76
	Severe NPDR	3	0.88
	PDR	12	3.53
	CSME	4	1.18
Family H/O DM	**Yes**	114	33.53
	No	226	66.47
Duration of Diabetes (in years)	**0.5-1**	71	20.88
	2-5	148	43.53
	6-10	83	24.41
	11-15	17	5.00
	>16	21	6.18

Out of the 340 , there were 138 male and 202 female subjects. More than 50% of the subjects were hypertensive. Only 19 patients were underweight. One fifths belonged to normal BMI category . The rest ranged from overweight to obese.

Majority of the subjects had an HbA1C value of more than 6.5, belonging in the frank diabetes criteria, with 8 subjects having an HbA1C value of more than 12.5. Only 35 subjects had an HbA1C value of less than 6.5

Haemoglobin values categorized most of the subjects from normal to moderate anemia. None of the subjects included in the study belonged to the category of severe or very severe anaemia.

More than 80% of patients had a serum creatinine value within normal limits. Most of the subjects were on treatment with oral hypoglycemic agents.

Less than 20% of the study population were smokers or had history of nicotine use in the past.

Over 60 % of the subjects did not have a family history of diabetes.

Majority of the subjects had diabetes from between 2-10 years. 68 were recently diagnosed diabetics and 21 had diabetes for more than 15 years.

Prevalence of Diabetic Retinopathy

Of the 340 subjects studied, 81 had diabetic retinopathy of varying severity. The total prevalence of diabetic retinopathy in a sample population of rural Belgaum thus is 81/340* 100 i.e **23.82%.**

Of this 19.11 % had non proliferative diabetic retinopathy and 3.53% had proliferative diabetic retinopathy. 1.18 % had Clinically Significant Macular Edema.

Assessment of risk factors implicated in the prevalence of diabetic retinopathy

1. **Gender**

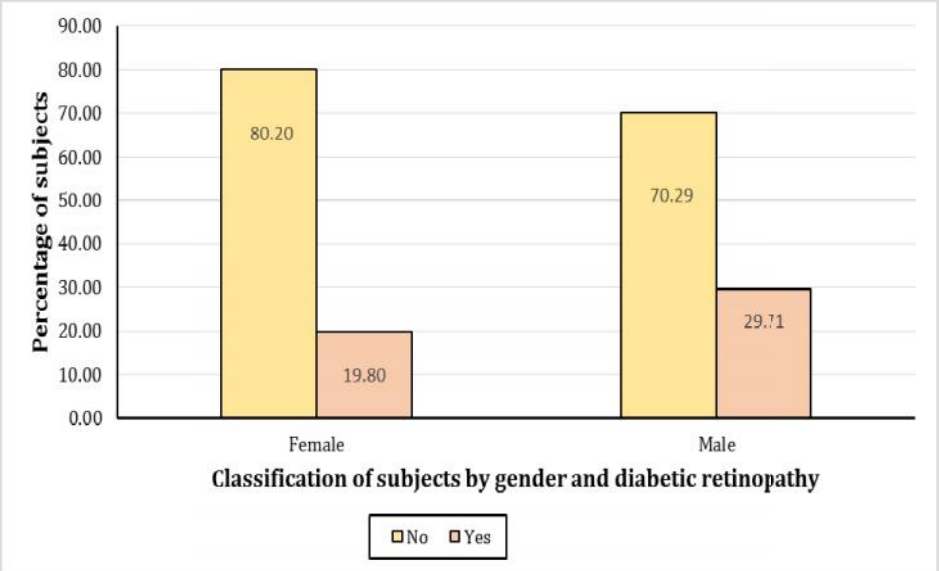
Table 1a: Comparison of gender with severity of diabetic retinopathy

Factor	Sub-category	Gender		p-value
		Female	Male	
Posterior Segment	Yes	40	41	0.04811
	No	162	97	

Above table gives the frequency table of gender and diabetic retinopathy. Chi-square test is used to test the independence between gender and diabetic retinopathy. Here p-value is significant therefore, they are dependent.

Odds of having retinopathy (1.71, CI:1.03-2.83) is more for males compared to females.

Figure 1: Distribution of subjects with gender and severity of diabetic retinopathy



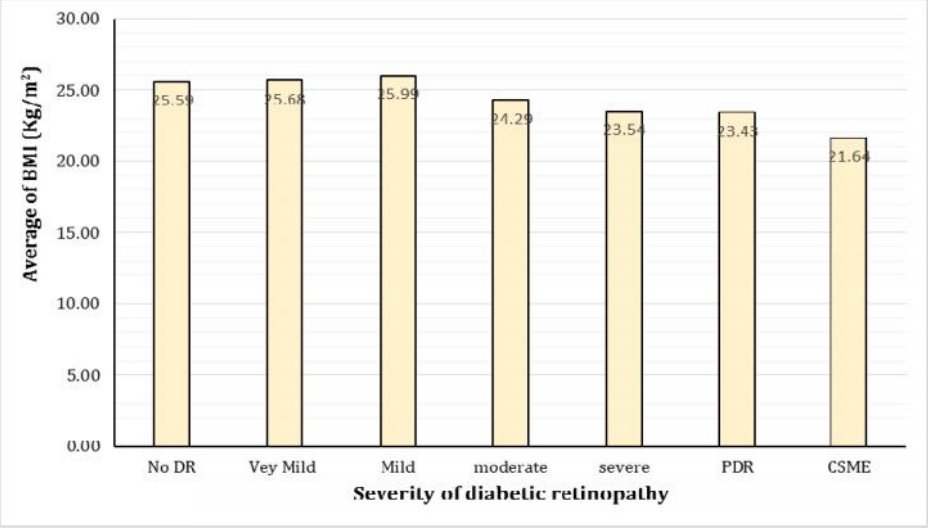
2. BMI

Table 2: Comparison of Body Mass Index with Diabetic Retinopathy

Factor	Category	BMI (Kg/m^2)	p-value
Posterior Segment	No diabetic retinopathy	25.58± 4.49	0.199
	Very mild NPDR	25.67± 4.32	
	Mild NPDR	25.99± 3.46	
	Moderate NPDR	24.28± 4.50	
	Severe NPDR	23.54 ± 2.63	
	PDR	23.42± 3.34	
	CSME	21.64± 1.14	

Above table gives the mean ± sd values of BMI (Kg/m^2) over the different levels of severity of diabetic retinopathy. ANOVA is used to test whether the mean level of BMI (Kg/ m^2) is same or not over the different levels of severity of retinopathy. Here p-value is not significant, hence we conclude that there was no significant difference in the mean level of BMI (Kg/m^2) over severity.

Figure 2: Average of BMI (Kg/m^2) over severity of diabetic retinopathy



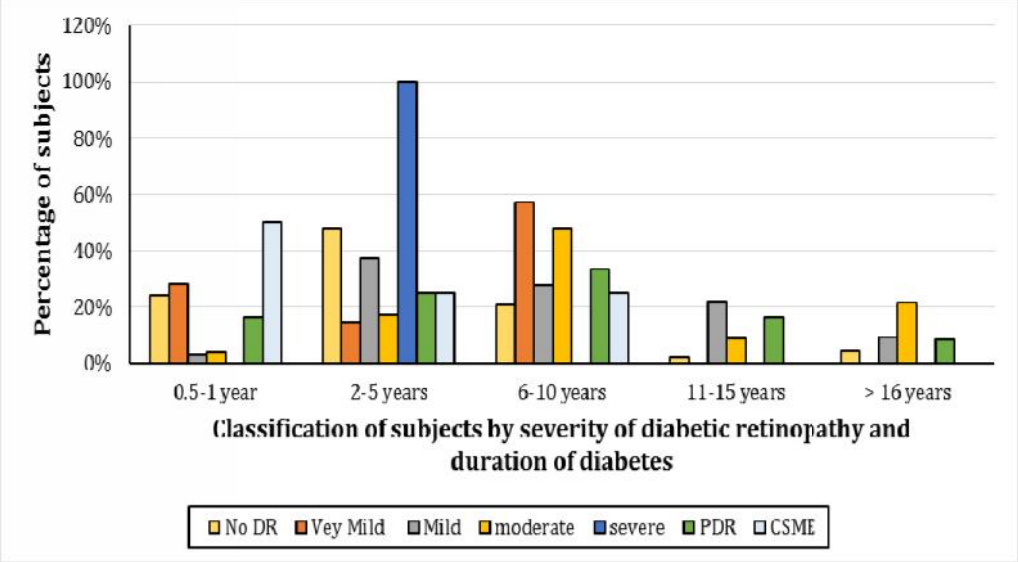
3. Duration of diabetes mellitus

Table 3: Comparison of Duration of Diabetes with Diabetic Retinopathy

Factor	Category	Duration of Diabetes (years)					p-value
		0.5-1	2-5	6-10	11-15	> 16	
Posterior Segment	No diabetic retinopathy	63	124	54	6	12	< 0.0001
	Very mild NPDR	2	1	4	0	0	
	Mild NPDR	1	12	9	7	3	
	Moderate NPDR	1	4	11	2	5	
	Severe NPDR	0	3	0	0	0	
	PDR	2	3	4	2	1	
	CSME	2	1	1	0	0	

From above table we can see that, there is association between duration of diabetes and diabetes retinopathy.

Figure 3: Distribution of subjects by severity of diabetic retinopathy and duration of diabetes



4. Glycemic control

Table 4: Comparison of HbA1c and posterior segment.

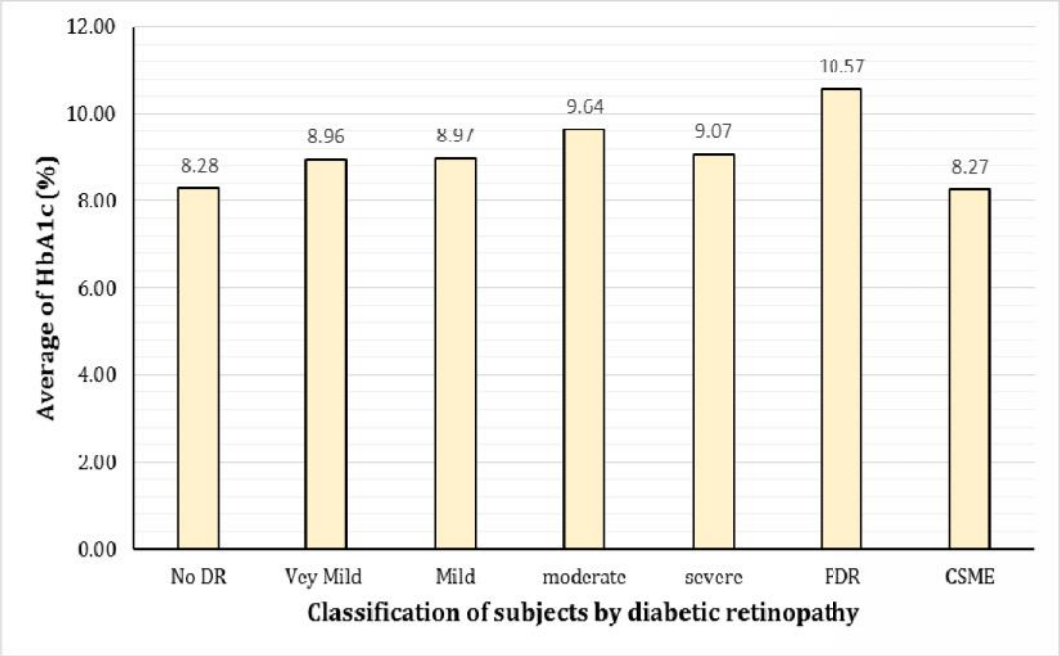
Factor	Sub-category	HbA1c category (in %)	p-value
Posterior Segment	**No diabetic retinopathy**	8.29 ± 1.77	< 0.00001
	Very mild NPDR	8.95 ± 2.14	
	Mild NPDR	9.01 ± 1.78	
	Moderate NPDR	9.63 ± 1.92	
	Severe NPDR	9.06 ± 2.76	
	PDR	10.56 ± 2.15	
	CSME	7.17 ± 0.59	

ANOVA is used to know whether there is any significant difference in the mean level of HbA1c (%) over severity of diabetic retinopathy. Here p-value is significant, it shows that there is significant difference in the mean level of HbA1c (%) over diabetic retinopathy. Tukey HSD test is used for post-hoc analysis, that is, mean of HbA1c is significantly different between which levels of severity. There is difference between the mean level of HbA1c between no diabetic retinopathy and moderate diabetic retinopathy (p-value = 0.011), and no diabetic retinopathy subjects and PDR subjects (p-value = 0.0005).

By Pearson's correlation test, 'r' value obtained is 0.215 and p-value for correlation test is less than 0.001. There is positive correlation between severity of HbA1c (%) and severity of retinopathy. As HbA1c severity increases there is increase

in severity of diabetic retinopathy. Below figure shows the distribution of subjects by diabetic retinopathy and HbA1c (%).

Figure 4: Distribution of average level of HbA1c (%) over severity of diabetic retinopathy.



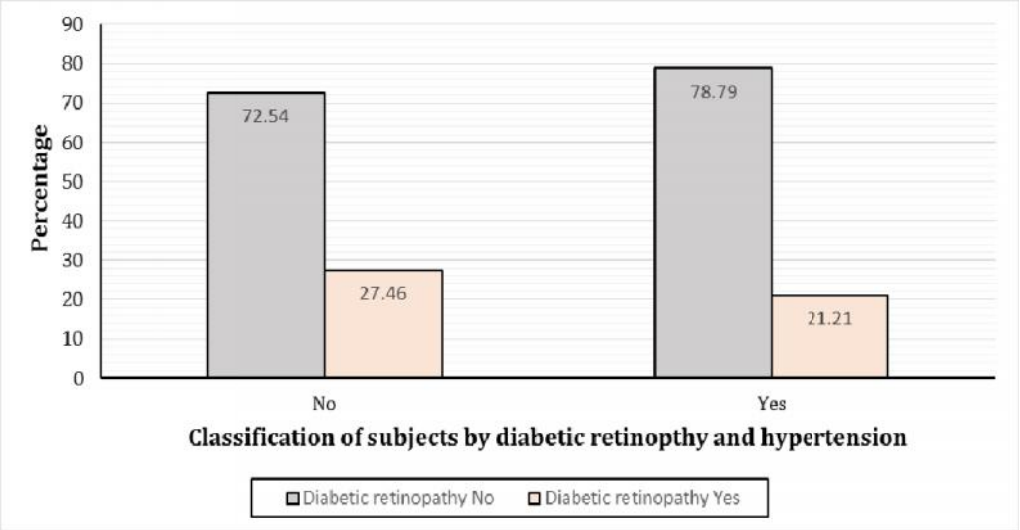
5. Hypertension

Table 5: Comparison of hypertension with severity of diabetic retinopathy

Factor	Sub-category	Hypertension		p-value
		No	Yes	
Posterior Segment	No	103	156	0.228
	Yes	39	42	

Above table is the cross table of hypertension with diabetic retinopathy. Chi-square test is used to test the independence between them. Here p-value is not significant, therefore, both the factors (hypertension and diabetic retinopathy) are independent.

Figure 5: Distribution of subjects by hypertension and severity of diabetic retinopathy.



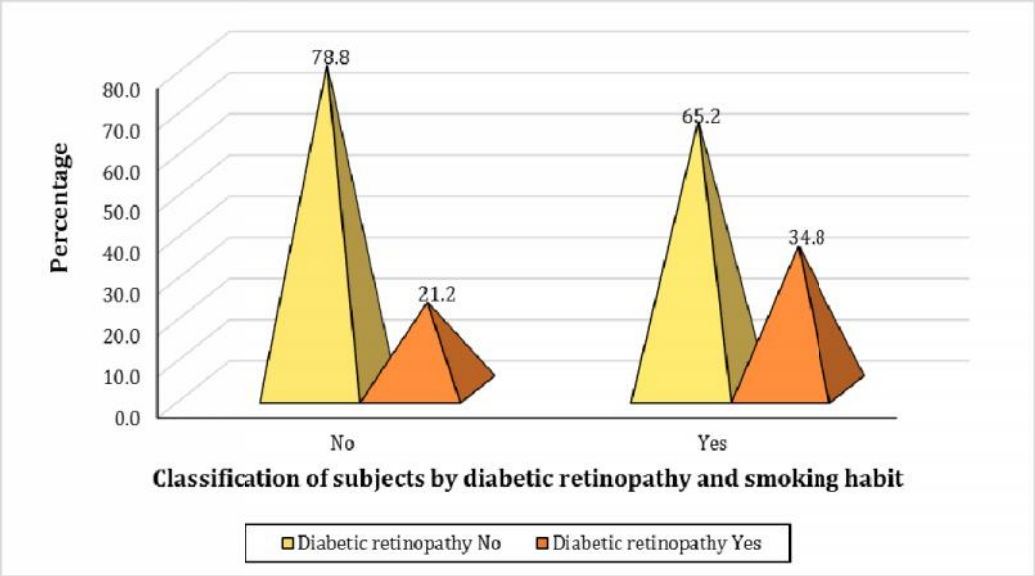
6. Smoking

Table 6: Comparison of smoking with diabetic retinopathy

Factor	Sub-category	Smoking		p-value
		No	Yes	
Posterior Segment	No	216	43	0.02917
	Yes	58	23	

From Chi-square test we can say that, smoking and diabetic retinopathy are dependent. Odds of having diabetic retinopathy (1.99, CI: 1.11-3.56) is more for the smokers compared to non-smokers.

Figure 6: Distribution of subjects by smoking habit and severity of diabetic retinopathy.



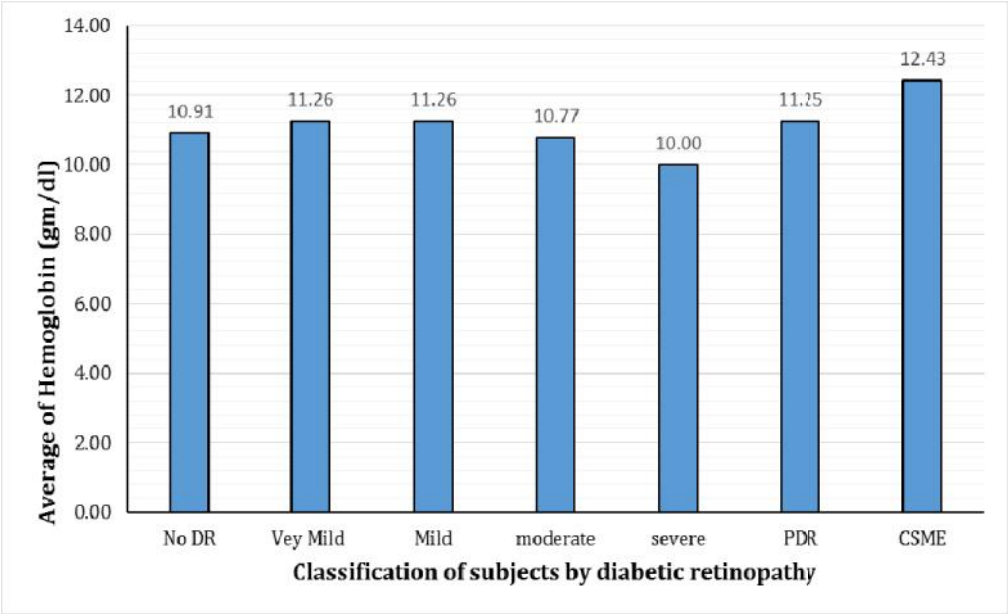
7. Anemia

Table 7: Comparison of Hemoglobin levels with diabetic retinopathy

Factor	Sub-category	Hemoglobin (gm/dl)	p-value
Posterior Segment	No diabetic retinopathy	10.90 ± 1.48	0.304
	Very mild NPDR	11.25 ± 2.77	
	Mild NPDR	11.26 ± 1.79	
	Moderate NPDR	10.77 ± 1.43	
	Severe NPDR	10.00 ± 1.91	
	PDR	11.25 ± 1.64	
	CSME	12.42 ± 1.33	

Above table gives the descriptive summary of hemoglobin over severity of diabetic retinopathy. ANOVA gives the p-value 0.304, which is not significant. There was no significant difference in the mean level of hemoglobin over severity of diabetic retinopathy.

Figure 7: Average of hemoglobin (gm/dl) over severity of diabetic retinopathy.



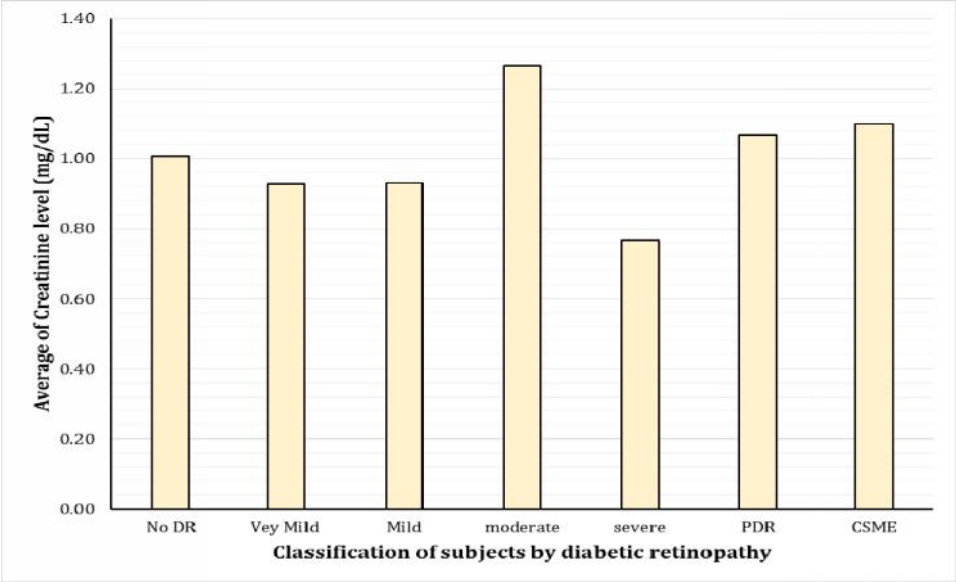
8. Renal status

Table 8: Comparison of creatinine level with diabetic retinopathy

Factor	Sub-category	Creatinine (gm/dL)	p-value
Posterior Segment	No diabetic retinopathy	1.01 ± 0.52	0.3488
	Very mild NPDR	0.92 ± 0.19	
	Mild NPDR	0.93 ± 0.21	
	Moderate NPDR	1.26 ± 1.74	
	Severe NPDR	0.77 ± 0.23	
	PDR	1.06 ± 0.19	
	CSME	1.10 ± 0.28	

In ANOVA, equal variance assumption is violated, so Kruskal-Wallis test is carried out for mean comparison. By Kruskal-Wallis test, there was no significant difference in the mean of creatinine level (mg/dL) over the severity of diabetic retinopathy.

Figure 8: Average creatinine (mg/dL) over severity of diabetic retinopathy



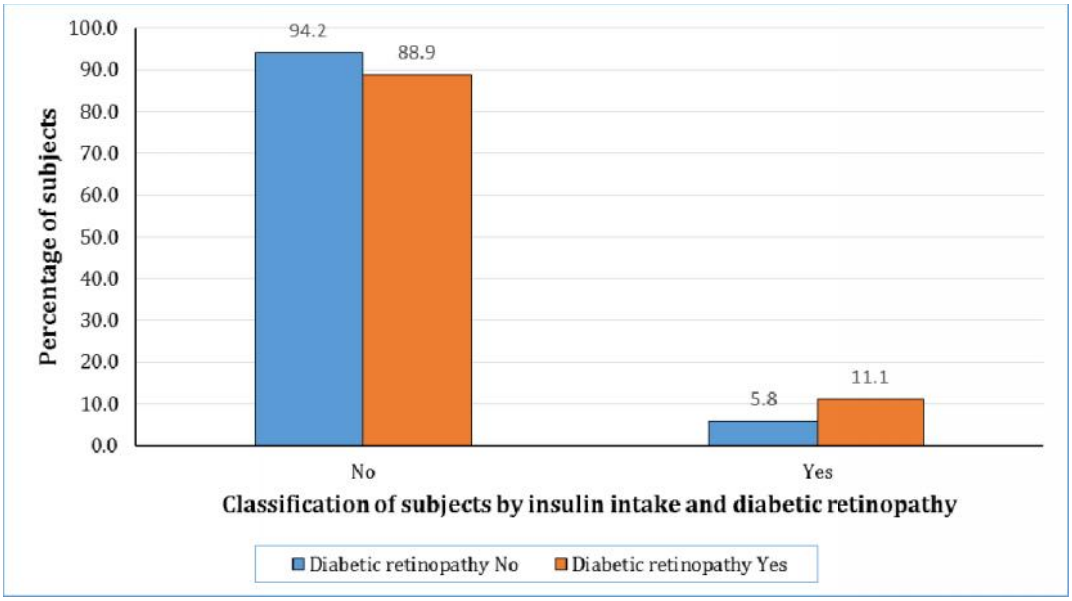
9. Insulin use

Table 9: Comparison of insulin intake with severity of diabetic retinopathy

Factor	Sub-category	Insulin intake		p-value
		No	Yes	
Posterior Segment	Yes	72	9	0.1667
	No	244	15	

Here p-value is not significant for Chi-square test, it shows that insulin intake and diabetic retinopathy are independent.

Figure 9: Distribution of percentage of subjects according to severity of retinopathy and insulin intake



10. Family history

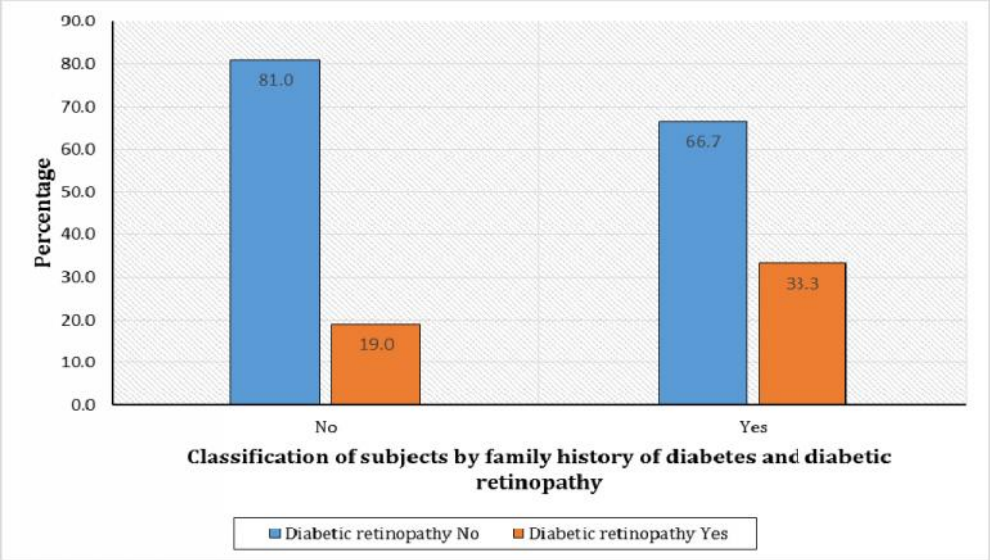
Table 10: Comparison of family history of diabetes with severity of diabetic retinopathy

Factor	Sub-category	Family H/O Diabetes		p-value
		No	Yes	
Posterior Segment	No	183	76	0.00529
	Yes	43	38	

Chi square test is used to check the independence of family history of diabetes and diabetic retinopathy. Here p-value is significant, therefore family history of diabetes and diabetic retinopathy are dependent.

Odds of having diabetic retinopathy (2.12, CI: 1.27-3.55) is more for the subjects with family history of diabetes compared to the subjects without family history of diabetes.

Figure 10: Distribution of subjects by family history of diabetes and severity of diabetic retinopathy.



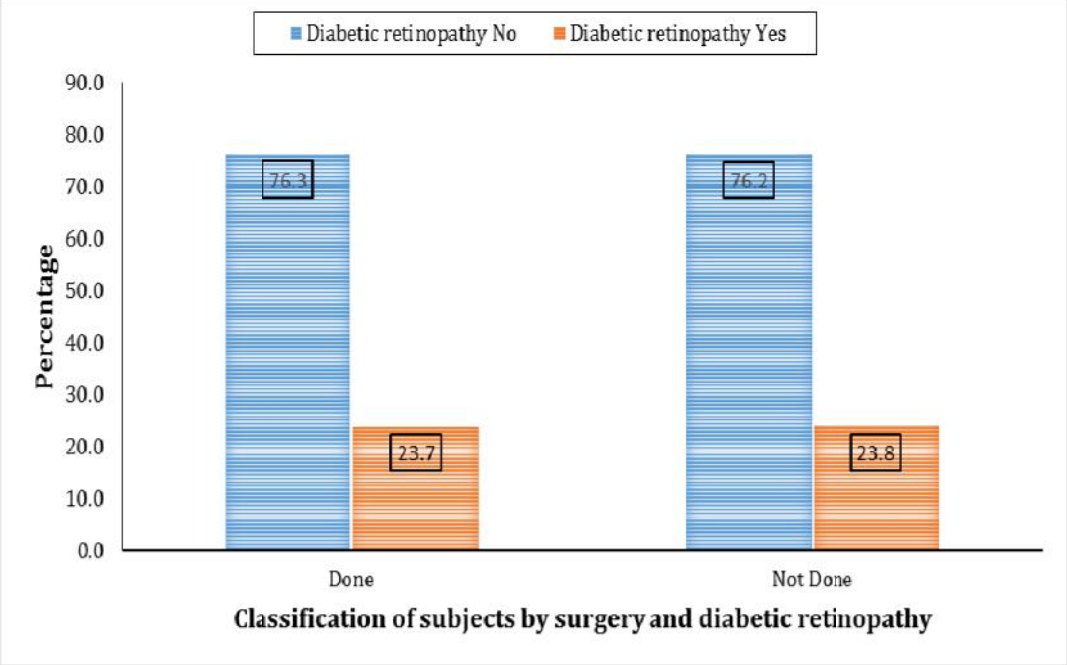
11. History of cataract surgery

Table 11: Comparison of surgery with severity of diabetic retinopathy

Factor	Sub-category	Surgery		p-value
		No	Yes	
Posterior Segment	No	230	29	1
	Yes	72	9	

Above cross table gives the frequency table of cataract surgery done and severity of diabetic retinopathy. Chi-square test is used to check the independence between surgery and diabetic retinopathy. Here p-value in the below table is not significant, therefore, surgery and severity of diabetic retinopathy are independent.

Figure 11: Distribution of subjects by surgery and severity of diabetic retinopathy.



DISCUSSION

Diabetic retinopathy is one of the major ocular diseases with significant public health implications in India . The International Diabetes Federation, in 2017 has estimated the prevalence of diabetes in Indian adults to be 8.8%, which amounts to a population of 72.9 million diabetics, much more than the previously estimated 40.9 million in the year 2000 .[70] This significant increase in prevalence can be due to numerous factors such as rampant urbanization, and resultant unhealthy lifestyles. It may also be due to increased life expectancy because of better access to improved health care.

In such a setting, estimation of the prevalence and risk factors of diabetic retinopathy, in a rural set up , with less access to specialized medical care requires utmost importance.

This will enable to develop better, cost effective targeted screening programmes with a view to prevent and manage vision threatening diabetic retinopathy.

PREVALENCE OF DIABETIC RETINOPATHY

The All India Ophthalmological Society Diabetic Retinopathy Eye Screening Study ,a cross sectional study conducted in 2014 ,which screened 6218 patients showed a prevalence of DR of 21.7%[71]

The Sankara Nethralaya Diabetic Retinopathy Epidemiology and Molecular Genetics Study Report 2(SN-DREAMS 2) conducted in Chennai, reported a higher prevalence of diabetic retinopathy in urban areas (18.0 %) [22]compared to rural areas

(10.8 %)[23].This may be secondary to the increasing wealth and dietary changes in urban areas, and also more likelihood of mortality as a result of diabetes related complications , owing to lesser access to healthcare facilities in remote areas.

The Chennai Urban Rural Epidemiology Study (CURES) eye study I by Raman et al, which screened 1414 known cases of diabetes showed a prevalence of 17.6 % in urban population.[72]

A population based assessment by Narendran et al among self reported diabetics in southern India showed a prevalence of 26.8%.[73]

In this study, the prevalence of diabetic retinopathy in a sample population of rural Belgaum was studied. It showed a prevalence of **23.82 %** in the 340 patients screened. Of this, 19.11 % comprised NPDR, 3.53 % PDR and a 1.18% CSME. The higher prevalence , in a rural set up can be because of the lesser number of subjects included.

A similar study conducted in rural population of Ramanagara and Chikaballapura districts of Karnataka, which screened 321 patients, showed a prevalence of 21.2 %.[69]. NPDR comprised 18.08 % and PDR comprised 3.12%.

A cross sectional study conducted in rural area of Villupuram district, Tamil Nadu by Nadarajan et al ,which screened 105 type 2 diabetic subjects showed prevalence of DR in any eye to be 32.5%.[74]

Another study conducted in Pravara Rural Hospital in Loni, Maharshtra showed a prevalence of 44.4%. This high prevalence can be resultant of the fewer subjects considered.(88).[75]

RISK FACTORS ASSOCIATED WITH DEVELOPMENT OF DIABETIC RETINOPATHY

Gender

In this study, there were 138 male and 202 female subjects. Diabetic changes were present in 40.59% of the males and 59.41 % of the females . Odds of having retinopathy is more in the male gender.

Similar study in Villupuram, Tamil Nadu by Nadarjan et al showed a statistically insignificant (p value of 0.65)higher prevalence of DR in males.[74]

The study conducted by Bharati et al in rural Karnataka showed a statistically significant(pvalue= 0.05) association of male gender with diabetic retinopathy. [69]

The WESDR study observed more chance of PDR in type 1 diabetes in men as compared to women[76], but concerning the prevalence or long term incidence, there was no statistically significant variation.[77]

Body mass index (BMI)

In this study, the prevalence of any diabetic retinopathy was higher in subjects with a BMI of 23.4 % or more as compared to those with lower BMIs. But, this association is statistically insignificant (p value of 0.19)

In the WESDR study, patients who were obese at baseline (BMI> 31 kg/sq m for men and > 32.1 kg/sq m for women) had 35 % more chance for progression of retinopathy, when compared to those who had a normal BMI at baseline.[68]

In the Ramanagara and Chikkaballapura district study , subjects with a BMI>25 were associated with a higher prevalence of diabetic retinopathy (p value=0.04)[69]

Duration of diabetes

Duration of diabetes continues to be the most significant risk factor for the development for diabetic retinopathy in this study also, in concurrence with the global epidemiological data on DR.

The association between both these variables had a statistically significant p value of less than 0.0001%.

In a study conducted by Khan et al in rural areas of Kanchipuram and Thiruvallur districts of Tamil Nadu, India, among 1190 subjects, the prevalence of DR was 11.5 % in individuals with onset of diabetes before 40 years compared to 10.0% in those with an older age onset.[78]

In a study conducted by Rajalakshmi et al with 150 type 1 and 150 type 2 Asian Indian diabetics, duration of diabetes mellitus had a significant association with diabetic retinopathy (odds ratio of 1.99 per 5 years in type 1 DM and 2.21 per 5 years in type 2 DM).[79]

The CURES Eye Study-4 also supported the positive association between duration of diabetes and diabetic retinopathy($p<0.0001$).[72]

In a study conducted by PK Rani et al, aimed at estimating the prevalence and risk factors of diabetic retinopathy in a rural population of self reported diabetes,

longer duration of diabetes(odds ratio of 1.07 per year) had a significant correlation with development of diabetic retinopathy.[80]

Glycemic control

In this study, glycemic control was demonstrated by the plasma values of glycated haemoglobin (HbA1C) as compared to either random or fasting plasma glucose concentration. Patients with HbA1C values of more than 8.95 ± 2.14 had diabetic retinopathy as compared to those with lower HbA1C values(more optimal glycemic control).

The positive association between higher HbA1C levels and retinopathy had a statistically significant p value of less than 0.0001. The average HbA1C values for patients with PDR was 10.56 ±2.15.

In a 2009 study on the relation between glycated haemoglobin and microvascular complications by Sabananayagam et al, the ideal threshold values for detecting mild and moderate retinopathy were 6.6% with a 87% sensitivity and 77.1% specificity.[81]

In an analysis of glycemic thresholds for diabetic retinopathy by Colaguiri et al , HbA1C thresholds for any retinopathy was set between 6.0-6.4 %.[82]

A study by Park et al in 2011, showed the ideal glycemic threshold for detecting any diabetic retinopathy with maximum sensitivity and specificity to be 6.3 mmoL/L of fasting plasma glucose and 6.2% HbA1C.[83]

Smoking

In this study, the number of smokers to non smokers was less (69 and 274). Of the smokers, 23 had diabetic retinopathy. The p value was statistically significant 0.029.

Mostly due to it's effect of vasoconstriction of microvasculature [59] and enhancing the platelet aggregation and adhesiveness[60], smoking is expected to have a deleterious effect on retinopathy. But most epidemiologic data like the WESDR have not found any association between smoking and the retinopathy in diabetics.[61]

Studies have only shown borderline significant association between pack years smoked and progression to proliferative retinopathy in older onset insulin taking subjects.

In the present study, details such as pack years smoked and other forms of nicotine use were not recorded. Therefore , the association of smoking and retinopathy remains ambiguous.

Anemia

In this study, there are 83 patients with mild (Hb 10-11 g/dl) and 79 patients with moderate (Hb 7-10 g/dl) anemia, comprising mostly women. There was no significant difference in the mean value of haemoglobin over the severity of diabetic retinopathy (p value=0.304).

Rani et al ,in a study of 1414 patients , demonstrated that type 2 diabetics with anemia had 1.80 times more risk of developing retinopathy than those without anemia[55]

In the ETDRS study, David et al observed that anemic patients (with a haematocrit lower than 40 % in males and 32% in females) had a higher risk of development of proliferative retinopathy and resultant vision loss.

The lack of association between haemoglobin levels and diabetic retinopathy in the present study may be due to the paucity of patients with significant anemia in this group.

Serum creatinine

In this study, there were only 85 patients with a serum creatinine value of more than 1.2 mg/dl. But, detailed history regarding other features of diabetic nephropathy were not elicited.

There was no significant difference in the mean of creatinine level over the presence or severity of diabetic retinopathy. It had a statistically insignificant p value of 0.348.

A correlative study of diabetic retinopathy with microalbuminuria by Garg et al though , has shown a statistically significant association between the grade of microalbuminuria and severity of diabetic retinopathy ($p< 0.001$) [84]

A similar association (p value < 0.001) has also been observed by Mohan et al between microalbuminuria and development and increasing severity of DR and CSME.[85]

Insulin use

Multiple studies have shown early worsening of DR with intensive glycemic control by insulin. The Sankara Nethralaya –Diabetic Retinopathy Epidemiology and Molecular Genetics Study (SN-DREAMS, Report number 35) reported a significant association between longer duration(> 5 years) before commencing insulin therapy overall with presence of DR(38 % vs 62% with a p value of 0.013). This may be attributed to the harmful effects of long term hyperglycemia on the retinal microvasculature, owing to the delay in initiation of insulin therapy.[51]

The present study had only 24 insulin users. But, as per Chi-square test, both insulin intake and diabetic retinopathy are independent. .

Hypertension

In the present study, there was no significant association between hypertension and the presence of diabetic retinopathy (p value=0.228). Both are independent factors.

According to the UKPDS study , each 10 mm Hg decrease in mean systolic blood pressure resulted in a 13% reduction in microvascular complications. A threshold was not observed for a retinopathy endpoint though.[52]

The present study shows higher incidence of CSME among diabetes patients with associated hypertension than non hypertensives.

The WESDR study showed a higher risk of developing macular edema in diabetics who had associated hypertension.[53]

History of cataract surgery

In the present study, 38 subjects had undergone previous cataract surgery. Details regarding the type of surgery, duration of surgery and intra or post operative complications of the surgery were not known. Among them, 9 had diabetic retinopathy changes. But, the p value (1) was not statistically significant.

Hong et al in a cohort study of 190 patients, with a 12 month follow up period, observed an incidence of 28.2 % DR in pseudophakic eyes in comparison to 13.8 % in phakic eyes.[67]

Family history of diabetes

The present study has shown a positive association between family history of diabetes and presence of diabetic retinopathy (p value= 0.005). This might indicate the role of genetic predisposition.

CONCLUSION

The prevalence of diabetic retinopathy in rural Belgaum as estimated by this study is 23.82 %. This can even be an underestimation, considering the fact that, the people who voluntarily attend such screening camps are in better health than the non participants.

Although it was present more in males, as compared to females, this did not amount to any statististical significance .

Among the risk factors assessed, the major factors were longer duration of diabetes mellitus, impaired glycemic control as indicated by higher HbA1C values , family history of diabetes and smoking.

Other factors such as BMI, Serum creatinine, haemoglobin level, insulin use ,history of cataract surgery and hypertension did not have any statistically significant correlation with retinopathy.

The burgeoning diabetic burden in India, with a significant section in rural India warrants major advances in wholesome diabetic care.

Patients should be made aware regarding retinopathy and it's implication on vision. They should be counselled for regular follow up and yearly dilated fundus examination .

Since, only three of the twelve PDR patients advised referral to the base hospital turned up for further management, the government should implement adequate measures to provide basic vitreoretinal care at a primary level.

SUMMARY

In this study of 340 known diabetic subjects, who underwent detailed fundus examination, 81 had diabetic retinopathy with varying levels of severity. Most of those affected with diabetic retinopathy were males.

Among the risk factors assessed, the duration of diabetes and HbA1C had the most significant association with diabetic retinopathy. Other significant risk factors were family history of diabetes and smoking.

Hypertension, BMI, anemia, serum creatinine and history of previous cataract surgery did not have a significant correlation with diabetic retinopathy.

The awareness regarding diabetic retinopathy is very less in the rural polulation of Belagavi district.

If the results of this study are extrapolated to the rest of rural India, (with caution, considering the study population might not be entirely representative of the rural population of India) ,the number of diabetic patients affected by sight threatening diabetic retinopathy will be quite significant.

Eye care infrastructure needs to develop at a rapid pace to deliver timely and adequate services to such a large population in need, in the remote areas.

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ANNEXURE I – CONSENT FORM

STUDY ID NO: _____

TITLE OF THE STUDY

"PREVALENCE AND RISK FACTORS OF DIABETIC RETINOPATHY AMONG KNOWN DIABETIC PATIENTS OF RURAL POPULATION OF BELGAUM DISTRICT: A ONE YEAR CROSS SECTIONAL STUDY"

PRINCIPAL INVESTIGATOR: _____

GUIDE: _____

INTRODUCTION AND PURPOSE:

This study is designed to study the prevalence of diabetic retinopathy among known diabetics in a rural population and to study the associated risk factors. Better awareness of this, will help in identifying the risk factors ,and to provide treatment to the underprivileged rural areas.

PROCEDURE:

I request you to kindly participate in the study titled **'PREVALENCE AND RISK FACTORS OF DIABETIC RETINOPATHY AMONG KNOWN DIABETIC PATIENTS OF RURAL POPULATION OF BELGAUM DISTRICT: A ONE YEAR CROSS SECTIONAL STUDY'**. If you agree to participate in the study, please provide the details pertaining to the study. We will check visual acuity, anterior segment, optic disc changes and macular changes. For detailed eye examination ,we will dilate the eye and record fundus photographs with a retinal camera. Blood samples will be withdrawn and investigations performed to assess risk factors of diabetic retinopathy.

BENEFITS: Results will help to study retinal changes in diabetic patients.

RISKS: No proven side effects

ALTERNATIVES:

If patient is not willing to take part in the study, his / her treatment or any other further investigations the patient wants to undergo, in future, in KLE will not be affected by his / her decision.

VOLUNTARYPARTICIPATION/WITHDRAWAL:

Taking part in this study is voluntary. I may choose not to take part in this study, or if I decide to take part I can later change my mind and withdraw from the study. My decision will not change the present or future health care or other services that I receive. The study doctor or the sponsor may stop my participation in this study. I will tell of any important new findings that may change my willingness to continue to take part. If I choose not to take part in the study I will receive the standard treatment for patients with my condition.

COSTS: NIL

COMPENSATION: In the event that I become injured as a result of taking part in this study, treatment will be offered to me. No reimbursement, compensation or free medical care is given.

CONFIDENTIALITY:

All information collected about me during the course of the study will be kept confidential to the extent permitted by the law. The code numbers will identify me in this research record. Information from this study may be published but my identity will be confidential in any publication.

CONSENT TO PARTICIPATE IN RESEARCH STUDY

I voluntarily agree to take part in this study by signing on the line below. I may withdraw at any time. I am not giving up any of my legal rights by signing this form. My signature below indicates that I have read this entire consent form or it has been read to me, and has been explained to me in my vernacular language and had all my questions answered.

AUTHORIZATION TO PUBLISH RESULTS: When the results of the study are published or discussed, in a conference, no information will be displayed that would disclose your identity. Any information that is obtained in connection within this study and that can be identified with me will remain confidential.

QUESTIONS:

If any enquiries in the future or in case of research related injury or illness, you may contact following people.

Even if you have any queries in future, you may contact thefollowing person

1. Dr.ROOPA BELLAD $_{M.D(Paed),DCH}$, Professor of Pediatrics, Chairman of JNMC Institutional Ethics Committee on Human Subjects Research, J N Medical College, Belagavi.

CONSENT TO PARTICIPATE IN RESEARCH TRIAL

I, Mr./Ms./ Mrs voluntarily agree to participate in this study. By signing this consent form, I am not giving up any of my legal rights. I may withdraw from the study anytime. I am signing the consent form after having read or been read for me in vernacular language, including the risks and benefits and having all my questions answered.

Subject Name :

Signature or left thumb impression:

Witness Name :

Signature or left thumb impression:

Investigator's Name:

Signature of Investigator:

Date:

Place:

ANNEXURE II

PROFORMA

GENERAL INFORMATION

PATIENT ID NUMBER:

NAME: _____

AGE: _____ GENDER: F/M CONTACT NUMBER: _____

ADDRESS: _____

_____

_____

Has informed consent been given? YES/NO

CHIEF COMPLAINTS

Diminution of vision: RE/LE/BOTH EYES_____ days/months/years

Duration: RE: _____ days/months/years

LE: _____ days/months/years

HISTORY OF PRESENTING ILLNESS

Diminution of vision: Gradual/Sudden
Progressive/Static
Painless/Painful
For distance/For near/For both distance and near

Diplopia: Present/Absent
Coloured halos: Present/Absent
Black spots before the eyes: Present/Absent
Dryness: Present/Absent
Redness: Present/Absent
Discharge: Present/Absent
Clear/Whitish
Serous/Mucoid
Spectacle use: Distance/Near/Both
Duration: _____ days/months/years
Last refraction done: _____ days/months/years

back

PAST HISTORY

Ocular surgery: Yes/No
Type of Surgery:
_____
Duration: _____ days/months/years

Ocular trauma Yes/No

Diabetes Yes/No
Duration: _____ days/months/years

Hypertension: Yes/No
Duration: _____ days/months/years

Any other medical disorders:
_____
_____
_____

PERSONAL HISTORY

Smoking: Yes/No
Duration: _____ days/months/years

Alcohol: Yes/No
Duration: _____ days/months/years

Other addictions: Yes/No
Duration: _____ days/months/years

DIABETIC HISTORY

Type of diabetes I/II

Duration _____days/months/years

Family history of diabetes Yes/No

Medication for diabetes Oral/Insulin

Duration _____days/months/years

If on Insulin, duration from diagnosis of diabetes to start of insulin use

Duration _____days/months/years

Other diabetic complications Kidney/Heart/Vascular/Other

_____

GENERAL PHYSICAL EXAMINATION

General appearance: Well-built/Moderately built/Poorly built/Emaciated
Pallor: Present/Absent If present: Mild/Moderate/Severe
Height: _____cm Weight: _____kg BMI_____

Pulse: _____ beats/minute BP: _____ mmHg

SYSTEMIC EXAMINATION

CVS: Normal/Abnormal
Specify:

_____

RS: Normal/Abnormal
Specify:

_____

CNS: Normal/Abnormal
Specify:

_____

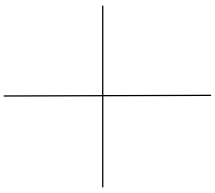
Per abdomen: Normal/Abnormal
Specify:

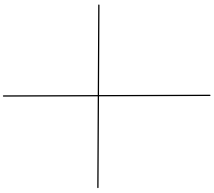
_____

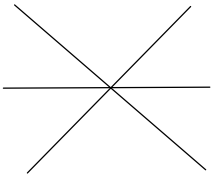
OCULAR EXAMINATION

Head posture: Erect/Tilted
Visual axis: Parallel/Deviated
Facial symmetry: Symmetrical/Asymmetrical

Extra-ocular movements: Normal/Restricted/Partially restricted

RE: 

LE: 

Binocular: 

N- Normal R-Restricted

VISUAL ACUITY:

	RE	LE
DISTANT		
PINHOLE		
NEAR		

	OD	OS
LID		
ADNEXA		
CONJUNCTIVA		
CORNEA		
ANTERIOR CHAMBER		
IRIS		
PUPIL A. Size B. Shape C. Direct D. Indirect E. Near reflex	 _____ in mm Present/Absent Present/Absent Present/Absent	 _____ in mm Present/Absent Present/Absent Present/Absent
LENS	Clear/Opaque Aphakia/Pseudophakia Immature/Mature/Hypermature/ Snowflake	Clear/Opaque Aphakia/Pseudophakia Immature/Mature/Hypermature/ Snowflake

ANTERIOR SEGMENT FINDINGS

_____
_____
_____
_____
_____
_____

DIRECT OPHTHALMOSCOPY

Fundus Examination	OD	OS
GLOW		
MEDIA		
DISC 1. Size 2. Shape 3. Colour 4. NRR 5. Vessels 6. Lamellar Dot Sign 7. Haemorrhagic Spots 8. Other Signs		
C:D RATIO		
BLOOD VESSELS		
BACKGROUND		
MACULA		

INDIRECT OPHTHALMOSCOPY

Fundus Examination	OD	OS
GLOW		
MEDIA		
DISC 1. Size 2. Shape 3. Colour 4. NRR 5. Vessels 6. Lamellar Dot Sign 7. Haemorrhagic Spots 8. Other Signs		
C:D RATIO		
BLOOD VESSELS		
BACKGROUND		
MACULA		

DIABETIC RETINOPATHY

STAGE

-NO DIABETIC RETINOPATHY

-VERY MILD NPDR

-MILD NPDR

-MODERATE NPDR

-SEVERE NPDR

-VERY SEVERE NPDR

-MILD PDR

-MODERATE PDR

-HIGH RISK PDR

-DIABETIC MACULAR EDEMA

ADVICE

a.3 monthly dilated fundus examination

b.6 monthly dilated fundus examination

c.Yearly dilated fundus examination

d.Refer to base hospital for further management

BLOOD INVESTIGATIONS

Haemoglobin _____g/dl

Random Blood Sugar_____mg/dl

Mini RFT

Blood Urea_____mg/dl

Serum Creatinine_____mg/dl

HbA1C _____ %

ANNEXURE-III- ETHICAL CLEARANCE LETTER

K.L.E.UNIVERSITY'S
JAWAHARLAL NEHRU MEDICAL COLLEGE,
NEHRU NAGAR, BELAGAVI-590010 (KARNATAKA-INDIA)
(Accredited 'A' Grade by NAAC)

Website: http//www.jnmc.edu
E-Mail : dome@jnmc.edu

Phone: (+ 91-(0)831 Office : 2471350
Principal: 2471701
Fax No. +91 (0)831 – 2470759

Ref: MDC/DOME/ **Date: 27/11/2017**

To,

REG. NO. BK0117001

Sub: Institutional Ethical Clearance for the study.

With reference to the above, we wish to inform you that your proposed research project titled **"PREVALENCE AND RISK FACTORS OF DIABETIC RETINOPATHY AMONG KNOWN DIABETIC PATIENTS OF RURAL POPULATION OF BELGAUM DISTRICT– A ONE YEAR CROSS SECTIONAL STUDY",** is ethical and justifiable. The proposed research project has been cleared by the JNMC Institutional Ethics Committee on Human Subjects Research.

(Dr. Arathi Darshan)
Member Secretary
JNMC Institutional Ethics Committee
on Human Subjects Research,
J.N.Medical College, Belagavi.

(Dr. Roopa M Bellad)
Chairman,
JNMC Institutional Ethics Committee
on Human Subjects Research,
J.N.Medical College, Belagavi.

17

ANNEXURE IV – PHOTOGRAPHS

I. SCREENING CAMPS

Ia. Examining anterior segment

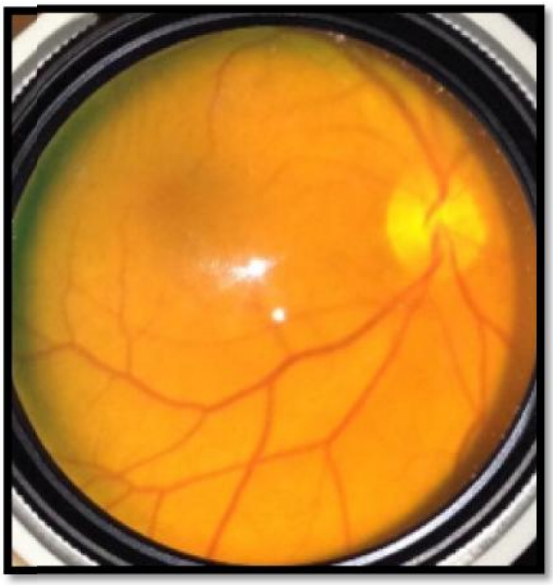
Ib. Patient particulars and blood investigations

Ic. Patient counseling

Id. Recording fundus images

II. FUNDUS IMAGES

1. NORMAL FUNDUS

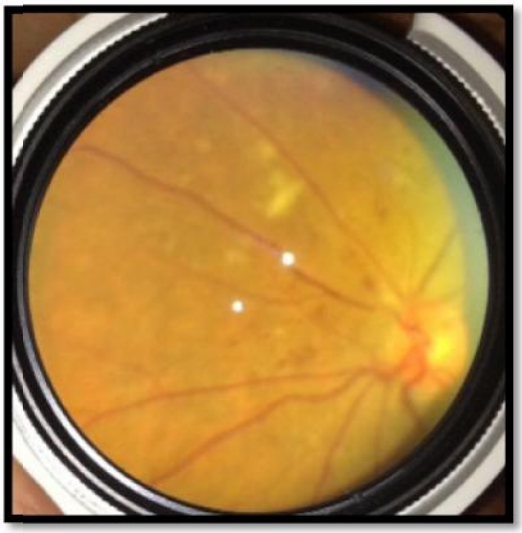


1a

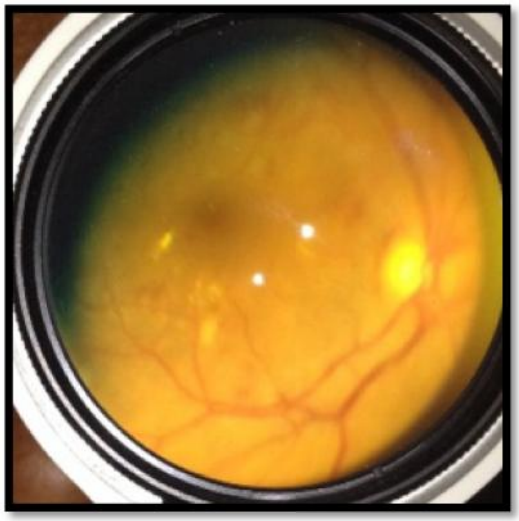
1b

1c

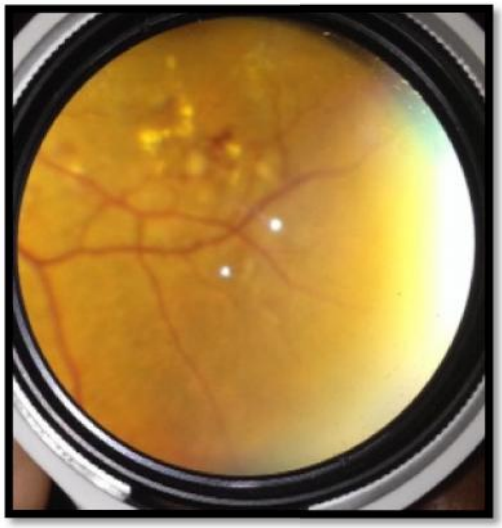
2. NON PROLIFERATIVE DIABETIC RETINOPATHY



2a



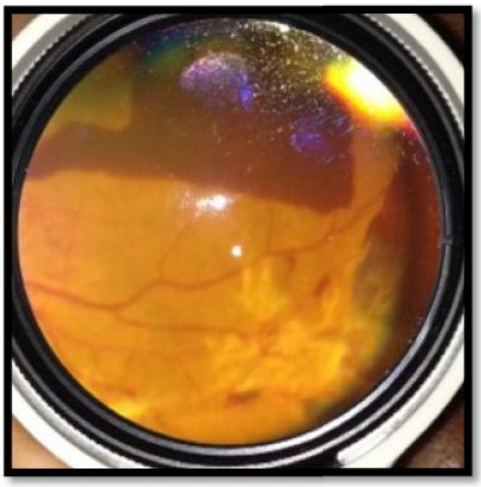
2b



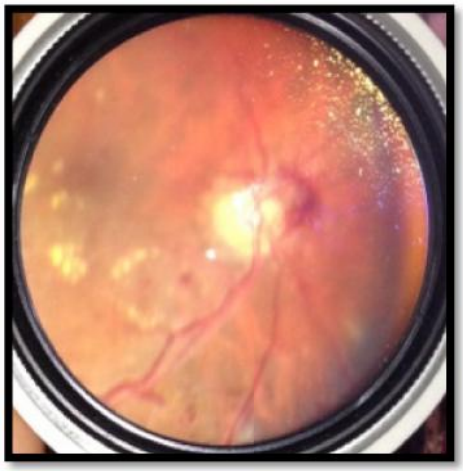
2c

3. PROLIFERATIVE DIABETIC RETINOPATHY

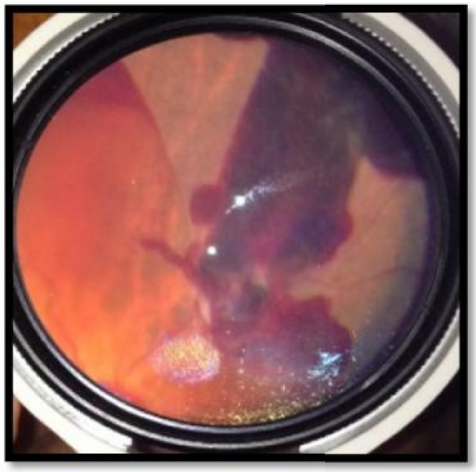
3a



3b

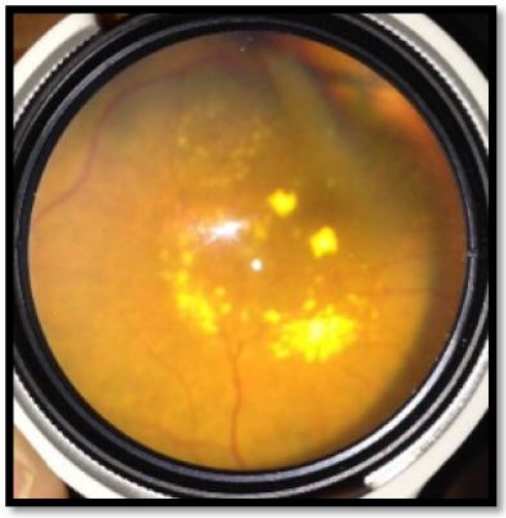


3c



3d

4. CSME



ANNEXURES V - MASTER CHART

Sl No	age/sex	dm dum	htn	bmi	hb	hba1c	creat	insulin	smoking	re	le	as od	as os	ps od	ps os	family	rbs	bp	
1	48/m	4 years	no	22.08	9.5	6.5	0.8	no	no	6.6	6 by 6	g	g	n	n	plus	210	130/80	
2	42/m	3 years	no	26.56	11.5	6.7	0.7	no	yes	6.6	6.6	g	g	n	n	plus	248	130/80	
3	55/f	4 years	12 years	27.48	9.5	9.2	0.8	no	no	cf 1m	6 .9	g	g	n	n	plus	210	140/80	
4	70/f	10 years	10 years	26.41	9	13.1	0.9	no	no	6.12	6.12	pciol	pciol	n	n	plus	345	170/140	
5	68/m	10 years	3 years	20.76	16.6	10.8	0.7	no	yes	6.36	6.12	g	pciol	v.mild npdr	v.mild npdr	nil	230	120/80	
6	65/m	3 years	3 years	21.81	12	9.9	0.9	nil	yes	6.9	cf 3m	pciol	g	n	n	nil	251	120/80	
7	57/f	7 years	nil	27.3	10	10.6	1.1	nil	no	6.6	6.6	g	g	n	n	nil	160	110/70	
8	62/m	10 years	10 years	29.06	10	10.3	0.9	nil	yes	6 by 24	6 by 24	g	g	n	n	nil	343	140/92	
9	58/f	2 years	5 years	21.68	10.5	6.2	0.7	nil	no	6.6	6.6	g	g	n	n	plus	428	120/80	
10	40/f	6 years	nil	24.39	11	11.7	1.2	nil	yes	6.6	6.6	g	g	n	n	nil	324	120/80	
11	40/f	2 years	nil	25	12	7.9	1	nil	nil	6.6	6.9	g	g	n	n	plus	313	110/70	
12	52/m	5 years	nil	31.2	12	7.1	0.8	nil	no	6.9	6.9	g	g	n	n	nil	97	130/80	
13	62/m	10 years	7 years	29.07	10.8	9.5	1.1	nil	yes	6.12	6.9	g	g	n	n	nil	289	120/80	
14	55/f	6 years	6 years	27.5	9.8	10.5	1.3	nil	no	6.12	6.12	g	g	v.mild npdr	v.mild npdr	plus	180	120/80	
15	46/m	15 years	nil	22.26	13	12.5	0.8	nil	yes	6.6	6.9	g	g	mod npdr	mod npdr	nil	600	130/90	
16	65/f	2 years	2 years	20.76	9.8	12	0.9	no	yes	cf 3m	cf 3m	brownish	g	severe npdr eith csme	mod npdr with severe macular edema	nil	540	110/70	
17	66/f	6 years	nil	24.56	9.4	10.6	0.9	no	yes	6 by 60	6 by 36	g	g	mod npdr	mod npdr	yes	260	130/80	
18	63/m	6 years	6 years	23.75	10.8	7.7	1	nil	no	6.6	6.9	g	pciol	n	n	nil	270	140/90	
19	44/m	12 years	12 years	26.87	12.1	6.8	0.9	nil	no	6.6	6.6	g	g	n	n	yes	209	140/90	,cva 1 year back
20	52/f	12 years	12 years	27	10.8	10.2	0.7	nil	no	6.6	6.6	g	g	mild npdr	mod npdr	yes	301	140/80	
21	70/f	20 years	15 years	17.57	10.8	5.5	0.8	nil	no	cf 2m	cf 3m	g	g	n	n	yes	106	110/70	
22	55/f	6 months	1 month	27.73	10.8	6	0.9	nil	no	6.6	6.6	g	g	n	n	nil	189	110/70	
23	50/f	2 years	nil	20.41	10.8	7.8	0.8	nil	no	6.6	6.6	g	g	n	n	nil	138	130/80	
24	62/f	20 years	no	22.5	11	8	0.8	yes-20 y	no	6.6	6.6	g	g	mod npdr	mod npdr	nil	411	170/90	p.neuropathy
25	55/f	12 years	12 years	30.51	11.4	6.6	2.9	yes-12 y	no	6.24	6.18	g	g	n	n	nil	347	160/80	
26	76/f	1 month	nil	25.51	11	8	1.4	nil	no	cf 1.5 m	6.9	g	pciol	n	n	nil	180	130/80	
27	55/f	10 years	nil	21.29	10	5.4	1.6	nil	no	6 by 24	cf 1.5 m	g	g	mod npdr	mod npdr	nil	90	130/80	
28	45/f	8 years	nil	24.05	12.8	11.4	1.5	nil	no	cf 1.5 m	cf 1m	g	g	mod npdr	mod npdr	nil	408	180/90	

29	55/f	5 years	nil	36.73	11.5	6.2	0.9	nil	no	6.12	6.9	g	g	irma	irma	nil	122	170/90	
30	40/f	2 years	nil	22.54	10.3	8.9	1.2	nil	no	6.9	6.6	g	g	n	n	nil	399	130/80	
31	60/m	10 years	nil	24	11.9	6	1	y-8 years	no	cf 2m	cf 2m	g	g	mod npdr	mod npdr	nil	429	140/80	
32	73/m	1 year	nil	23.5	11	6.7	1	nil	no	6 by 12	cf 2m	pciol	g	n	n	nil	120	120/70	
33	50/f	6 mon	yes	22.06	10	6.6	1.7	nil	no	6.12	6.12	g	g	n	n	nil	114	120/70	
34	48/f	9 years	no	26.66	12.2	8	1	nil	no	6.6	6.6	g	g	mild npdr	mild npdr	nil	405	150/80	
35	50/m	12 years	no	27.57	11.2	6.8	1.5	nil	no	6.6	6.6	g	g	n	n	yes	255	160/90	
36	45/m	2 years	no	25.73	11.5	8	1.5	yes-2 y	no	6.6	6.6	g	g	n	n	nil	234	140/80	
37	49/m	1 year	no	24.63	13.2	10.4	2.5	yes-1y	no	6.6	6.6	g	g	n	n	nil	214	120/80	
38	50/f	4 years	no	32.53	11	7.2	1.3	yes-2 years	no	6.6	6.6	g	g	n	n	nil	115	140/80	
39	50/f	7 years	no	17.39	9.1	12	1	nil	no	6.12	6 by 18	g	g	n	n	nil	101	140/90	
40	60/m	5 years	nil	26.1	10.4	8.6	0.9	nil	no	6.12	6.9	g	g	n	n	nil	149	130/80	
41	65/m	2 years	nil	26.71	11.2	6.5	1.6	nil	no	cf 0.5 m	6.12	g	g	n	n	nil	295	140/100	
42	66/m	6 years	nil	20.47	11.2	6.4	1.3	nil	no	6.6	6.9	g	g	n	n	yes	203	140/90	
43	68/f	10 years	no	33.97	10.2	6.6	1.2	nil	no	6.9	6.6	g	g	n	n	nil	235	140/100	
44	52/m	2 years	2 years	23.84	12	7.9	1	nil	no	6.12	6.12	g	g	mild npdr	mild npdr	plus	220	124/76	
45	40/m	5 years	5 years	24.35	12.8	9.6	0.6	nil	yes	6.6	6.6	g	g	mild npdr	mild npdr	plus	188	130/90	
46	47/m	8 years	3 years	32.45	10.2	7.6	1	nil	no	6.18	6.9	g	g	mild npdr	drusen	plus	198	120/80	
47	63/m	25 years	15 years	27.34	12.2	9.6	1.2	nil	no	6.9	6.18	g	g	mod npdr	mod npdr	nil	324	140/90	
48	55/m	3 years	3 years	28.3	13.2	9.1	0.8	nil	no	6.18	6.9	g	g	htn ret	htn ret	nil	210	130/80	
49	68/f	8 years	nil	21.6	10.8	9	1.1	nil	no	6.24	6.9	g	g	n	n	yes	188	120/80	
50	65/f	6 years	3 years	22.07	11.2	9.2	0.9	yes-6 y	no	6.6	6.6	g	g	n	n	nil	268	130/80	
51	50/f	3 years	3 years	29.56	12.2	7.1	0.7	no	no	6.24	6.18	g	pciol	n	n	yes	204	130/80	
52	65/f	10 years	10years	29.68	11.2	6.1	1.2	nil	no	cf 1m	cf 1.5m	pciol	pciol	n	n	yes	166	130/90	
53	75/f	4 years	6 years	22.83	11.8	8.6	0.7	nil	no	6.9	6.6	g	g	n	n	nil	176	110/70	
54	58/f	10years	10 years	28.06	11.2	10	1	y-9 y	no	6 by 60	cf 2m	g	g	n	n	nil	180	130/90	
55	70/f	10 years	8 years	30.66	11.4	10.3	0.9	nil	nil	cf 2m	cf 3m	pciol	g	n	n	nil	210	120/70	
56	60/f	4 years	4 years	31.08	11.6	13	0.5	nil	nil	6.18	6.12	g	g	n	n	nil	196	120/80	
57	60/f	5 years	1 year	22.94	10.2	7.6	1	nil	no	6.6	6.6	pciol	pciol	n	n	nil	200	110/80	
58	44/f	10 years	nil	31.91	9.8	11.8	0.8	nil	no	6.6	6.9	g	g	v.mild npdr	v.mild npdr	nil	393	130/80	
59	53/f	8 months	3 months	22.86	11.8	8.1	0.9	nil	no	6.6	6.6	g	g	n	n	yes	214	130/100	
60	61/f	5 years	5 years	21.6	9.2	8.6	1.2	nil	no	6.12	6.12	g	g	n	n	yes	202	110/70	
61	58/f	6 years	6 years	29	10.5	8.9	1.3	nil	no	6.18	6.18	pciol	pciol	n	n	nil	194	170/80	
62	67/m	5 years	5 years	28.75	11.8	10.4	1.2	nil	no	6.9	6.6	g	g	n	n	yes	206	150/90	
63	67/f	6 years	4 years	28.98	11.2	8.5	1.4	nil	no	6.36	6.24	g	g	n	n	yes	148	120/90	
64	65/M	4 years	no	24.16	10.5	9	0.4	nil	no	6.36	6.9	pciol	pciol	n	n	nil	200	160/110	
65	55/f	2 years	no	30.61	10.5	7.1	0.8	nil	no	6.12	6.12	g	g	n	n	nil	180	130/80	
66	41/f	3 years	no	28.57	10	9.4	0.9	nil	no	6.6	6.6	g	g	n	n	nil	220	130/80	
67	55/m	7 years	no	29.77	11	9.5	0.9	nil	no	6.9	6.6	g	g	n	n	nil	238	110/60	
68	55/m	1 year	1 year	28.88	11.5	10.9	0.9	nil	yes	6.9	6.9	g	g	n	n	nil	214	130/90	

69	55/f	1 year	1 year	24.13	9	9.2	0.4	nil	no	cf 3.5 m	6.36	g	g	drusen	mac hole	nil	204	130/100	
70	49/m	4 years	nil	34.13	12	8.3	0.9	nil	yes	6.6	6.6	g	g	n	n	yes	156	130/90	
71	42/f	3 years	3 years	38.26	11	10.4	0.8	nil	no	6.9	6.9	g	g	n	n	yes	204	130/100	
72	58/f	3 years	3 years	23.29	10	7.4	0.9	nil	no	6.9	6.6	g	g	n	n	nil	198	130/90	
73	62/m	4 years	4 years	27.08	12	10.5	0.9	nil	yes	6.18	6.18	g	g	mild npdr	mild npdr	nil	208	160/80	
74	49/m	12 years	no	23.87	11	11.1	0.9	nil	yes	6.9	6.9	g	g	mild npdr	mild npdr	yes	228	120/70	
75	40/f	5 years	no	22.85	9	9.8	0.7	nil	no	6.24	6.12	g	g	mild npdr	mild npdr	yes	240	100/70	
76	42/f	10 years	no	31.31	9	9.6	0.9	nil	no	6.9	6.9	g	g	mild npdr	mild npdr	yes	234	130/80	
77	41/m	7 years	7 years	38.15	12	11.4	0.8	nil	yes	6.9	6.6	g	g	mod npdr	mod npdr	yes	346	180/130	
78	45/m	8 years	no	26.22	12	9	0.8	nil	yes	6.6	6.6	g	g	mild npdr	mild npdr	no	209	120/80	
79	65/f	8 years	8years	33.33	10	11.3	0.9	nil	no	6.18	6.12	g	g	mod npdr	mod npdr	no	220	130/90	
80	62/m	20 years	no	23.75	10	10.6	0.8	nil	yes	6.12	6.12	g	g	mod npdr	mod npdr	yes	293	110/70	
81	65/m	1 year	1 year	23.04	8	7.2	0.8	nil	yes	6.18	cf3m	g	g	n	n	no	170	100/70	
82	50/f	8 years	10 years	35.86	7.5	8	1	nil	no	6.24	6.24	g	g	n	n	yes	218	150/90	
83	48/m	9 months	no	22.61	9	6.8	0.9	nil	no	6.6	6.18	g	g	n	n	nil	420	110/70	
84	63/f	6 years	6 years	20.32	10	6.2	0.8	nil	no	cf 2m	6.36	g	pciol	n	n	no	90	110/70	
85	67/m	5 years	no	19.78	12	12.1	0.9	nil	no	6.24	6.12	g	pciol	n	n	no	186	120/70	
86	70/f	2 years	1 year	23.94	7.5	6.4	0.4	nil	tobacco	6.9	6.9	g	g	n	n	no	127	140/90	
87	68/m	3 years	no	23.95	10	7.6	0.3	nil	yes	6.6	6.6	pciol	pciol	n	n	no	186	130/80	
88	60/f	3 years	3 years	30	8	7.3	0.9	nil	no	6.12	6.12	g	g	n	n	no	117	140/80	
89	58/m	2 years	5 years	26.1	12	7.2	0.5	nil	yes	6.6	6.6	g	g	n	n	nil	168	130/80	
90	68/m	2 years	2 years	25.17	12	6.6	0.9	nil	no	cf 2.5 m	6.6	g	g	n	n	yes	92	190/130	
91	43/f	8 months	1 month	32.39	10	6.8	0.8	nil	no	6.6	6.12	g	g	n	n	no	351	140/90	
92	65/f	10 years	10 years	17.11	9	11.3	1.2	nil	no	cf 3m	cf 2m	g	g	n	n	no	335	110/70	
93	40/m	1.5 years	1 year	17.55	10	12.3	0.7	yes-1.5 years	no	6.12	6.24	g	g	n	n	yes	266	140/90	
94	60/f	5 years	5 years	28.98	8	10.2	0.8	nil	no	6.12	6.12	g	g	n	n	yes	470	110/70	
95	50/f	2 years	no	30	9	7.1	1	nil	no	6.12	6.12	g	g	n	n	yes	229	110/70	
96	54/m	5 years	no	32.87	10	7	0.7	nil	yes	6.9	6.9	g	g	n	n	no	225	140/80	
97	65/f	12 years	12 years	28.78	7.5	8	0.7	nil	no	cf 2.5 m	cf 3m	g	g	mild npdr	mild npdr	no	171	130/80	
98	43/f	20 years	6 years	25.82	11.4	11.7	0.4	nil	no	6.18	6.12	g	g	n	n	yes	173	170/110	
99	45/f	6 months	1 week	32.12	10	10.1	0.4	nil	no	6.12	6.9	g	g	n	n	yes	270	130/80	
100	70/m	1year	12 years	27.71	11.2	7.9	0.8	nil	no	cf 2.5 m	cf 2.5 m	g	g	n	n	yes	150	150/100	
101	52/m	3 years	5 years	23.15	12.8	11.3	0.5	nil	yes	6.9	6.9	g	g	n	n	no	260	140/90	
102	66/m	1 year	1.5 years	31.5	12.4	5.6	0.4	nil	yes	cf 0.5 m	cf 3m	g	g	n	n	yes	180	200/100	
103	58/f	5 years	6 years	22.63	8	7.3	1	nil	no	6.24	6.24	g	g	n	n	no	143	130/70	
104	65/f	6 years	6 years	28.57	9	7	1.3	nil	no	cf 1m	cf 1m	g	g	n	n	no	117	130/80	
105	80/f	20 years	2 years	21.39	7	6.2	0.5	nil	tobacco	6.6	6.6	g	g	n	n	yes	70	120/70	
106	62/f	20 years	25 years	27.02	8.2	8.3	0.6	nil	no	6.36	6.36	pciol	pciol	n	n	no	564	180/100	
107	60/f	6 years	6 years	34.34	8	7.1	0.6	nil	no	6.6	6.6	g	g	n	n	yes	184	140/90	
108	50/f	8 years	8 years	24.78	8.4	6.5	0.6	nil	no	6.18	6.18	g	g	n	n	yes	210	140/90	

109	55/f	5 years	no	23.86	8.2	6.5	0.5	nil	no	6.36	6.36	g	g	severe npdr eith csme	severe npdr	yes	386	140/90	
110	42/m	2 years	no	17.84	10	10.7	0.4	yes-2 y	no	6.6	6.36	g	g	mod npdr	mod npdr	yes	324	120/80	
111	41/m	6 months	no	19.82	12	6.6	0.8	nil	yes	6.12	6.18	g	g	n	n	yes	92	80/60	
112	65/f	8 years	8 years	22.44	9	6.8	0.9	nil	no	6.24	6.18	g	g	n	n	yes	74	160/90	
113	40/f	6 years	no	25.33	8.4	9.2	0.8	nil	no	6.9	6.6	g	g	mod npdr	mod npdr	yes	104	140/90	
114	61/m	6 months	6 months	23.82	11.4	7.1	1	nil	yes	cf 2m	cf 3m	g	g	n	n	no	240	150/100	
115	71/m	4 years	4 years	23.33	12	13.2	1.1	yes-3y	no	6 by 24	6 by 60	pciol	pciol	stable pdr post laser	stable pdr post laser		70	160/90	ihd
116	55/m	2 years	1 year	25.7	13	6.8	0.9	no	yes	6.18	6.12	g	g	n	n	no	163	140/70	
117	55/f	1 year	no	20	8.8	6.4	0.7	no	no	6.12	6.18	g	g	n	n	yes	268	110/70	
118	42/f	5 years	1 month	27.58	9.2	11.4	0.8	no	no	cf 3m	cf 2.5 m	g	g	mod npdr with csme	mod npdr with csme	yes	321	160/90	
119	45/f	4 years	no	17.08	8.6	10.6	0.9	yes-3 years	no	6.6	6.6	g	g	mod npdr with csme	mod npdr with csme	no	450	80/50	
120	67/f	6 years	3 years	23.64	8.8	5.8	1	no	no	6.12	6.12	g	g	n	n	no	212	130/80	
121	52/f	3 years	no	25.67	9	6.6	0.8	no	no	6.9	6.9	g	g	n	n	yes	252	170/90	
122	65/f	3 years	3 years	21.75	8	12.4	1.2	nil	no	cf 2.5 m	cf 3m	pciol	pciol	pdr	pdr,subhyaloid hmrg	no	129	180/90	
123	79/m	8 years	9 years	19.37	9	6.4	1	y-2 mon	no	6.36	cf 0.5 m	pciol	g	n	n	no	402	190/60	
124	68/m	5 years	no	18.33	8.4	6.6	0.8	yes	no	6.9	6.6	g	g	n	n	yes	212	90/60	
125	60/m	1 year	no	26.95	10.2	8.8	0.9	no	no	6.6	6.6	g	g	v.mild npdr	v.mild npdr	no	269	130/70	
126	60/f	5 years	no	21.9	9	6.3	0.8	no	no	6.9	6.6	g	g	n	n	no	143	150/70	
127	45/f	3 years	3 years	26.66	9.2	5.8	0.8	no	no	6.9	6.12	g	g	n	n	yes	326	190/100	
128	60/f	4 years	4 years	19.23	8.2	7.9	0.9	no	no	6.6	6.9	g	g	v.mild npdr	v.mild npdr	no	104	130/80	
129	60/m	1 year	no	21	13.9	7.9	1.5	no	yes	6.18	6.12	g	g	csme	csme	no	96	130/90	
130	50/f	5 years	no	26.89	10	6.8	0.6	no	no	6.12	6.18	g	pciol	n	n	no	401	130/80	
131	68/f	4 years	6 years	31.06	13.6	6.7	1.1	no	no	6.18	6.24	g	g	n	n	no	109	120/80	
132	60/f	5 years	no	34.69	11.7	11.3	1.1	no	no	cf 0.5 m	6 by 12	g	g	n	n	no	398	120/80	
133	43/m	1 year	no	26.67	14.2	11.1	1.1	no	no	6.18	6.12	g	g	n	n	no	387	120/70	
134	50/f	6 months	1 week	21.62	12.9	8.3	0.9	no	no	6.36	6.24	g	g	n	n	no	187	150/100	
135	63/f	3 years	7 years	28.88	10.5	8.7	0.9	no	no	6.24	6.18	g	g	n	mild npdr	no	174	120/70	
136	50/f	5 years	5 years	28.8	11	8.4	1.1	no	no	6.12	6.9	g	g	n	n	yes	300	150/100	
137	65/f	15 years	15 years	31.08	10.7	5.8	1.2	no	no	6.18	6.12	g	g	mild npdr	mild npdr	yes	138	130/70	
138	65/f	2 years	no	23.14	10	7.5	1.4	no	no	6.36	6.36	g	g	mild npdr	mild npdr	no	254	140/80	
139	48/f	8 mon	3 years	28.76	14	6.4	1	no	no	6.12	6.9	g	g	n	n	no	176	110/70	
140	60/f	6 months	no	27.77	11.4	6.6	1.3	no	no	6.12	6.12	g	g	mac scar	mac scar	no	184	140/90	
141	65/m	2 years	4 years	33.78	14.9	7.1	1.2	no	yes	6.12	6.24	g	g	n	n	yes	148	130/90	
142	66/m	2 years	2 years	27.34	12.8	6.4	1.4	no	no	6.24	6.24	g	g	n	n	yes	101	130/90	
143	42/f	7 months	no	25.11	12.4	7.2	1.1	no	no	6.6	6.6	g	g	n	n	yes	122	120/80	
144	53/m	2 years	no	26.66	14	10.5	1.2	no	yes	6.12	6.12	g	g	n	n	yes	118	120/80	
145	60/f	12 years	no	24.12	10.5	15.1	1.3	no	no	6.24	cf 2m	g	g	early pdr	pdr, vitreous hmrg	yes	401	140/90	
146	65/f	6 months	5 years	24.37	10.9	7.6	1.9	no	no	cf 3m	6.6	pciol	g	n	n	no	189	140/70	
147	42/f	8 months	2 years	21.77	13	7.4	1.1	no	no	6.18	6.18	g	g	csme	csme	no	274	120/70	
148	45/f	1 year	no	33.8	12	9.4	0.7	no	no	6.18	6.18	g	g	n	n	no	327	120/80	

149	60/f	5 years	2 years	19.5	10.9	8.2	0.9	no	no	cf 1m	cf 1m	g	g	n	n	no	304	130/70	
150	55/f	6 months	no	22.22	10.6	9.8	1	no	no	6.6	cf 0.5 m	g	g	mild npdr	mild npdr	no	124	140/80	
151	55/f	1 year	1 year	23.8	10.8	6.9	1.1	no	no	6.12	6.12	g	g	n	n	no	218	140/80	
152	50/f	10 years	5 years	23.62	10	9.3	1	no	no	6.18	6.36	g	g	mild npdr with mac hole	pdr	yes	190	130/80	
153	65/f	6 months	1 year	21.89	10.5	8	1	no	no	6 by 60	6.36	g	pciol	n	n	no	219	160/90	
154	52/f	4 years	no	30.54	10.1	10.2	1.2	no	no	6.6	6.9	g	g	n	n	no	371	130/80	
155	60/m	5 years	no	27.3	9.6	9.8	1.1	no	yes	6 by 60	6.6	g	g	n	n	no	276	140/80	
156	84/m	8 years	1 year	24.2	10.2	6.7	0.9	no	no	6 by 60	6 by 36	pciol	pciol	n	n	no	162	160/90	
157	60/f	4 years	2 years	24.4	10	8.4	0.9	no	no	6.36	6.36	g	g	n	n	no	218	120/70	
158	65/f	16 years	no	25.3	10	12.1	1.2	no	yes	6.18	6.18	g	g	mild npdr	mild npdr	yes	392	150/90	
159	50/m	10 years	no	27.8	11	9.4	1	yes 4 years	no	6.9	6.9	g	g	mild npdr	mild npdr	yes	412	140/70	
160	60/f	6 mon	no	28.1	9.8	7.6	0.8	no	no	6.6	6.6	g	g	n	n	no	251	140/80	
161	60/f	3 years	no	26.7	7	7.5	0.7	no	no	6.18	6.18	g	g	n	n	no	267	150/90	
162	60/f	4 years	no	22.2	9	8.4	1.1	no	no	6.18	6.18	g	g	n	n	no	252	150/90	
163	60 /f	5 years	9 years	28.1	9.4	7.1	1	no	no	6 by 60	6 by 60	g	pciol	n	n	no	303	140/90	
164	55/f	6 years	no	31.1	9.2	8.6	1.3	no	no	6.12	6.12	g	g	n	n	no	256	150/80	
165	62/f	10 years	10 years	24.4	10	9.2	0.7	no	no	6 by 60	6 by 60	g	g	mod npdr	mod npdr	yes	380	150/70	
166	67/f	4 years	5 years	26.7	10	9.5	0.8	yes 2 years	no	6 by 60	6 by 60	g	g	n	n	yes	296	150/90	
167	50/m	10 years	no	22.5	10	8.1	0.8	no	no	6.18	6.18	g	g	n	n	yes	189	130/70	
168	65/f	6 mon	no	22.9	9.2	7.8	1	no	no	6.36	6.36	g	g	n	n	yes	246	140/80	
169	55/m	17 years	no	20.8	10	16	1.2	no	no	6.36	6.36	g	g	n	n	yes	200	150/80	
170	63/m	3 years	8 years	29.4	10	7.5	1.2	no	no	6 by 60	6 by 60	g	pciol	n	n	yes	412	130/80	
171	51/m	2 years	2 years	26	12	8.7	0.9	no	yes	6 .6	6.6	g	pciol	mild npdr	sev npdr	yes	413	120/80	
172	62/f	6 mon	1 year	22.2	9	7	0.8	no	no	6.12	6.12	g	g	n	n	no	150	140/80	
173	60/m	6 mon	6 months	17.6	12.4	13.1	0.8	no	no	6.12	6.6	g	g	n	n	no	70	160/80	
174	63/m	3 years	1 year	24.2	10	7	1	no	yes	6.18	6.18	g	g	n	n	no	150	150/80	
175	76/m	4 years	4 years	18	9.8	5.7	0.8	no	yes	6 by 60	6 by 60	pciol	pciol	n	n	no	150	150/80	
176	53/m	3 years	no	21	10.2	9.6	1.1	no	no	6.18	6.12	g	g	n	n	yes	171	110/70	
177	61/f	1 year	1 month	17.8	9.6	9.7	1.4	no	no	6 by 60	6 by 60	g	g	mod npdr csme	trac RD , PDR	yes	243	130/70	
178	45/m	3 years	no	20	11.4	10	1	no	no	6 by 60	6 by 60	pciol	g	n	n	no	331	120/80	
179	61/m	2 years	no	25.4	11.6	11.7	0.9	no	no	6.12	6.12	g	g	mild npdr	mild npdr	yes	328	160/80	
180	56/f	10 years	2 years	28.9	10.8	10.1	0.8	no	no	6.12	6.18	g	g	n	n	no	280	110/70	
181	50/m	5 years	5 years	31.3	12.4	8.9	0.9	no	yes	6.18	6.12	g	g	n	n	no	205	120/80	
182	61/m	11 years	8 years	26.2	12	8.3	1.3	no	no	6.12	6.36	g	g	n	n	no	150	160/80	
183	60/f	2 years	2 years	26.7	10.2	8.2	0.6	no	no	6.18	6.18	g	g	n	n	yes	200	150/70	
184	60/f	1 year	1 year	16.4	9.4	12	0.8	no	no	6.12	6.18	g	g	n	n	no	230	150/80	
185	52/m	6 years	2 years	29.1	12.2	11	1	4 years	no	6.12	6.12	g	g	n	n	no	200	130/90	
186	69/m	6 mon	5 years	24.2	9.8	7	1	no	yes	6.12	6.12	g	g	n	n	no	276	160/80	
187	54/m	2 years	no	22.3	12.4	8.2	1.4	no	no	6.18	6.36	g	g	n	n	no	294	130/70	
188	64/m	10 years	6 years	18.4	11.2	9.5	1.2	no	no	6.12	6.36	g	g	n	n	no	346	160/80	

189	60/f	1.5 years	1.5 years	19	10	10.8	1.4	no	no	6.18	6.18	g	g	n	n	no	200	140/80	
190	76/m	2 years	no	23.8	10.2	7.9	1	no	yes	6 by 60	6 by 60	g	g	n	n	no	111	150/80	
191	66/m	17 years	no	22.2	10.6	10.2	0.9	no	no	6 by 60	6by 60	g	g	mod npdr csme	mod npdr csme	yes	380	130/70	
192	75/f	6 mon	8 years	23.8	9.6	7	1.3	no	no	6 by 60	6 by 60	pciol	pciol	n	n	no	98	120/70	
193	45/f	3 years	no	23.8	11.2	8.2	0.8	no	no	6.12	6.18	g	g	n	n	no	238	150/100	
194	55/f	20 years	20 years	23.4	11.4	8	1	3 years	no	6.18	6.18	pciol	pciol	mod npdr csme	mod npdr csme	no	250	150/90	
195	43/m	4 years	no	25	12.6	10.6	0.8	no	no	6.12	6.12	g	g	n	n	no	400	140/80	
196	42/m	1.5 years	no	26.6	13.4	6.6	1.2	no	yes	6.12	6.36	g	g	mild npdr	mild npdr	no	200	120/80	
197	40/f	3 years	no	26.6	12.2	9.2	0.6	no	no	6.12	6.12	g	g	n	n	no	300	140/80	
198	63/f	1 year	1 year	24.8	10.6	7.6	0.7	no	no	6 .36	6.36	g	g	n	n	no	200	140/80	
199	70/f	4 years	4 years	22.2	9.2	11.4	1.2	no	no	6 by 60	6 by 60	g	pciol	n	n	no	380	130/80	
200	55/m	2 years	no	26.2	12.6	8	0.9	no	yes	6 .12	6.12	g	g	mild npdr	mild npdr	no	160	150/80	
201	73/m	5 years	5 years	22	10.2	8.2	1.3	no	yes	6.12	6.12	g	g	n	n	no	188	160/80	
202	49/f	8 years	8 years	27.3	11.2	6.4	1	no	no	6.12	6.12	g	g	v.mild npdr	v.mild npdr	yes	93	140/90	
203	67/m	16 years	16 years	23.4	11	6.8	1.2	no	no	6.18	6.36	g	g	n	n	no	160	160/80	
204	64/m	25 years	10 years	30.5	10.6	7	1.1	10 years	no	6.12	6 by 60	pciol	g	n	n	no	170	160/80	
205	68/m	5 years	no	16.7	13.4	8.3	0.7	no	no	6.12	6.9	g	g	n	n	no	253	120/70	
206	68/m	8 years	8 years	25.1	11.1	6.2	1.4	no	yes	6 by 60	6.12	g	g	n	n	no	89	130/80	
207	40/m	2 years	no	27.9	13.5	8.6	0.8	no	yes	6.6	6.6	g	g	n	n	no	197	140/100	
208	59/m	5 years	no	24.2	11.1	11.2	0.7	no	no	6 by 60	6 by 60	g	g	n	n	no	357	130/80	
209	68/f	8 years	no	25.8	11.6	7.3	0.8	no	no	6.24	6.12	g	g	n	n	no	134	110/70	
210	60/f	2 years	no	25.2	11	6.5	0.9	no	no	6 .6	6.6	pciol	g	n	n	no	110	140/90	
211	60/f	1 year	2 years	22.5	11.3	9.2	1.2	no	no	6.6	6.9	g	g	n	n	no	236	140/80	
212	65/m	6 mon	6 months	30	12	13.7	0.9	no	yes	6 .6	6.6	pciol	pciol	n	n	no	407	170/90	
213	41/m	3 years	no	31.9	12.4	9.9	0.6	no	no	6.6	6.6	g	g	n	n	no	392	110/70	
214	70/f	4 years	3 years	31.1	11.2	6.5	1.1	no	no	6 byb 60	6 by 60	g	g	n	n	no	186	100/60	
215	55/f	17 years	17 years	23.5	11.8	9.4	1.3	no	no	6.9	6.6	g	g	n	n	no	269	110/70	
216	60/f	4 years	4 years	38.7	12	11.3	1.1	no	no	6.24	6.18	g	g	n	n	no	427	130/70	
217	50/f	8 years	8 years	25.5	11.4	8.3	0.9	no	no	6.12	6.6	pciol	g	n	n	yes	368	120/70	
218	67/f	10 years	10 years	39.4	12.2	7.5	1.2	no	no	6 by 60	6 by 60	g	g	drusen	drusen	no	215	150/80	
219	49/f	6 mon	no	31.4	11.8	12.3	0.8	no	no	6.36	6.12	g	g	n	n	no	387	150/90	
220	60/f	1 year	1 year	33.1	12	8.6	1.1	no	no	6.36	6.36	g	g	n	n	yes	313	130/80	
221	50/f	1 year	no	27.9	12.4	7.6	8	no	no	6.6	6.6	g	g	n	n	yes	151	110/70	
222	60/f	8 years	8 years	35.2	12.2	6.3	0.7	4 years	no	6.6	6.9	g	g	n	n	yes	186	150/90	
223	50/f	10 years	10 years	29.6	11.8	10.3	0.8	10 years	no	6.12	6.9	g	g	n	n	yes	367	140/90	
224	63/m	17 years	17 years	30.1	11.6	12.7	0.8	no	no	6 .6	6.6	pciol	pciol	mild npdr	mild npdr	yes	407	150/80	
225	55/f	4 years	4 years	33.6	11.8	8.3	0.9	no	no	6.6	6.6	g	g	n	n	yes	302	120/60	
226	65/f	10 years	10 years	21.8	11.2	9.7	0.9	no	no	6.9	6.12	g	g	mild npdr	mild npdr	yes	218	140/70	
227	69/f	6 mon	6 months	37.4	11.8	8.4	0.8	no	no	6.9	6.6	pciol	pciol	n	n	no	171	120/70	
228	50/f	7 years	6 years	28.4	12	10.7	1	no	no	6.6	6.9	g	g	n	n	yes	243	110/60	

229	62/f	1.5 years	no	28.4	11.6	10	1.1	no	no	6.18	6.12	g	g	n	n	no	338	120/70	
230	76/m	4 years	4 years	29.2	11.6	7.8	1.2	no	no	6.9	6.36	pciol	g	n	n	no	244	140/90	
231	68/m	20 years	20 years	26	12.2	11	1.1	no	no	6.6	6.12	g	g	n	n	no	406	130/90	
232	60/f	10 years	no	26.5	11.8	8.2	0.9	no	no	6.6	6.6	g	g	n	n	no	211	120/70	
233	40/f	6 mon	no	35.7	12.4	10.6	1.3	no	no	6.6	6.6	g	g	n	n	no	253	110/70	
234	53/m	1 year	no	23.1	12.6	9.8	0.8	3 months	no	6.36	6.6	g	g	mod npdr with csme	mod npdr	no	229	140/80	
235	58/m	11 years	10 years	24.2	10.1	6	0.9	no	yes	6.6	6.6	g	g	mild npdr	mild npdr	yes	108	120/80	
236	45/f	2 years	no	29.2	12.8	8.7	0.8	no	no	6.9	6.6	g	g	n	n	yes	220	130/70	
237	49/f	3 years	3 years	30	12.7	6.1	1.4	no	no	6.6	6.6	g	g	n	n	yes	141	130/80	
238	70/m	17 years	17 years	22.8	11.8	8.1	1.2	no	no	cf 4m	6.24	g	g	high risk pdr	high risk pdr	no	221	160/100	
239	85/f	1.5 years	1.5 years	26.3	9.7	7.4	0.7	no	no	6.18	6.6	g	g	n	n	no	224	110/70	
240	60/f	4 years	12 years	25	11.8	11.5	0.9	no	no	6 by 60	6 by 60	g	g	n	n	yes	326	130/70	
241	67/f	12 years	no	24.1	11	7.3	0.6	no	no	6.6	6.6	g	g	n	mild npdr	yes	150	150/70	
242	58/f	5 years	9 years	25.8	10.6	10.9	0.8	no	no	6.24	<6 by 60	g	g	htn ret	htn ret, macular scar	no	200	140/70	
243	62/m	6 years	no	24.2	10.5	9.5	1.2	no	no	6.6	6.9	g	g	n	n	no	239	130/80	
244	75/f	10 years	14 years	36.9	12.2	11.4	1	no	no	6.9	6.6	pciol	pciol	n	n	no	256	150/70	
245	64/m	6 years	no	24.1	13	10.9	0.9	no	no	6.36	6.18	g	g	early pdr	n	no	186	150/100	
246	80/f	16 years	15 years	29.8	12.9	8.9	1.3	1.5 years	no	6.12	6.9	pciol	pciol	n	n	yes	316	150/60	
247	40/f	3 years	no	32.2	9.6	8.4	0.8	no	no	6.6	6.12	g	g	n	n	yes	273	110/60	
248	55/f	20 years	no	23.8	10.2	6.4	0.8	no	no	cf 5m	cf 3m	g	g	n	n	no	128	130/80	
249	59/f	15 years	10 years	34	10.8	11.7	0.6	no	no	6.6	6.18	g	g	mild npdr	drusen	no	282	140/70	
250	60/m	2 years	no	17.8	13.2	5.2	1.2	no	no	cf 3m	cf 3m	g	g	n	n	no	129	100/60	
251	68/f	1 year	no	24.1	11.8	6.1	1	no	no	cf 2m	6.18	g	pciol	n	n	yes	114	140/70	
252	60/f	3 years	no	28.1	12.8	8.9	0.9	no	no	6.6	6.6	g	g	n	n	no	381	110/60	
253	55/f	6 mon	no	32.3	11.9	7.4	0.8	no	no	6.12	6.36	g	g	n	n	no	254	110/60	
254	60/f	2 years	no	30.7	9.2	6.3	0.9	no	no	6.6	6.6	g	g	n	n	no	158	140/80	
255	48/m	14 years	4 years	29	10.2	8.8	1.5	no	no	6.9	6.9	g	g	mild npdr	mild npdr	yes	296	130/80	
256	40/f	1 year	2 years	23.1	12.2	6.8	0.7	no	no	6.9	6.9	g	g	n	n	no	112	110/80	
257	50/m	10 years	no	27.5	11.8	7.2	0.8	no	yes	6.9	6.9	g	g	mild npdr	mild npdr	yes	222	150/90	
258	50/m	2 years	2 years	27.2	12.4	7	0.9	no	no	cf 3m	cf 2m	g	g	n	n	yes	214	110/90	
259	70/m	6 mon	no	26.2	11	8.3	1.1	no	yes	6.12	6.12	g	g	n	n	no	285	120/90	
260	50/f	3 years	no	23.2	9.5	9.6	1.2	no	no	6.12	6.12	g	g	n	n	yes	269	120/80	
261	55/f	1 year	no	22.6	8.2	7.8	0.8	no	no	6.6	6.12	g	g	n	n	yes	229	130/80	
262	68/m	1 year	no	28.4	12	8.2	0.6	no	yes	6.24	6.36	g	g	mac hole	mac hole	no	228	120/80	
263	59/f	6 years	no	28	9.6	7.6	1.4	no	no	cf 4m	cf 3m	g	g	n	n	no	203	130/70	
264	52/f	1.5 years	no	18.4	7	9.3	0.8	no	no	6.9	6.9	g	g	mild npdr	n	no	228	130/80	
265	56/f	3 years	no	22.6	9.5	10.5	0.9	no	no	6 by 60	6.24	g	pciol	n	n	np	344	120/90	
266	50/f	6 mon	2 years	23.7	9.6	6.5	1.3	no	no	6 by 60	6.36	g	g	n	mac scar	no	115	140/100	
267	45/f	1 year	1 year	24.1	9.8	11.3	1.4	no	no	6.6	6.6	g	g	n	n	yes	359	150/100	
268	84/m	13 years	10 years	21.8	10	8.2	1.2	no	no	6.12	6.12	g	g	htn ret	htn ret	yes	222	110/70	

269	62/f	2 years	2 years	20	9.6	7.8	0.8	no	no	6 by 60	cf 4m	g	g	n	n	no	212	100/80	
270	65/f	6 mon	2 years	17.3	9.6	7.6	0.9	no	no	6.6	6.6	g	g	drusen	drusen	no	194	120/90	
271	62/f	6 mon	6 months	18	10	8.3	0.8	no	no	cf 3m	6 ny 60	brownish	g	n	n	no	274	140/100	
272	60/f	5 years	5 years	19.8	9	8.1	1	no	no	6 by 60	cf 2m	g	pw	n	n	no	250	130/90	
273	60/f	3 years	25 years	32.7	10.2	10.8	1.1	no	no	6.18	6 by 60	pciol	g	n	n	no	348	140/90	
274	50/f	2 years	no	26	9.8	11.2	1.3	no	no	6.12	6.18	g	g	n	n	no	388	150/80	
275	60/f	4 years	no	17.3	10.2	11.4	0.9	no	no	6 by 60	6 by 60	g	g	n	n	no	447	138/80	
276	60/f	2 years	6 months	23.8	9.8	7.9	0.7	no	no	6.9	6.12	g	g	n	n	yes	191	110/70	
277	60/m	2 years	no	25	12.2	8	0.8	no	yes	6 by 60	6 by 60	g	g	n	n	yes	190	120/90	
278	70/f	1 year	2 years	32.5	10	8.2	1	no	no	6 by 60	6 by 60	pciol	g	vit hmg	n	no	140	190/90	
279	70/f	6 mon	2 years	18.3	9.8	7.9	0.6	no	no	6.24	6.36	pciol	g	n	n	no	223	140/90	
280	45/m	6 mon	no	26.1	13	6.5	0.9	no	yes	6 .36	6.24	g	g	n	vmild npdr	no	133	100/70	
281	50/f	6 mon	2 mon	27.7	10.6	9.8	0.8	no	no	6.24	6.24	g	g	n	n	no	353	140/80	
282	40/m	7 mon	7 mon	27.5	10	8.3	0.8	no	no	6.12	6.9	g	g	n	n	no	173	180/100	
283	63/m	6 mon	1 year	24.7	12	7.5	1.2	no	yes	6.6	6.6	g	g	n	n	yes	172	110/70	
284	46/m	12 years	2 years	25.5	13.2	10.4	0.8	no	yes	6 by 60	6.24	g	g	mild npdr	mild npdr	no	380	120/70	
285	53/m	3 years	1.5 years	28.6	13.4	9.8	0.9	no	no	6.18	6.9	g	g	n	n	no	294	150/80	
286	52/f	6 mon	no	23.2	10.8	7.4	1.1	no	no	6.9	6.18	g	g	n	n	yes	186	140/80	
287	55/f	6 mon	6mon	20	9.8	8.1	1.3	no	no	6 by 60	6.36	g	g	n	n	no	226	140/70	
288	78/m	8 years	no	24.3	10.8	7.8	0.8	no	yes	6.36	6.36	g	g	n	n	no	208	110/70	
289	70/f	5 y	2 mon	24.4	10.2	9.6	1.4	no	no	6.36	cf 3m	pciol	g	n	n	no	339	160/90	
290	70/m	4 years	no	24.5	12.2	8.8	0.8	no	no	6.36	6.24	g	g	n	n	no	295	130/70	
291	78/m	12 years	6 years	23.6	10.6	7.2	1.6	no	yes	6.9	6.9	g	pciol	n	n	no	209	130/80	
292	75/m	5 years	5 years	22.8	10.8	8.3	1.2	no	no	6.18	6.9	g	g	n	n	yes	222	130/80	
293	68/m	5 years	5 years	23.2	11.2	8.4	0.9	no	yes	6.36	6.12	g	g	n	n	yes	234	120/90	
294	71/m	8 years	8 years	20.6	10.8	6.6	0.9	no	no	6.6	6 by 60	g	g	n	dme	no	194	120/80	
295	43/m	5 years	5 years	24.2	16	10.3	1	no	no	6.9	6.6	g	g	mild npdr	n	yes	226	130/80	
296	45/m	6 years	no	23.8	12.4	7.4	0.8	no	no	6.6	6.6	g	g	n	n	no	204	120/80	
297	49/m	5 years	5 years	24.6	13.2	8.2	0.6	no	no	6.6	6.6	g	g	n	n	no	258	130/80	
298	50/f	10 years	no	22.4	12.4	12.4	0.8	2 years	no	6.6	6.6	g	g	mod npdr	mod npdr	no	400	130/80	
299	70/m	5 years	5 years	20.6	11.8	8.5	1.2	no	no	6.9	6.6	g	g	n	n	no	265	120/90	
300	53/f	8 years	no	23.2	12.6	8.6	1.2	no	no	6.12	6.6	g	g	drusen	n	no	192	120/80	
301	65/f	4 years	4 years	20.4	11.6	7.5	0.6	no	no	6.18	6.36	pciol	g	mod npdr	mild npdr	no	202	110/70	
302	69/m	2 years	no	22.2	12	6.2	0.8	no	no	6.24	6.18	g	pciol	n	n	no	146	110/80	
303	59/f	10 years	10 years	23.6	12.6	6.8	0.8	no	no	6.6	6.6	g	g	n	n	no	164	100/70	
304	42/f	6 years	3 years	24.2	12.2	8.2	1.3	no	no	6.6	6.6	g	g	n	n	no	246	120/90	
305	61/f	6 years	no	20.8	11.2	8.6	1.1	no	no	6.24	6.36	g	g	n	n	no	284	110/80	
306	77/m	8 years	no	21.4	11.6	7.2	1.2	no	yes	6 by 60	6.18	aphakic	pciol	mod npdr	mild npdr	yes	186	120/90	
307	50/f	4 years	no	23.6	12.6	5.8	0.6	no	no	6.9	6.9	g	g	n	n	no	123	130/80	
308	63/m	10 years	1 month	23.4	12.6	11.4	0.8	no	yes	6.36	6.36	pciol	pciol	pdr	pdr	yes	324	120/80	

309	53/f	3 years	no	22.8	12.8	10.2	0.9	no	no	6 by 60	6.12	g	g	pdr	mild npdr	no	272	120/70	
310	58/f	1 year	1 year	23.6	11.8	6.8	1.1	no	no	6 by 9	6.9	g	g	n	n	no	210	110/80	
311	67/f	5 years	no	21.6	10.8	8	1.2	no	no	6.18	6.18	g	g	n	n	no	245	110/70	
312	56/m	6 years	6 years	22.4	13.3	7.4	0.8	no	yes	6.6	6.6	g	g	n	n	no	178	130/80	
313	72/m	10 years	10 years	21.8	12.4	6.8	0.9	no	no	6.9	6.9	g	g	mild npdr	n	yes	204	120/80	
314	57/m	4 years	6years	23.6	13.2	6.4	0.9	no	yes	6.6	6.9	g	g	drusen	n	no	202	120/80	
315	50/f	6 mon	4mon	22.4	11.8	5.8	1.3	no	no	6.12	6.6	g	g	n	n	yes	164	110/70	
316	74/f	4 years	4 years	21.8	11.6	6.4	0.7	no	no	6.12	6.18	g	g	n	n	yes	236	110/80	
317	47/m	9 years	no	23.6	13.4	8.5	1.2	no	no	6.9	6.9	g	g	pdr	mild npdr	no	276	140/80	
318	66/f	5 years	12 years	20.8	11.6	8.4	1.1	no	no	6.12	6.6	g	g	n	n	no	305	130/90	
319	69/f	10 years	10 years	22.2	11.8	7.2	0.7	6 years	no	6.12	6.12	g	g	n	n	yes	158	130/80	
320	66/m	3 years	no	23.2	12	6.8	0.9	no	yes	6.9	6.9	g	g	v.mild npdr	csme	no	156	120/80	
321	61/m	5 years	5 years	22.5	13.2	10	1	no	yes	6.9	6.9	g	g	mild ndr with csme	mild npdr with csme	no	202	130/90	
322	75/f	15 years	15 years	21.3	11.3	9.8	0.8	no	no	6.18	6.24	pciol	pciol	mild npdr	pdr	yes	318	140/80	
323	57/m	5 years	no	23.7	12.8	7.4	0.8	no	yes	6.9	6.9	g	g	n	n	no	215	110/80	
324	70/f	4 years	no	22.6	9.2	8	0.7	no	no	6.9	6 .36	g	g	n	n	no	186	120/70	
325	74/m	10 years	yes	20.6	14.1	7.6	1.2	no	yes	6.36	6.24	g	g	n	n	no	212	110/70	
326	65/m	1.5 years	yes	24.3	12.3	6.8	1.5	no	yes	6.36	6.36	g	g	n	n	no	196	120/80	
327	68/f	5 years	yes	22.8	10	8.2	1.3	no	no	6.24	6.9	g	g	n	n	no	200	130/70	
328	65/f	6 mon	yes	23.4	15.5	7.4	0.8	no	no	6 by 60	6.36	g	g	n	n	no	178	110/80	
329	62/f	2 years	yes	23.8	8.8	7.4	0.7	no	no	6.36	6.36	g	g	n	n	no	182	110/70	
330	62/m	10 years	yes	24.6	12.1	7.8	1.5	no	yes	6.12	6.12	g	g	n	n	no	194	130/90	
331	58/f	8 years	no	23.2	12.2	7.6	1	no	no	6.24	6 by 60	g	g	n	n	no	155	120/70	
332	56/f	5 years	no	24.2	12.2	6.8	1	no	no	6 by 60	6 by 60	g	g	n	n	no	204	110/80	
333	70/m	20 years	yes	22.8	12.8	7	1	no	no	6 by 60	6 by 60	g	g	n	n	no	212	120/80	
334	76/m	30 years	yes	24.6	13.7	7.6	1	no	no	6 .18	6.24	g	g	mild npdr	mild npdr	no	198	130/90	
335	65/f	1 year	no	22.8	11.8	6.8	0.9	no	no	6 by 60	6.36	g	g	n	n	no	182	120/80	
336	62/f	2 years	yes	23.2	7.8	6.8	0.9	no	no	6 by 60	6.36	g	g	n	n	no	176	130/80	
337	68/f	1 year	no	24.4	8.6	8.2	1.1	no	no	6.12	6.9	g	g	n	n	no	198	130/80	
338	60/m	6 years	yes	25.2	8.3	8.5	9.2	no	no	6 by 60	6.18	g	g	mod NPDR	mod NPDR	no	208	130/80	
339	65/m	5 years	yes	24.2	9.6	8	1.5	no	no	6 by 60	6.12	g	pciol	n	n	no	202	130/90	
340	70/f	3 years	no	22.6	9	7.4	0.8	no	no	6.36	6.36	g	g	n	n	no	102	130/90	

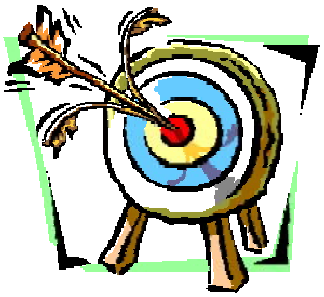
C

ANNEXURE-VI

KEY TO MASTER CHART

Dm durn	-	Duration of diabetes
Htn	-	Hypertension
Bmi	-	Body Mass Index
Hb	-	Haemoglobin
Hba1c	-	Glycosylated haemoglobin
Creat	-	Serum Creatinine
Re	-	Right eye
Le	-	left eye
As od	-	Anterior segment right eye
As os	-	Anterior segment left eye
ps od	-	Posterior segment right eye
ps os	-	Posterior segment left eye
family	-	Family history of diabetes
rbs	-	Random blood sugar
bp	-	Blood pressure

Introduction



Objectives

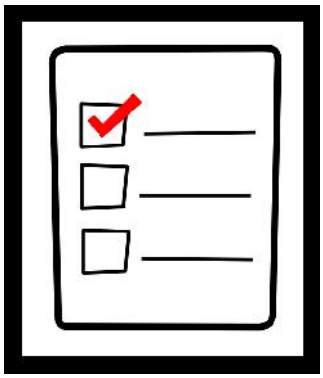
Review of Literature

Methodology

Results

Discussion

Conclusion

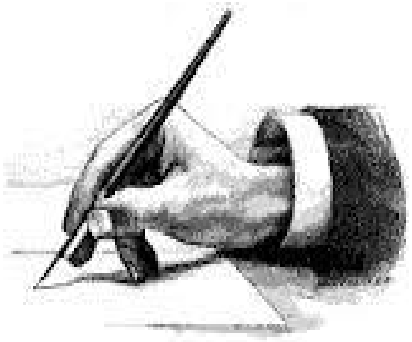


Limitations

Recommendations

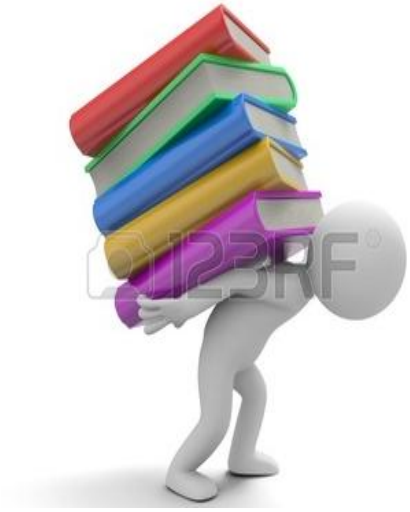
Summary

Bibliography



Annexure-I

Annexure-II



Annexure-III

Annexure-IV

Annexure-V