"ONE YEAR CROSS-SECTIONAL STUDY TO DETERMINE OCULAR CHANGES IN DIABETIC END STAGE KIDNEY DISEASES AT KLES DR. PRABHAKAR KORE HOSPITAL AND MEDICAL RESEARCH CENTRE, BELGAUM"

By

Dr. NAGBHUSHAN S. CHOUGULE

Dissertation submitted to the
KLE University, Belgaum, Karnataka

In Partial Fulfillment
of the requirements for the degree of

M. S. (OPHTHALMOLOGY)

Under the Guidance of

Dr. S. B. PATIL MS, DOMS
Professor,

DEPARTMENT OF MEDICINE,
JAWAHARLAL NEHRU MEDICAL COLLEGE,
BELGAUM, KARNATAKA

MAY - 2010

KLE UNIVERSITY, BELGAUM,

KARNATAKA

DECLARATION

I hereby declare that this dissertation entitled **"ONE YEAR CROSS-SECTIONAL STUDY TO DETERMINE OCULAR CHANGES IN DIABETIC END STAGE KIDNEY DISEASES AT KLES DR. PRABHAKAR KORE HOSPITAL AND MEDICAL RESEARCH CENTRE, BELGAUM"** is a bonafide and genuine research work carried out by me under the guidance of **Dr. S. B. PATIL** **MS DOMS** Professor, Department of Ophthalmology, Jawaharlal Nehru Medical College, Nehru Nagar, Belgaum-590010.

Date:

Place: (Dr. NAGBHUSHAN S. CHOUGULE)

KLE UNIVERSITY, BELGAUM,

KARNATAKA

CERTIFICATE

This is to certify that the dissertation entitled **"ONE YEAR CROSS-SECTIONAL STUDY TO DETERMINE OCULAR CHANGES IN DIABETIC END STAGE KIDNEY DISEASES AT KLES DR. PRABHAKAR KORE HOSPITAL AND MEDICAL RESEARCH CENTRE, BELGAUM"** is a bonafide research work done by **Dr. NAGBHUSHAN S. CHOUGULE** in partial fulfillment of the requirement for the degree of **M.S. (OPHTHALMOLOGY).** This work has been carried out under my direct supervision and guidance and under the overall guidance of **Dr. S. B. PATIL** MS, DOMS, Professor, Department of Ophthalmology, Jawaharlal Nehru Medical College, Belgaum – 590 010.

Date:

Place: Belgaum

Dr. M. S. KHANPET MD DNB (Nephrol)
Professor,
Department of Medicine,
J. N. Medical College,
Nehru Nagar, Belgaum – 10

KLE UNIVERSITY, BELGAUM,

KARNATAKA

CERTIFICATE

This is to certify that the dissertation entitled **"ONE YEAR CROSS-SECTIONAL STUDY TO DETERMINE OCULAR CHANGES IN DIABETIC END STAGE KIDNEY DISEASES AT KLES DR. PRABHAKAR KORE HOSPITAL AND MEDICAL RESEARCH CENTRE, BELGAUM"** is a bonafide research work done by **Dr. NAGBHUSHAN S. CHOUGULE** in partial fulfillment of the requirement for the degree of **M.S. (OPHTHALMOLOGY).**

Date:

Place:

Dr. S. B. PATIL MS,DOMS
Professor,
Department of Ophthalmology,
J. N. Medical College,
Nehru Nagar, Belgaum – 10

KLE UNIVERSITY, BELGAUM,

KARNATAKA

ENDORSEMENT

This is to certify that the dissertation entitled **"ONE YEAR CROSS-SECTIONAL STUDY TO DETERMINE OCULAR CHANGES IN DIABETIC END STAGE KIDNEY DISEASES AT KLES DR. PRABHAKAR KORE HOSPITAL AND MEDICAL RESEARCH CENTRE, BELGAUM"** is a bonafide research work done by **Dr. NAGBHUSHAN S. CHOUGULE** under the guidance of **Dr. S. B. PATIL** MS, DOMS Professor, Department of Ophthalmology, J. N. Medical College, Nehru Nagar, Belgaum-590010.

Dr. R. K. DANDUR MS,DOMS
Professor and Head,
Department of Ophthalmology,
J. N. Medical College,
Nehru Nagar, Belgaum – 10

Date:
Place: Belgaum

Dr. V. D. Patil MD,DCH
Principal,
J. N. Medical College,
Nehru Nagar, Belgaum – 10

Date:
Place: Belgaum

KLE UNIVERSITY, BELGAUM,

KARNATAKA

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(Dr. NAGBHUSHAN S. CHOUGULE)

Place :

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I bow my head in respect before God Almighty.

Date:

Place: **Dr. NAGBHUSHAN S. CHOUGULE**

LIST OF ABBREVIATIONS USED

BDR	:	Background diabetic retinopathy
CBMT	:	Capillary basement membrane thickening
CCF	:	Congestive cardiac failure
CSME	:	Clinically significant macular oedema
DCCT	:	Diabetes Complications and Control trial
DF	:	Degrees of freedom
DR	:	Diabetic retinopathy
DRS	:	Diabetic Retinopathy Study
DRVS	:	Diabetic Retinopathy vitrectomy Study
ETDRS	:	Early Treatment of Diabetic Retinopathy study
FAZ	:	Foveal Avascular zone
FBS	:	Fasting blood sugar
FFA	:	Fundus fluorescein angiography
GCL	:	Ganglion cell layer
GFR	:	Glomerular filtration rate
HTN	:	Hypertension
IDDM	:	Insulin dependent diabetes mellitus
ILM	:	Internal Limiting Membrane
IPL	:	Inner plexiform layer
IRMA	:	Intraretinal microvascualr abnormalities
MA	:	Microaneurysms
MODY	:	Maturity onset of diabetes in the young
N	:	Normal
NFL	:	nerve fiber layer

NIDDM	:	Non-Insulin dependent diabetes mellitus
NPDR	:	Non-Proliferative diabetic retinopathy
NVD	:	Neovascularization of disc
NVE	:	Neovascularization elsewhere
ONL	:	Outer Nuclear layer
PDR	:	Proliferative Diabetic Retinopathy
PPBS	:	Post-prandial blood sugar
PPDR	:	Pre-proliferative diabetic retinopathy
RBS	:	Random blood sugar
RD	:	Retinal detachment
RPE	:	Retinal pigment epithelium
S Chol	:	Serum Cholesterol
S. Creat	:	Serum Creatinine
VA	:	Visual acuity
WESDR	:	Wisconsin Epidemiological Study of Diabetic Retinopathy

ABSTRACT

Background and objectives

Diabetic nephropathy that is Kimmelsteil Wilson lesion or intercapillary glomerulonephritis is progressive kidney disease causes angiopathy. This syndrome is seen in chronic diabetes. Diabetic nephropathy is most common cause of kidney failure and end stage kidney disease. Present study was undertaken to find ocular changes and complications associated with diabetic end stage kidney diseases.

Methodology

The present one year cross-sectional study was conducted in the Department of Ophthalmology, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum during the period of January 2008 to December 2008 on 50 patients with diabetes mellitus and undergoing renal haemodialysis. The patients were subjected to general physical examination and systemic examination. Ocular examination was carried out to assess best corrected visual acuity, intraocular pressure and detailed examination of anterior and posterior segment.

Results

In the present study male (74%) preponderance was seen. Fifty percent (50%) of the patients were in the age group of > 60 years. Thirty two (32%) of patients had duration of renal dialysis less than six months. Twenty six (26%) eyes had duration of vision loss within a year with duration of diabetes upto four years. Blurring of vision was most important symptom noticed among the

patients. Patients with decreased vision < 6/24 were about (47%). Most of them were of gradual onset and remaining patients were having vision of 6/6 to 6/18 in 53%. Eighty percent 80% of eyes had diabetic retinopathy in one or other form. Overall ocular changes seen in the patients were diabetic retinopathy (48%), hypertensive retinopathy (12%) and cataract (9%). Proliferative diabetic retinopathy was the commonest (50%) cause of visual impairment.

Conclusion and interpretation

The study may be concluded that patients with diabetic end stage kidney diseases are at high risk of ocular morbidities. Timely screening and treatment may help to reduce the ocular morbidities in this group.

Key Words

Best corrected visual acuity; End stage kidney disease; Diabetes mellitus; Diabetic retinopathy; Diabetic nephropathy.

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INTRODUCTION

Diabetes Mellitus is a clinical syndrome characterized by hyperglycaemia due to absolute or relative deficiency of insulin. Now in the modern era diabetes mellitus is a burning issue and its incidence is increasing day by day. Its long term complication leads to microvascular complications like neuropathy, retinopathy, and nephropathy. Diabetes affects vasculature in retina and kidneys.

Diabetic nephropathy that is Kimmelsteil Wilson lesion or intercapillary glomerulonephritis is a progressive kidney disease which causes angiopathy. This syndrome is seen in chronic diabetes. Diabetic nephropathy is most common cause of kidney failure and end stage kidney disease.[1]

Chronic renal failure (CRF) is irreversible and progressive process that results in end stage renal disease (ESRD) where patient has to be dependent on renal replacement therapy for survival. Deterioration of eyesight is due to diabetic retinopathy, ischemic optic neuropathy, central retinal vein occlusion and cortical blindness. Ocular morbidity may be directly due to hypertension, uremia and anemia; some are related to the causes leading to chronic renal failure. Some effects are due to haemodialysis.

Retinopathy is often asymptomatic in its most treatable stage; delay in diagnosis can result in significant increase in the patient's risk of visual loss. Ocular condition is also an indicator of the metabolic control of the disease process. Similarly, an unknown case of chronic renal failure, with its ocular complications, may first present to an ophthalmologist.

In view of the above, the present study was undertaken to find ocular changes and its outcome and complications associated with diabetic end stage kidney diseases and to evaluate the degree of ocular status along with duration of diabetes in end stage kidney disease that is chronic renal failure.

OBJECTIVES

The objectives of the present study were to assess the ocular changes in patients with diabetic end stage kidney diseases.

REVIEW OF LITERATURE

DIABETES MELLITUS

Diabetes mellitus comprises a group of common metabolic disorders that share the phenotype of hyperglycemia. Several distinct types of diabetes mellitus exist and are caused by a complex interaction of genetics, environmental factors, and life style choices. Depending on the etiology of diabetes mellitus, factors contributing to hyperglycemia may include reduced insulin secretion, decreased glucose utilization, and increased glucose production. The metabolic dysregulation associated with diabetes mellitus causes secondary pathophysiologic changes in multiple organ systems. Diabetes mellitus is the leading cause of end-stage renal disease (ESRD), non-traumatic lower extremity amputation and adult blindness. With an increasing incidence worldwide, diabetes mellitus will be a leading cause of morbidity and mortality in the future.[2]

HISTORICAL ASPECTS

The History of Diabetes

Diabetes mellitus is a disease that was recognized in antiquity, but its history has been characterized by numerous cycles of discovery, neglect and rediscovery. Its history may be divided into four major periods that reflect different phases in the understanding and management of the disease. The 'ancient' period witnessed the first clinical descriptions of diabetes and complications. The 16^{th} to 18^{th} centuries have been termed the 'diagnostic' period, as diabetes mellitus was then identified as a separate disease entity, while

the mid to late 19th century may be regarded as the first 'experimental' period, during which the glucoregulatory role of the pancreas became clear and the biochemical disturbances of diabetes were initially characterized.[3]

The history of diabetes mellitus is as old as medicine itself. In the pre-Christian era, the "honey urine" was described by Susruta in Hindu medicine and was known in classical times and referred to as a "melting down of the flesh and limbs to urine" by Aretaeues of Cappadocia.

- In the pre-opthalmoscopic days, Richard Bright (1836) was the first to associate renal disease with visual failure.
- The original idea, that "albuminuric retinitis" (Liebreich, 1859) was correlated with albumin in the urine has long been discarded.
- In 1860, Von Graefe and Schweigger were among the earliest to ascribe the retinal lesions in renal disease to a generalized disease of the vascular system (arterio-phleb-sclerosis) which affected the kidney as well.
- In 1877, Mckenzie and Lowenstein were the first to discover capillary aneurysms in a case of glycosuria.
- In 1885, Jaegar described changes in the retina in diabetic patients with albuminuria.
- Later on, in 1890, Hirschberg made the first attempt to classify diabetic retinopathy.
- In 1891, Noyer and later Leber and Hirschberg found cases of diabetic re-stenosis without nephritis and described them as a separate entity.

- The value of the work of Volhard and Fahr (1913, 1918), Wagener (1929) and others is that it stressed the fact that the retinal changes are related to hypertension rather than to the state of the kidney and that it has established the importance of contraction of the arterioles.
- Few authors (Rochon – Duvigneaud, 1904; Leber, 1909; Widal et al, 1910, Achard, 1924 and others) contended that the retinal changes in renal disease were due to the accumulation of nitrogenous waste products – azotemic retinitis.
- Dejean (1932) and Villard and his colleagues (1933) considered an increase in toxic polypeptides in the blood as an aetiological factor. Chauffard et al (1912), Gaudissart (1922) and Chabanier et al (1924) associated the retinal changes with hypercholesterolemia.
- In 1936, Kimmelsteil and Wilson described a renal lesion in long standing diabetics, known since as intercapillary glomerulosclerosis or Kimmelsteil – Wilson syndrome and established that long-standing diabetics are susceptible to renal damage.
- The work of Ballantyne and Lowenstein (1943), Ashton (1949) and Fridenwald (1950) finally showed clinically and histologically that the retinopathy found in diabetes is specific to the disease and proved a close histological and biochemical similarity between the focal glomerular lesion and retinal microaneurysms.
- In 1945, Wagner established a close relationship between the nephropathy and retinopathy in diabetes.

- In 1951, Asthon and Day suggested that the severe grades of retinopathy are always associated with a renal lesion and nephropathy is not found in the absence of retinopathy.
- Engleson (1950) and Kornerup (1955) however found that nephropathy preceded the retinopathy in a high percentage of cases.[4]

Although it is clear that retinopathy and nephropathy are part of the same disease, there is little or no significant evidence of vascular changes elsewhere in the eye or the body similar to those seen in the retina (Fridenwald, 1950; Ashton, 1949, 1951).

CLASSIFICATION OF DIABETES AND OTHER CATEGORIES OF GLUCOSE REGULATION

Diabetes mellitus is classified on the basis of the pathogenic process that leads to hyperglycemia, as opposed to earlier criteria such as age of onset or type of therapy.[2]

TYPE 1 DIABETES MELLITUS

Immune Mediated Diabetes (Type 1A)

This form of diabetes, which accounts for only 5-10% of those with diabetes, results from a cellular mediated autoimmune destruction of the β-cells of pancreas. Markers of immune destruction of the β-cells include islet cell auto antibodies, autoantibodies to insulin, autoantibodies to glutamic acid decarboxylase (GAD65) and autoantibodies to the tyrosine phosphatases IA-2 and IA-2B. One and usually more of these auto antibodies are present in 85-90%

of individuals when fasting hyperglycemia is initially recognized. Also the disease has strong HLA associations, with linkage to the DQA and DQB genes.

In this form of diabetes, the rate of β-cell destruction is quite variable. Being rapid in some individuals (mainly infants and children) and slow in others (mainly adults). Some patients, particularly children and adolescents, may present with ketoacidosis as the first manifestation of the disease. Others have modest fasting hyperglycemia that can rapidly change to severe hyperglycemia and / or ketoacidosis in the presence of infection or other stress. Immune mediated diabetes commonly occurs in childhood and adolescence, but it can occur at any age, even in 8^{th} and 9^{th} decade of life.

Idiopathic Diabetes (Type 1B)

Some forms of type 1 diabetes have no known etiologies. These patients have permanent insulinopenia and are prone to ketoacidosis, but have no evidence of autoimmunity. This forms only a minority of patients with type 1 diabetes mellitus. Most are of African or Asian ancestry. Individuals with this form of diabetes suffer from episodic ketoacidosis and exhibit varying degrees of insulin deficiency between episodes.

This form of diabetes is strongly inherited. Lacks immunological evidence for β-cell autoimmunity, and is not HLA associated.

TYPE 2 DIABETES MELLITUS

This form of diabetes, which accounts for ~90-95% of those with diabetes, encompasses individuals who have insulin resistance and usually have relative (rather than absolute) insulin deficiency.

There are probably many different causes of this form of diabetes. Specific etiologies are not identified. Most patients with type-2 diabetes mellitus are obese, and obesity itself causes some degree of insulin resistance. Ketoacidosis seldom occurs spontaneously. This form of diabetes frequently goes undiagnosed for many years, as the hyperglycemia develops gradually. Nevertheless, such patients are at increased risk of developing macrovascular and microvascular complications.

TABLE 1: DIAGNOSTIC CRITERIA FOR DIABETES MELLITUS

The criteria for diagnosis of diabetes are shown in table.[2,5]

Criteria for the Diagnosis of Diabetes Mellitus
• Symptoms of diabetes plus random blood glucose concentration ≥11.1 mmol/L (200 mg/dL)[a] or • Fasting plasma glucose ≥ 7.0 mol/L (126 mg/dL)[b] or • Two-hour plasma glucose ≥ 11.1 mmol/L (200 mg/dL) during an oral glucose tolerance test[c]

[a] Random is defined as without regard to time since the last meal.
[b] Fasting is defined as no caloric intake for atleast 8 h.
[c] The test should be performed using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water.
(source:Adapted from ADA,2004)

Three ways to diagnose diabetes are possible and each in the absence of unequivocal hyperglycemia, must be confirmed, on a subsequent day by any one of the 3 methods, given in the table.

The use of the hemoglobin A1C (HbA1C) for the diagnosis of diabetes is not recommended at this time.

SCREENING FOR DIABETES

Diabetes is frequently not diagnosed until complications appear and approximately one third of all people with diabetes may be undiagnosed. However, there are no randomized trials demonstrating benefits of early diagnosis through screening of asymptomatic individuals. But wide spread use of FPG as a screening test for T-2 diabetes mellitus is justified in individuals at high risk.[2]

STANDARDS OF MEDICAL CARE IN DIABETES

Diabetes is a chronic illness that requires continuing medical care and patient education to prevent acute complications and to reduce the risk of long term complications.[2]

Physical examination

- Height and weight measurements (and comparison to norms in children and adolescents).
- Sexual maturation staging (during pubertal period).
- Blood pressure determination, including orthostatic measurements when indicated, and comparison to age-related norms.

- Fundoscopic examination.
- Oral examination.
- Thyroid palpation.
- Cardiac examination.
- Abdominal examination (e.g. for hepatomegaly).
- Evaluation of pulses by palpation and with auscultation.
- Hand/finger examination.
- Foot examination.
- Skin examination (for acanthosis nigricans and insulin-injection sites).
- Neurological examination.
- Signs of diseases that can cause secondary diabetes (e.g. hemochromatosis, pancreatic disease).

Laboratory evaluation

- A1C.
- Fasting lipid profile, including total cholesterol, HDL cholesterol, triglycerides, and LDL cholesterol.
- Test for microalbuminuria in type 1 diabetic patients who have had diabetes for at least 5 years and in all patients with type 2 diabetes; some advocate beginning screening of pubertal children before 5 years of diabetes.
- Serum creatinine in adults (in children if proteinuria is present).
- Thyroid stimulating hormone (TSH) in all type 1 diabetic patients; in type 2 if clinically indicated.
- Electrocardiogram in adults, if clinically indicated.

- Urinalysis for ketones, protein, sediment.

COMPLICATIONS OF DIABETES

Diabetes has both acute and long term complications.[5] They are:

Acute

- Diabetic ketoacidosis
- Hyperglycemic Hyperosmolar state
- Hypoglycemia

Long term:

- Retinopathy
- Nephropathy
- Neuropathy
- Ischemic heart disease
- Cerebrovascular disease
- Peripheral vascular disease
- Hypertension.

Ocular Complications

Conjunctiva	Sludging of blood, tortuous constricted blood vessels.
Cornea	Wrinkling of Descemet's membrane.
	Trigeminal neuropathy (Reduced corneal sensation)
	Abnormal epithelial basement membrane with delayed wound healing. Punctuate keratopathy

Iris	Hydrops of pigment epithelium (Transient glycogen storage, disappears with normal blood sugars).
	Rubeosis iridis
	Transmission defects in pigment epithelium.
Lens	Variation in the refractive power.
	Snowflake (true diabetic cataract seen in IDDM).
	Premature onset of senile cataract.
Intraocular pressure	Decreased in acidosis and increased in neovascular glaucoma.
Oculomotor nerves	Neuropathy with muscle paralysis (Pupil frequently spared in III nerve paralysis.
Visual acuity	Transient variation refraction
	Photopsiae and diplopia in cerebral hypoglycemia.
	Reduced accommodation
Fundus	Diabetic retinopathy.
	Disc oedema
	Optic nerve atrophy.
	Lipaemia retinalis.

Diabetic retinopathy

Diabetic retinopathy is the most frequent cause of blindness among adults aged 20-74 years. During the first two decades of disease, nearly all patients with type 1 diabetes mellitus and >60% with type 2 diabetes mellitus have retinopathy. In type 2 diabetes mellitus, 21% of patients have retinopathy at first diagnosis.

Diabetic Nephropathy

Diabetes has become the most common single cause of endstage renal disease (ESRD) world wide. About 20-30% of patients with type 1 or type 2 diabetes mellitus develop evidence of nephropathy, but in type 2 diabetes a considerably smaller fraction of these progress to ESRD. However, because of much higher prevalence of type 2 diabetes mellitus, these patients constitute over half of patients with nephropathy needing dialysis.

The diabetic nephropathy progresses from appearance of low but abnormal levels of (≥ 30mg to 299 mg/day or 20µg/min) albumin in urine (stage of microalbuminuria) to stage of macroalbuminuria / clinical albuminuria (≥300mg/dl or ≥200µg/min) to ESRD. Progress from microalbuminuria to macroalbuminuria usually takes 10-15 years. ESRD develops in 50% of type 1 diabetic individuals with clinical nephropathy within 10 years and in 75% by 20 years. But in type 2 diabetes mellitus, even after 20 years of overt nephropathy only 20% progress to ESRD.

ORIGIN OF THE MICROANGIOPATHY IN DIABETES MELLITUS

Microangiopathy is a specific disorder of the small blood vessels, which causes much morbidity and mortality in diabetic patients.[6] The major susceptibility factors for the microangiopathy include duration of the disease, metabolic control, genetic factors and the presence of hypertension.

The mechanism of the development of microangiopathy is incompletely understood, but relate to;

1. Anatomical or ultrastructural factors
2. Biochemical factors
3. Abnormalities of hemostasis.

The central feature appears to be chronic hyperglycemia, which is causally related to these factors and culminates in tissue ischemia.

ANATOMICAL FACTORS

Capillary Basement Membrane thickening (CBMT):

The histological hallmark of microangiopathy is capillary basement membrane thickening.[7] The major structural element involved in CBMT is type IV collagen and Heparin sulphate is the major proteoglycan together with laminin and fibronectin.[8,9]

Heparin sulphate produced by endothelial cells is highly negatively charged and produces a regular lattice – work of anionic sites that hinders the filtration of negatively charged proteins like albumin.

In diabetes, there appears to be an impaired synthesis of proteoglycans and an increase in hydroxylysine and it's glycosidically linked disaccharide units.

These alterations lead to the abnormal packing of the peptide chains producing excessive leakiness the membranes.

Loss of Microvascular Intramural Pericytes:

An early and seemingly invariable feature is the degeneration of the capillary pericytes. The mechanism by which pericytes are specifically lost early

in diabetic retinopathy is unknown. It may be related to the action of sorbitol pathway.

Aretriolar Hyalinosis:

Hyaline thickening of the arteriolar wall occurs as a function of aging and mild hypertension, which is accelerated kin diabetes. The enhanced incidence of hyalinosis is likely to be a manifestation of the increased endothelial cell permeability associated with diabetes. Reduced caliber of the terminal retinal arterioles consequent to the mural thickening may contribute to the risk of occlusion and capillary closure downstream.

BIOCHEMICAL FACTORS

Sorbitol (Polyol) Pathway :

The sorbitol or polyol pathway converts glucose to sorbitol and has been implicated in the pathogenesis of many diabetic complications.[10]

It is possible that increased flux through the polyol pathway causes increased NADPH utilization resulting in less NADPH being available[11] for conversion of anti-oxidants back to their free radical scavenging reduced form. This increased utilization of NADPH may render the tissues less able to deal with oxidative stress.

Non Enzymatic Glycosylation:

In the presence of persistent hyperglycemia, glucose chemically attaches to protein, non-enzymatically to form a stable product – ketoamine or Amadori

product. In long lived tissue proteins such as collagen, the ketoamine then undergoes to series of reactions resulting in the development of advanced glycosylation end products (AGE Products).[12]

AGE products are resistant to degradation and continue to accumulate indefinitely on long-lived protein. They are quantitatively identified by their characteristic brown pigment fluorescence (Protein Browning) and participate in protein cores-linking. This could lead to trapping of albumin and lgG within the basement membrane. One study has reported a significant relationship between collagen browning and microangiopathy, where AGE-correlated fluorescence was related to the severity of retinopathy and nephropathy.[13]

Protein Fluorescence, Free Radical Activity and Antioxidant Status

Free radicals which are a violently reactive chemical species having unpaired electron spins will also include oxidation of protein amino acid residues as well as lipid peroxidation. Increased free radical activity in diabetes is suggested from studies examining lipid peroxidation. There are reports of increased lipid peroxidation in diabetes particularly in relation to microangiopathy.[14,15]

Free radicals and their lipid hydroperoxide products may be directly cytotoxic to vascular vascular endothelial cells. Free radicals are produced continuously during many metabolic processes and are rapidly eliminated by antioxidants like reduced glutathione and vitamin C and E.

In diabetes, however there is a reduced concentration of these antioxidants. The reduction in the antioxidant reserve in diabetic patients may be due to competition for NADPH, which is a co-factor required to re-cycle the oxidized free radical.

Protein Kinase C Activity:

Hyperglycemia is associated with increased cellular protein kinase C activity in cultured endothelial cells. This may have a role in the microangiopathy.

ABNORMALITIES OF HEMOSTASIS

The combination of reduced endothelial cell production of PGI2 and the activators of fibrinolysis, together with increased platelet reactivity and increased factor VII production, produces a thrombotic tendency. This leads to microthrombus formation and small vessels occlusion and thus contributes to the abnormalities of blood flow in the small vessels.

Factor VII produced in the endothelial cell is increased in patients with early diabetic retinopathy, a situation that would promote microthrombus formation.[16]

Prostacyclin PGI2 also produced in the endothelial cell is a powerful vasodilator, which antagonizes platelet aggregation and platelet adherence to the vascular wall. There is a reduced level of circulating PGI2 in diabetic patients.[17]

Plasminogen activator, which converts plasminogen to plasmin acting to promote fibrinolysis, has also been reported to be low in diabetics.[18]

Abnormalities in platelet function mirror all the above abnormalities in diabetes. Thromboxane A2 is increased in platelets taken from patients with vascular complications.[19] This agent is a potential vasoconstrictor and causes platelet aggregation.

The platelets also carry powerful mediators of the microcirculation such as serotonin and platelet derived growth factors. Increased platelet aggregation is well described in diabetics on the basis of measuring proteins released from the platelets on aggregation.

Eg. B – Thromboglobulin and platelet factor. Both techniques have detected increased platelet reactivity in diabetic microangiopathy.

The mechanisms of development of microangiopathy is likely to be complex, involving a number of different biochemical pathways. Increased knowledge of these pathways allows hypotheses to be constructed, which can be tested. Further understanding of pathogenesis will suggest a number of therapeutic approaches, which may lead in the future to important therapeutic options.

DIABETIC RETINOPATHY – AETIOPATHOGENESIS, CLASSIFICATION AND CLINICAL FEATURES

Introduction

Diabetic retinopathy is a common cause of legal blindness in developed countries and now in developing countries between the ages of 45 and 65 years.[20,21,22] The risk of blindness in diabetic is 12 to 20 times higher than in non-diabetics.

Many diabetics, even with good control develop severe retinopathy. This may be due to genetic factor, which otherwise protect from or predispose to microvascular disease. Many of these blind patients also have systemic complications like renal failure and cardiovascular disease.

There is as yet no way to prevent the development of retinopathy, but emphasis is placed on the early detection and treatment of its blinding complications. By direct ophthalmoscopy, the attending physician may detect Four of five diabetic patients as having diabetic retinopathy even before the development of visual impairment. Treatment with laser photocoagulation in the early stages or even with early diabetic muscular oedema will reduce the development of severe visual loss.

Blindness in patients with diabetic retinopathy is a consequence of the occurrence of diabetic maculopathy or proliferative diabetic retinopathy and vitreous hemorrhage and its sequelae.

Diabetic maculopathy may be a consequence of increased vascular permeability or retinal hypoxia due to capillary closure in the region of the posterior pole. Neovascularization, which is a hallmark of proliferative diabetic retinopathy, is a form of an aberrant reparative process in the course of which fragile new vessels grow from post capillary venules. The stimulus for the neovascularization is extensive retinal hypoxia due to closure of a large part of capillary network.

Flourescein angiography is one of the important investigational tools available to a clinical ophthalmologist to evaluate the functional integrity of the retinal vasculature, retinal pigment epithelium and other layers of the retina.

Though evaluation of the fundus vasculature with a direct opthalmoscope and by slit lamp biomicroscopy provides a wealth of information regarding the retinal changes in diabetes, fluorescein angiography plays an important role in understanding the disease process as also the rationale for different treatment modalities in various stages of diabetic retinopathy. An understanding of the role of fluorescein angiography in patients with diabetic retinopathy is predicated on an understanding of the evolution of the diabetic retinal microangiopathy and of the pathophysiology of the disease process.

Epidemiology

Diabetes Mellitus affects 1- 5% of the overall population. The overall prevalence of retinopathy among diabetics is approximately 26 to 40%.[23] The prevalence of diabetic retinopathy is higher in IDDM (40%) than in NIDDM (20%).

Ocular symptoms occur in 20 – 40% at the clinical onset of the disease, but the symptoms are mainly caused by changes in the refraction rather than the retinopathy. In juvenile diabetics, proliferative diabetic retinopathy is uncommon in patients younger than 20 years of age.

Background diabetic retinopathy is an almost invariable consequence of diabetes mellitus, but proliferative diabetic retinopathy occurs in only 60% of diabetic patients even after 40 years of diabetes suggesting the presence of multiple risk factors.

Risk factors for diabetic retinopathy

1. ***Duration of diabetes***

The duration of diabetes is the single, most important factor. 60% of patients develop diabetic retinopathy after 15 years and 100% after 30 years of diabetes. It is extremely rare for development of retinopathy with 5 years of the onset of diabetes, but about 5% of Non-Insulin dependent diabetics have background diabetic retinopathy at presentation.

2. ***Metabolic control :***

Good metabolic control of diabetes will not prevent the development of retinopathy, although it will delay it by a few years. Conversely, poorly controlled patients may develop retinopathy sooner than well-controlled diabetics may. In some patients, worsening of the retinopathy has been observed during the first few months of improved blood glucose control.

3. Type of Diabetes Mellitus

Proliferative diabetic retinopathy is more prevalent in Type I Diabetes Mellitus probably due to different metabolic factors, different age group and higher mean blood glucose levels.

Macular oedema is more prevalent as a function of disease duration in Type II Diabetes mellitus.

Although Type II Diabetes mellitus has severe ocular complications, Type II Diabetes mellitus form most of the clinical cases of diabetic eye disease because of their overall average numbers.

After 20 years, 100% of patients with IDDM and 60% of patients with NIDDM will have diabetic retinopathy.

4. Systemic factors

Miscellaneous factors, which may have an adverse effect on diabetic retinopathy, include advancing age, pregnancy, systemic hypertension, in particular elevated diastolic blood pressure, renal disease, proteinuria, hyperlipidemia and anemia.

5. External factors

External factors like metabolic control and diabetic diet, smoking, alcohol and oral contraceptive pill possibly interfere with the course of diabetic retinopathy.

6. Genetic factors

There is a strong association between proliferative diabetic retinopathy and the presence of HLA – DR phenotypes 4/0, 3/0 and X/X.

7. Endocrinal and Metabolic factors

Pituitary gland and other endocrinal disorders as well as physiological states like puberty influence the natural course of diabetic retinopathy probably due to the circulating levels of growth hormone.

8. Ocular factors

The ocular factors that modify the natural history of diabetic retinopathy include myopia, amblyopia, glaucoma, posterior vitreous detachment, old chorioretinopathy, cataract surgery and rubeosis iridis.

Extensive myopia with choroidal degeneration, amblyopia, glaucoma and extensive chorioretinopathy all protect against diabetic retinopathy and act by reducing the metabolic requirements of the retina.

Pathogenesis of diabetic retinopathy

Diabetic retinopathy is a microangiopathy affecting the retinal pre-capillary arterioles, capillaries and venules, the larger vessels may not be involved. The retinopathy in diabetes has features of both, microvascular occlusion and leakage.

Microvascular occlusion

Pathogenesis

The factors though to be responsible for the microvascular occlusion include;

- Thickening of the capillary basement membrane.
- Capillary endothelial cell damage and proliferation.
- Changes in the red blood cells leading to defective oxygen transport.
- Increased stickiness and aggregation of the platelets.

The consequence of retinal capillary non perfusion is retinal ischemia, which, in turn causes retinal hypoxia, initially, the non-perfused area is located in the midretinal periphery. The two main effects of retinal hypoxia are the following.

1. Arteriovenous shunt: Associated with significant capillary occlusion ("Drop-out") which runs from venules to arterioles. As it is unclear whether or not these lesions represent new vessels, they are often referred to as "intraretinal microvascular abnormalities" (IRMA).

2. Neovascularisation is though to be caused by a "vasoformative substance" elaborated by the hypoxic retinal tissue in an attempt to revascularize hypoxic area of the retina. These substances promote neovascularisation on the retina (NVE) and optic nerve head (NVD) (proliferative DR) and on the iris (rubeosis iridis).

Microvascular leakage

Pathogenesis

The cellular elements of retinal capillaries consists of endothelial cells and pericytes (mural cells). The tight junctions of the endothelial cells constitute the inner blood retinal barrier. The pericytes are wrapped around the capillaries and are thought to be responsible for the structural integrity of the vessel wall. In normal healthy individuals, there is one pericyte to each endothelial cell, whereas in diabetic patients, there is a reduction in the number of pericytes. This reduction in pericytes is thought to be responsible for distention of the capillary walls and a breakdown of the blood – retinal barrier, leading to the leakage of plasma constituents into the retina. Microaneurysms are saccular pouches, which may form as result of local capillary distension. They may either leak or become thrombosed.

The consequences of increased vascular permeability are haemorrhage and retinal oedema, which may either be diffuse or localized.

1. Diffuse retinal oedema is caused by extensive capillary dilatation and leakage.

2. Localised retinal oedema is caused by focal leakage from microaneurysms and dilated capillary segments. Chronic localized retinal oedema leads to the deposition of hard exudates at the junction of healthy and oedematous retina. The exudates, which are composed of lipoprotein and lipid filled macrophages, typically surround leaking microvascular lesions forming a

circinate pattern. In some eyes they absorb spontaneously over a period of months or years, either into the healthy surrounding capillaries or by phagocytosis of their lipid content. In other cases, more chronic extravasation leads to enlargement of the exudates and deposition of cholesterol.

Systems of classification

Diabetic retinopathy does not lend itself easily to classification since the various lesions do not allow one another in sequence and one or other of the fundamental changes may dominate. Classification or more correctly staging of diabetic retinopathy has been attempted since 1890 with the objective of recording the natural history of the disease, the time for intervention and evaluation its efficacy. Most of the early classifications fell by the wayside due to overlapping of stages, lack of sequential consistency in stages and more fundamentally ignorance and lack of universal opinion about the pathogenesis, histopathology and pathophysiology of this complex multisystem disease.

Of the many classifications spawned forth the past century (1890 to 1990) only a few have been of lasting value and importance.

1. Hirschberg's classification: The first attempt 1890.
2. Ballantyne and Michaelson's classification.
3. Michaelson's classification: Basically a pathological classification.
4. Scott's classification: Allowed for variation in retinopathy features.
5. Alaerts and Slosse: Progression of vascular and exudative lesions.
6. Lee et al: Lesions were graded by severity.

7. Duke-Elders classification: The basic staging into simple and proliferative DR described in 1960 is still followed today.
8. O'Hare grading system: Derived by a committee to formulate a treatment protocol.
9. Hammersmith grading system: First used fundus photography for recording and grading DR, using standard photographs for comparison.
10. Vahex classification: Purely on the basis of ophthalmoscopic findings.
11. Airlee – House classification: Comprehensive recording and evaluation methods, form the basis of the modern ETDRS classification.
12. Modified Airlee-House classification: Basis of the modern ETDRS classification.
13. Kanski's classification.

Hirschberg classification

1. Inflammatory
2. Hemorrhagic
3. Pigmentary

Ballantyne and Michaelson classification

Microlesions	Microaneurysms alone or accompanied by minute hemorrhages or punctate exudates
Macrolesions	Dot and blot hemorrhages
Vascular damage	Gross damage to retinal veins
Destructive changes	Intraocular hemorrhages, retinitis proliferans, retinal detachment and glaucoma

Mixed forms	Diabetic changes associated with atherosclerosis or hypertension.

Scotts Classification

Stage I	a. Capillary microaneurysms
	b. Venous changes like looping, coiling or distension
Stage II	a. Punctate hemorrhages with or without discrete flecks of exudates.
	b. Larger round or blot hemorrhages with confluent exudates.
Stage III	a. Numerous exudates and hemorrhages.
	b. Hemorrhages in the vitreous
Stage IV	a. Retinitis proliferans, retinal detachment and other gross degenerative changes

Alaerts and Slosses Classification

Segmental dilatation of veins	Not represented
Microaneurysms at the posterior pole	Punctate exudates
Small microthrombotic haemorrhages	Increase of exudates with few confluent groups.
Segmental dilatation of larger veins	Plaques of larger exudates formed by confluence
Retinitis proliferans, Vascular proliferation	Larger spreading exudates
Retinal detachment, glaucoma	Degeneration of retina

Duke elders classification

Dobree classified this into three stages later incorporated by Duke Elder.

Preretinopathic stage	Uniform dilatation of larger veins
Simple diabetic retinopathy	• Capillary microaneurysms • Retinal hemorrhages and exudates • Late changes in retinal veins • Hypertensive and arteriosclerotic lesions. • Other changes like lipidemia retinalis, xanthosis retinae and pigmentary disturbances.
Proliferative diabetic retinopathy	• Stage I: Stage of naked vessels • Stage II: Condensation of connective tissue around naked vessels. • Stage of cicatrization

Airlee house classification

This system proposes fundus pathology, angiography, ophthalmoscopy, slit lamp biomicroscopy, fundus drawings and detailed written descriptions.

Grade 0	-	Components absent
Grade I	-	Components less severe
Grade II	-	Components more severe

Non proliferative	• Hemorrhage and/or microaneurysms
	• Hard and soft exudates
	• Venous abnormalities
	• Intra-retinal microvascular abnormalities (IRMA)
	• Retinal oedema with or without macular oedema
Proliferative	• Neovascularisation within 1 disc diameter of disc
	• Neovascularisation in area other than the optic disc.
	• Fibrous proliferation within 1 disc diameter of disc.
	• Fibrous proliferation in areas other than the optic disc.
	• Phase of proliferation: Grade 0 – within in one fourth disc diameter of surface of attached retina.
	• Retinal elevation.
Vitreous hemorrhage	• Pre-retinal hemorrhage
	• Vitreous hemorrhage
	• History of vitreous hemorrhage

CLASSIFICATION (MODIFIED FROM AMERICAN ACADEMY OF OPTHALMOLOGY)

Non Proliferative Diabetic Retinopathy (NPDR)

1. Mild NPDR

At least one retinal microaneurysm and one or more of the following : retinal hemorrhage, hard exudate, soft exudate.

2. Moderate NPDR

Hemorrhages or microaneurysms or both in atleast on quadrant and one or more of the following: soft exudates, venous beading and IRMA.

3. Severe NPDR

Hemorrhages or microaneurysms or both in all quadrants, venous beading in two or more quadrants, IRMA in at least one quadrant.

PDR

1. Early PDR

One or more of the following:

- NVE
- NVD
- Vitreous or preretinal hemorrhage
- NVE< ½ disc area.

2. High risk PDR

One or more of the following.

- NVD > ¼- $^{1}/_{3}$ disc area
- NVD with vitreous or preretinal hemorrhage
- NVE > ½ disc area. Preretinal or vitreous hemorrhage.

3. ***Advanced PDR***

High risk PDR, traction retinal detachment involving macula or vitreous hemorrhage obscuring ability to grade NVD or NVE.

- IRMA – Intraretinal microvascular abnormalities.
- NVE – Neovascularisation elsewhere.
- NVD – Neovascularisation disc.

Diabetic retinopathy progresses from mild non-proliferative abnormalities to moderate and severe non-proliferative diabetic retinopathy to proliferative diabetic retinopathy. Macular edema can develop at all stages of diabetic retinopathy. NPDR usually develops late in first decade or early 2^{nd} decade of type–2 diabetes mellitus. PDR usually develops within 5 years of NPDR. Pregnancy, poor glycemic control, hypertension and cataract surgery accelerate these changes. UKPDS study revealed that for every percentage reduction of HbA1C (eg. From 8 to 7%), there was a 35% reduction in risk of retinopathy and tight BP control (to < 150/85 mmHg) results in 34% reduction in progression of retinopathy.

Kanski's Classification

It is basically a management oriented classification with the recognition of an additional pre-proliferative stage.

Background diabetic retinopathy	• Microaneurysms (Usually temporal to the macula) • Hard exudates • Retinal oedema • Dot and blot haemorrhage

Pre proliferative	• Vascular changes – Venous beading, looping, sausaging, arteriolar narrowing or obliteration. • Dark – blot hemorrhages representing retinal infarcts. • Multiple cotton – wool spots. • Intra-retinal microvascular abnormalities (IRMA)
Proliferative diabetic retinopathy	• Neovascularisation – May develop along the vascular arcades (NVE) or at the optic disc (NVD). • Vitreous detachment • Pre-retinal or vitreous hemorrhage. • Retinal detachment and detachment and retinitis proliferans
Diabetic maculopathy	• Ischemic maculopathy • Exudative maculopathy • Oedematous maculopathy • Clinically significant macular oedema (CSME) • Non significant macular oedema
	Miscellaneous factors • Cystoid macular oedema • Macular hole • Foveal exudates • Renal failure

Features common to vascular retinopathies

Vascular retinopathies	• Microaneurysms, hard and soft exudates • Superficial and deep retinal hemorrhages • Neovascularisation, vitreous hemorrhage and fibrous proliferation. • Tractional retinal detachment • Leakage, staining of tissue and pooling of dye from leaking vascular abnormalities (the abnormal permeability response) and absence of dye due to closure of vessels (the ischemic response) on fluorescein angiography.
Features characteristics of diabetic retinopathy	• Evolution and progression of the lesions. • Location, combination and distribution of lesions within the fundus. • Age, bilaterally symmetrical lesions with medical history of associated diabetes mellitus.

DIABETIC RETINOPAHTY – DIAGNOSIS AND MANAGEMENT

The early diagnosis of diabetic retinopathy is necessary to prevent the sequelae and complications of this disease.

Though evaluation of the fundus vasculature with a direct ophthalmoscope and by slit lamp biomicroscopy provides a wealth of information regarding the retinal changes in diabetes, fluorescein angiography plays an important role in understanding the pathophysiology of the disease process and

the rationale for different treatment modalities in various stages of diabetic retinopathy.

An understanding of the evolution and stages of diabetic retinopathy and their clinical characteristics precedes the ability to understand and use fluroscein angiography optimally as an investigation too.

Fluorescein angiography in diabetes mellitus

The work of Dr. Maumenee (1954) stimulated a cascade of studies that firmly established fluorescein angiography as a research and clinical too to delineate and elucidate fundus circulation and histopathology.

One of the most common and useful applications of fundus fluorescein angiography (FFA) is diabetic retinopathy.

It may be used to identify the stages of diabetic retinopathy, to study the progression of the disease through the stages, to indicated the need for intervention, to assess the visual prognosis and to follow-up the natural course of the disease or the efficacy of treatment.

Angiographic plan for FFA in diabetic retinopathy

1. Red free photographs of the optic disc and macula in both eyes are taken.
2. Control photograph with a fluorescein filler in place before the injection of dye is taken to check the dual filter system for autofluorescence and pseudofluorescence.

3. Primary disc and macula : Depending on the age of the patient, 8 to 12 seconds after injection of the dye (Sodium fluorescein), 6 photographs are taken of the primary disc and macula at an interval of 1.5 to 2 seconds.
4. Quadrants of the primary eye : The next four photographs, taken 20 – 30 seconds after the injection, are for the quadrants. For orientation, the nasal, superior and inferior photographs are taken with the edge of the disc at the edge of the photograph and the temporal photograph with the fovea at the edge of the photograph.
5. The optic disc and macula of the opposite eye is then photographed.
6. the four quadrants of the opposite eye are photographed sequentially.
7. Late photograph : The primary disc and macula are photographed followed by the secondary disc and macula.

Recommendations for fundus fluorescein angiography

In general, in absence of macular oedema, FFA is not required at any stage of NPDR and in the presence of CSME, FFA is required at any stage of NPDR.

In general,

1. Any stage of NPDR with CSME – FFA indicated.
2. Any stage of NPDR without macular oedema – FFA not necessary.
3. Mild NPDR to Early PDR with non-cystoid macular oedema – FFA may be done occasionally.
4. High risk PDR with non-cystoid macular oedema – FFA indicated.

Interpretation of fundus fluorescein angiography

The angiographic interpretation of diabetic retinopathy is done in three ways:

1. Defects of fluorescence.
2. Staging of diabetic retinopathy.
3. Diabetic retinopathy lesions in different phases of the angiogram.

Defects of fluorescence

The first step in interpreting any angiogram is to recognize the two fundamental abnormalities of fluorescence, whether excessive or reduced.

Hypofluorescence

1. Blocked retinal fluorescence : Vitreous hemorrhage, Pre-retinal or nerve fiber layer hemorrhages.
2. Blocked choroidal fluorescence : Deep retinal maerial like oedema fluid, hard exudates, dot and blot hemorrhages.
3. Vascular filling defects (VFD) : Retinal vascular filling defects in capillary non-perfusion, optic nerve head vascular filling defects in anterior optic ischemic neuropathy (AION).

Hyperfluorescence

1. Pre-injection fluorescence: Pseudofluorescence may be the result of poorly matched filters where any white glistening tissue may fluorescence. Auto fluorescence is never seen in any lesion of DR.

2. Pigment epithelial window defect : Not typically seen unless sever cystoid macular oedema present resulting in retinal degeneration or macular hole.
3. Abnormal retinal and disc vessels : Tortuosity and dilatation of vessels, anastomoses (IRMA), NVD, NVE, microaneurysms.
4. Leak : Vitreous leak is seen as a cotton ball type of hyperfluorescence surrounding new vessles.

In a disc leak, an early hyperfluorescence is seen with extensive peripapillary leakage.

In a retinal leak, intravascular retinal fluorescence in late phases is abnormal and indicates cystoid or non-cystoid retinal oedema. Non-cystoid oedema may be focal or diffuse.

Staging of the diabetic retinopathy

1. Mild NPDR : At least one microaneurysm and minimal hemorrhages.
2. Moderate NPDR : Definite presence of soft exudates, venous changes and IRMA.
3. Severe NPDR : Venous changes in all two or more quadrants and more severe hemorrhages, microaneurysms and IRMA.
4. Very severe NPDR : Presence of two or more lesions or severe NPDR without NVE.
5. Early PDR : with early NVE/NVD or both.
6. High risk PDR : with NVD>1/3 disc are associated with pre-retinal or vitreous hemorrhage.

Diabetic retinopathy lesions in different phases of the angiogram

1. Pre-arterial phase : No typical lesions of DR are evident in this phase.
2. Arterial phase : Neovascularization, either NVD or NVE may be seen. A feeder vessel may be seen in NVD.
3. Arterio-venous phase : Most lesions of diabetic retinopathy are evident n this phases it is a microangiopathy. Microaneurysms hemorrhages, IRMAs, venous beading, exudates, capillary non-perfusion (CNP) areas, macular ischemia and abnormalities in the foveal avascular zone (FAZ) are seen. Most of these pathologies re more distinctly evident in the early arterio-venous phase.
4. Venous phase : New vessels and leaks are evident which are diagnosed in the early phases.
5. Macular oedema : Hyperfluorescence seen in the late phases.

Management of diabetic retinopathy

A. Diabetes without Retinopathy
    - Two to four year follow-up.
    - Metabolic control of diabetes.
    - Attention to and prompt referral for associated systemic disease like renal failure, hypertension and anemia.

B. NPDR without CSME
    - Four to six monthly or annual follow – up; earlier if vision falls.
    - Control of diabetes and associated systemic diseases.

C. NPDR with CSME

- Laser photocoagulation : Argon laser, 200μ spot size, 0.2 second duration, moderately intense burn (100mW), focal to leaking microaneurysms, grid to areas of oedema.
- Produces obliteration of microaneurysms, resolution of oedema and resorption of hard exudates.
- There is a better visual acuity in treated compared to untreated eyes at 3 year follow up (ETDRS study).
- Follow up for 4 to 6 months, re-treat if necessary and watch for new vessels.

D. NPDR with diffuse macular oedema

- Grid laser more beneficial than no treatment.
- Attention to the general health.

E. Moderate to severe NPDR

- Needs no laser treatment.
- No treatment benefits (ETDRS study)

F. PDR without high risk characteristics

- Observe, follow-up every 2 to 4 months or earlier if symptomatic.
- No evidence that laser treatment in better than none (ETDRS study).

G. PDR with high risk characteristics (Figure 7.10).

- Prompt laser treatment.
- Pan retinal photocoagulation (Figure 8.2) : Argon laser, 200-500μ spot size, 0.2 second duration, about 1200 moderately intense

burns (100-300mW), about 1 laser burn apart, disc to equator sparing the macula.

- Single or multiple sessions, select a definite order in treating different quadrants.
- Prevents severe visual loss at two and five years (ETDRS study).
- Follow-up after two months.
- If al new vessels have involuted, follow-up after four to six months.
- Fill in laser if new vessels persist, new smaller spots, between previous burns towards the disc and equator, towards but not into the macula.
- If new vessels persist despite adequate laser, close observation for pre retinal or vitreous hemorrhage.
- The role of peripheral cryotherapy is controversial.
- Vitreous hemorrhage after adequate laser is mostly due to posterior vitreous detachment and is likely to clear. For non-clearing hemorrhages, vitrectomy ahs shown good results.

H. Vitreous hemorrhage

- If retrohyaloid, it clears on its own. If not, vitrectomy may be considered.
- Attention must be given to the underlying retinal changes.
- If the hemorrhage is within the internal limiting membrane or the vitreous gel, vitrectomy must be considered.

I. Fibrous tissue and fractional retinal detachment

- If there is no distortion or elevation of the macula, there is no need for treatment.
- If the fibrous tissue distorts the macula, tractional retinal detachment involves the macula or there is a combined tractional and rhegmatogenous retinal detachment, surgical treatment is considered.

Medical treatment of diabetic retinopathy

The medical treatment of diabetic retinopathy is largely unsatisfactory

1. Diet, Vitamins, Flavinoids, Sex hormones, anabolic steroids, anti coagulants, Clofibrate, Persantin and calcium dobesilate have been tried and were found to be ineffective.
2. Aspirin, Sorbinil, Ticlodipine were all ineffective in controlled clinical trials.
3. Pentoxyphylline and Tolrestat have been used.
4. Aminoguanidine ahs been found to be useful in experimental animal models.
5. The most promising medical line of treatment is the Angiotenisin converting enzyme inhibitors like Lisinopril. These drugs have been shown trial, Lisinopril was found to reduce the progression of diabetic retinopathy in non-hypertensive individuals.[24]

CLINICAL TRIALS IN DIABETIC RETINOPATHY

There are four major clinical trials in diabetic retinopathy conducted by the National Eye Institute in the late 70's and 80's which are worth mentioning for their landmark contributions towards the understanding of the pathophysiology and treatment modalities of diabetic retinopathy. These results of these studies are still being published even today.

1. Diabetic Retinopathy Study (DRS)
2. Early treatment of Diabetic Retinopathy study (ETDRS)
3. Diabetic Retinopathy Vitrectomy Study (DRVS)
4. Diabetic Control and Complications Trial (DCCT)

The early Treatment for Diabetic Retinopathy Study (ETDRS) was a prospective, controlled, randomized, multicentric clinical trial done in 22 clinical centers in the United States during the period from December 1979 to June 1989, during which 3711 patients were studied. The study group published its first report in 1985.[25]

The purpose of this study was to answer three fundamental questions.

1. When is the right time to begin photocoagulation in diabetic retinopathy?
2. What is the effectiveness of photocoagulation for diabetic macular oedema?
3. What is the role of aspirin in altering the progression of diabetic retinopathy?

The modified Airlee – House classification was first published by the DRS group in the DRS Report No. 7 in 1981 which provided standard fundus photographs for staging of the disease by comparison.

The ETDRS group defined clinically significant macular oedema in its first report in 1985 and subsequently developed systems for assessing the severity of diabetic retinopathy in 1991, in reports 10 and 11.

The highlights of these studies are briefly mentioned below.

DRS AND ETDRS STUDY

Highlights

1. Multicentric, prospective, randomized, controlled studies.
2. Posed important questions.
3. Defined different levels of diabetic retinopathy.
4. Randomized patients into treatment and no-treatment groups.
5. Ensured quality control.
6. Published findings periodically.

Important definitions

1. Clinically significant macular oedema was defined.
2. Four risk factors were identified in proliferative diabetic retinopathy.
    - New vessels on or within one disc diameter of the optic disc.
    - Moderate to severe new vessels on the disc > standard photographs or new vessels elsewhere. ½ disc diameter.

- Pre-retinal or vitreous hemorrhage.

ETDRS RESULTS

1. Laser treatment is better than none, in clinically significant macular oedema.
2. Significant visual loss was reported in 24% treated and 12% untreated eyes during a 3 year follow-up.
3. Scatter laser treatment may not be beneficial in patient with mild to moderate NPDR and is not useful as an alternative to grid photocoagulation in CSME.
4. In proliferative diabetic retinopathy with CSME, treatment of the CSME followed by pan – retinal photocoagulation I spaced sessions, with less intense and slightly wide – spaced burns is beneficial.
5. Pan-retinal photocoagulation was found to reduce the visual loss by more than 50% in high-risk eyes.
6. Aspirin, in the dose of 650mg/ day did not have any beneficial effect on the retinopathy, was not associated with any higher risk of bleeding in proliferative diabetic retinopathy, showed the same mortality rates as in other subjects without diabetes and did not reduced the risk factors for cataract surgery.
7. A good correlation was reported between the ophthalmoscopic findings and fundus photographs in the detection of macular oedema.

Subretinal fibrosis was reported following the laser treatment of macular oedema.

The correlation between hard exudates and increased serum lipids and low-density lipoproteins (LDL) was reported. A 5.l5%, five year cumulative rate of pars plana vitrectomy was reported.

DRS RESULTS

Six risk factors were identified as the cause for continued visual loss following pan-retinal photocoagulation.

DCCT RESULTS

Tight metabolic control of diabetes delays the onset of retinopathy in insulin-dependent diabetics.

These landmark studies have clarified several important questions related to diabetic retinopathy and provided valuable guidelines to the clinical ophthalmologist in its management.

DIABETIC NEPHROPATHY – A PERSPECTIVE

Introduction

Renal disease is a common life threatening microvascular complication of diabetes mellitus characterized by the presence of persistent proteinuria, hypertension ad progressive renal insufficiency.

Definition

Diabetic nephropathy is defined as a multifaceted pathologic entity which spans the continuum from early renal hypertrophic changes to late stages of

structural destruction of the glomeruli, renal vasculature, interstitium and tubules.[26,27] However, it is now widely accepted that the classical clinical manifestation of this pathologic entity, overt continuous proteinuria, hypertension and declining glomerular filtration rates represent unequivocal though non-specific consequences of this continuum. Useful markers of the extent of renal structural changes, they are not specific for diabetes.[28,29]

The advanced lesions of diabetic nephropathy are, in their constellation, specific. Taken separately, many of the component abnormalities, such as glomerular basement membrane thickening, increased mesaginal matrix production, tubular basement membrane and mesangial thickening can be seen in a variety of renal disease. However, the characteristics of diabetic glomerular basement membrane thickening as seen by electron microscopy are rarely seen in disorders other than diabetes.[30] Finding these changes along with afferent and efferent hyalinosis, increased renal linear extra cellular membrane albumin and IgG localization are diagnostic of diabetic nephropathy.

Epidemiology

Throughout the industrialized world, diabetic nephropathy is the most common cause amongst patients receiving treatment for end-stage renal disease. In India, about 15-35% of patients with end-stage renal diseased have diabetic nephropathy. In patients with IDDM, nephropathy develops in 30 to 40% within 20 to 25 years.[31,32] Patients who develop diabetes between 11 and 20 years of age are most likely to develop nephropathy.

Long term studies have shown that only 10% of IDDM patients with proteinuria survive after 40 years of diabetes in contrast to more than 70% of these without proteinuria.[31] Death in these patients is due to the complications of uremia or cardiovascular disease.[33] The overall prevalence of nephropathy in Type II NIDDM patients is 2 to 16%. However, it may be as high as 50% in certain ethnic populations like black Americans, American Indians and Hispians.[32]

The risk of development of nephropathy rises with the duration of diabetes, with a cumulative risk of 50% after 20 years of the disease.[34] The risk is higher in diabetic offspring with diabetic renal disease or in the presence of elevated blood pressure before the onset of diabetes. About 25 to 30% of NIDDM patients with proteinuria show non-diabetic glumerular lesions and a similar proportion have absence of retinopathy.[35,36]

Aetiological factors

It is estimated that around 30% of diabetics go on to develop diabetic nephropathy. Among the diabetic population, the following factors predispose to the development of diabetic renal disease.

1. ***Genetic factors :***

It has shown that the erythrocyte Sodium – Lithium counter-transport is increased in patients destined to develop diabetic nephropathy. This increase in various cells is a marker of essential hypertension.[37]

2. Metabolic and Hormonal factors :

The changes of diabetic nephropathy develop only in the presence of an abnormal diabetic milieu. Undoubtedly, prolonged hyperglycemia plays a very important role in the causation of diabetic nephropathy. It is supposed to act by altered tubulo-glomerular feedback or autoregulation. Suboptimal glycemic control raises growth hormone levels, which stimulates renal hypertrophy and increases glomerual filtration rates. Hyperglucagonemia and raised levels of atrial natriuretic peptides could also e playing a role.

Hyperglycemia also stimulates cellular aldose reductase activity thereby leading to a reduction in tissue stores of myoinositol and cellular Na- K ATPase. Glucose is known to react in a non-enzymatic fashion with many protein compounds including glomerular basement membrane and masangial matrix component by non-enzymatic glycosylation which may further aggravate glomerular injury. Similar changes also take place in the other organs like skeletal muscles and eyes. Other glomerular basement membrane abnormalities seen are reduction in sialic acid, heparin sulphate and increase in hydroxylysine and isaccharide units. Advanced glycosylation end products (AGE products) are formed which alter the permeability of the blomerular basement membrane leading to proteinuria and later azotemia.

3. Hemodynamic Abnormalities :

It is suggested that increased blood glucose levels may be directly damaging the vascular endothelium and may be an additional factor in the causation of the long-term complications of diabetes mellitus.

Raised intra-glomerular flow and pressure seen early in the course of diabetes are thought to play a critical role in the initiation and progression of structural renal damage.

The following factors are thought to be the mediators of glomerular hyper filtration

a. Prolonged hyperglycemia
b. Insulopenia
c. Growth hormone excess.
d. Hyperglucagonemia
e. Abnormal polyol metabolism and depletion of cellular myoinositol.
f. Supernormal concentration of plasma organic acids.
g. Non-enzymatic glycosylation of structural proteins.

The precise means by which these hemodynamic changes ultimately lead to structural alterations are not defined. The various possibilities suggested are : increased mesangial matrix production, increased transglomerular passage of plasma proteins, defective mesangial clearance of large molecules, physical stress and shear stress causing endothelial damage and platelet activation.

4. The Remnant Kidney hypothesis

The remnant kidney hypothesis based on physiologic studies in animals[38] and clinical observations in man suggest[39,40] that compensatory mechanisms to reduced number of nephrons results in the establishment of hemodynamic forces

within the glomerulus that disrupt structure to produce functional consequences including proteinuria and hypertension. These forces ultimately lead to further nephron destruction. The influence of hypertension on the rate of decline of glomerular filtration rate in the nephropathic diabetic patient[41] is consonant with this hypothesis but not specific to diabetes. The clinical manifestations of diabetic nephropathy, overt proteinuria, hypertension and declining glomerular filtration rates have at their onset; essentially, no relationship to the number of hyalinized glomeruli. Yet the remnant kidney hypothesis may be the key to the development of clinical diabetic nephropathy.

Once clinical diabetic nephropathy is present, it is unlikely to be reversed by steps taken to influence steps taken to influence the diabetic state.

Stages in the developemnt of daibetic nephropathy

The natural history of renal disease in diabetes has been studied extensively. Morgensen and his colleagues[42] have identified five distinct phases in the course of the disease.

Stage I : The Hyeperfiltration – Hypertrophy stage

Compared to age matched controls, GFR is 20 to 40% higher in patients with newly diagnosed IDDM. Renal plasma flow also shows a similar elevation. These changes are accompanied by an increase in the kidney size by about 30%. They are related to the degree of glycemic control and tight metabolic control early in the course of the disease may reverse these changes towards normal.

Histological studies at this stage reveal an increase in the glomerular size and volume. The intra-glomerular filtration pressures are also elevated in experimental and animal studies.

Stage II Clinically Silent Stage of Structural Glomerular Lesion or Incipient Diabetic Nephropathy

Thickening of the glomerular basement membrane and mesangial expansion become apparent within 18 to 24 months of diagnosis in patients with supernormal glomerular filtration rates. These changes become more marked with the passage of time. During the alter part of this stage, urinary albumin excretion may show a transient increase (normal < 7μg/minute) during episodes of poor metabolic control or exercise.

Stage III Stage of Microalbuminuria

The stage of microalbuminuria, which is defined as 30-300mg of albumin excretion per day (20-200μg/min), is not detected by routine clinical uniralysis. It is detected by ELISA or Radio-immunoassay.[43,44] Presence of urinary tract infection and uncontrolled diabetes and hypertension ahs to be ruled out before assessing for microalbuminuria.

Microalbuminuria predicts progression[45] to clinical proteinuria and increased cardiovascular mortality. This increase in seen 5 to 15 years after the onset of diabetes and almost all patients show an elevation in blood pressure during transition form stage II to III. The glomerular filtration rate is either elevated or normal at the onset of this stage, but begins to decline inexorably

once the albumin excretion rates exceed 70µg/min. The risk of overt nephropathy has been estimated to be 20-35 times more after the threshold of albumin excretion rate is crossed. Detection of microalbuminuria is of utmost significance because further progression f diabetic nephropathy may be prevented with a tight control of diabetes and the use of anti-proteinuria drugs like ACE-inhibitors.

Stage IV – Clinical or Overt Diabetic Nephropathy

Clinical diabetic nephropathy is defined as proteinuria of more than 0.5 grams per day and a dipstick positive proteinuria, with hypertension and oedema.

The clinical diagnosis of diabetic nephropathy is evident when the following conditions are fulfilled.

1. Duration of diabetes of more than eight years.
2. Associated diabetic retinopathy, usually pre-proliferative or proliferative is seen in 90% of patients and its absence should lead to consideration of non-diabetic causes of proteinuria.
3. Associated diabetic polyneuropahty.
4. Presence of proteinuria, oedema and associated hypertension. An alternative cause for proteinuria/azotemia should be entertained if;
    - Known duration of diabetes mellitus is less than eight years.
    - Absence of fundus changes of diabetic retinopathy.
    - Active urinary sediments like RBC cells and granular casts are present.

A kidney biopsy may become essential to differentiate the causes of proteinuria in certain circumstances.

Stage V End-Stage Renal Disease

The interval from the diagnosis to the appearance of uremia varies from 15 to 25 years. This is associated with effects of uremic damage on end organs, like advanced albuminuric retinopathy, cardiac insufficiency, gastroparesis and other extra-renal vascular disease. Hyeprkalemia may develop due to hyporeninemic hypoaldosteronism, which may aggravate, the metabolic acidosis. Median survival in untreated patients is about seven months.

MANAGEMENT

Early identification of patients likely to develop progressive renal disease and appropriate intervention, form the mainstay of management. Reversal is not possible after overt diabetic nephropathy develops.[46] Intervention needs to be diverted to the following factors.

1. ***Glycemic control***

Good control of diabetes with insulin is required. Oral hypoglycemic agents are best avoided because of their prolonged and erratic action and chance of developing lactic acidosis (biguanides).

Control of blood glucose has a limited impact on progression after proteinuria becomes overt. Short term studies have shown that reduction of blood

sugar levels in early stages of the disease diminishes the urinary albumin excretion rates and rate of decline of glomerular filtration rates.[47]

2. Dietary Measures

High protein diet has been shown to accelerate the progression of diabetic nephropathy.

3. Anti-hypertensive Therapy

A good control of hypertension goes a long way in retarding the progression of renal failure in these patients. In the presence of advanced renal failure, ACE inhibitors are best avoided. The initial drug of choice may be a diuretic with supplementation of a calcium channel blocker.

4. Renal Replacement therapy (RRT)

Renal replacement therapy is required at an early stage in diabetic nephropathy compared to other causes of chronic renal failure. Usually, dialysis is initiated when the urinary creatinine clearance drops to 10-15ml per minute. Creation of an arterio-venous fistula in advance is of importance as these patients have problems in A-V fistula creation/maturation because of diffuse vascular disease.

a. Maintenance Hemodialysis (MHD)

Maintenance hemodialysis causes different problems in diabetic nephropathy.

- Relatively difficult vascular access.

- Repeated episodes of vascular hypotension during or post – dialysis.
- Repeated hypoglycemic episodes on dialysis.
- Diabetic retinopathy may show a worsening due to heparin use.

It is prudent to omit the dose of insulin and anti-hypertensive therapy prior to dialysis in these patients.

b. Continuous Ambulatory peritoneal Dialysis (CAPD)

Continuous ambulatory peritoneal dialysis offers more hemodynamic stability and obviates the problems of vascular access. Ineffective complications like peritonitis and the risk of intestinal perforation continue to pose a serious problem in the long run.

c. Renal Transplantation

The transplantation surgery has become a practical reality in diabetics after the introduction of Cyclosporin A as the sheet anchor of immunosuppressive regimen.

However there is an increased mortality in these patients due to infection and cardiovascular events in the post transplant period. A few reports of simultaneous pancreatic and kidney transplantation of β cell islet transplants with renal transplantation are coming in.

5. Pancreatic Transplantation

Heterotopic pancreatic transplantation besides being technically difficult has been associated with high graft loss. Recently, however, a two year graft survival of over 80% has been reported.[48]

Pancreatic transplantation has been unsuccessful in ameliorating pre-existing retinopathy and neuropathy in pre-uremic diabetics. Combined renal and pancreatic transplantation is now being affirmed as the ideal mode of management of diabetic nephropathy.

METHODOLOGY

The present study was conducted in the Department of Ophthalmology, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum on patients with diabetes mellitus who are on renal haemodialysis during the period of January 2008 to December 2008.

Study design

One year cross-sectional study.

Study period

The present study was conducted during January 2008 to December 2008.

Method of collection of data

Source of Data

Patients with diabetes mellitus who are on renal haemodialysis at KLES, Prabhakar Kore Hospital and Medical Research Centre, Belgaum.

Sample size

A sample size of 50 cases.

Sampling procedure

The sample size was calculated considering number of patients with diabetes mellitus who are on renal haemodialysis at KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum over last three years.

Selection criteria

Inclusion Criteria

- Patients diagnosed to have chronic renal failure in diabetes mellitus.
- Patients who are known case of diabetes.
- Patients who are on renal dialysis.

Exclusion Criteria

- Comatose patients.
- Patients who are not willing to undergo procedures.

Procedure

The study is conducted in Department of Ophthalmology at KLES Prabhakar Kore Hospital and Medical Research Centre, Belgaum during one year duration. The study was approved by the Ethical and Research Committee of Jawaharlal Nehru Medical College, Belgaum.

After finding the suitability as per inclusion and exclusion criteria patients were selected for the study and briefed about the nature of the study, the interventions used and written informed consent was obtained (Annexure–I). Further, descriptive data of the participants like name, age, sex, detailed history, were obtained by interviewing the participants and clinical examination and necessary investigations were recorded on predesigned and pretested proforma (Annexure-II).

After taking informed consent of all the eligible patients were subjected to detailed examination like history, general physical examination and systemic examination. Ocular examination consisted of;

1. History
2. Best corrected visual acuity recorded (BCVA)
3. Intraocular pressure
4. Detail examination of anterior and posterior segment

Pupil was dilated with tropicamide for Indirect ophthalmoscopy with 20 diopter lens followed by macular edema was classified on the basis of early treatment diabetic retinopathy study. Other investigations done according to need were;

1. Fundus fluorescein angiography
2. Visual field
3. Fundus photography
4. Schirmer test

After detailed ocular examination patients were subjected to following investigations.

1. Hemoglobin.
2. Total leukocyte count (TLC).
3. Differential leukocyte count.
4. Erythrocyte sedimentation rate (ESR).
5. Serum urea.

6. Serum creatinine.

Special investigations like, serum calcium, serum electrolytes and urine routine and microscopic examination was carried out if necessary.

Statistical analysis

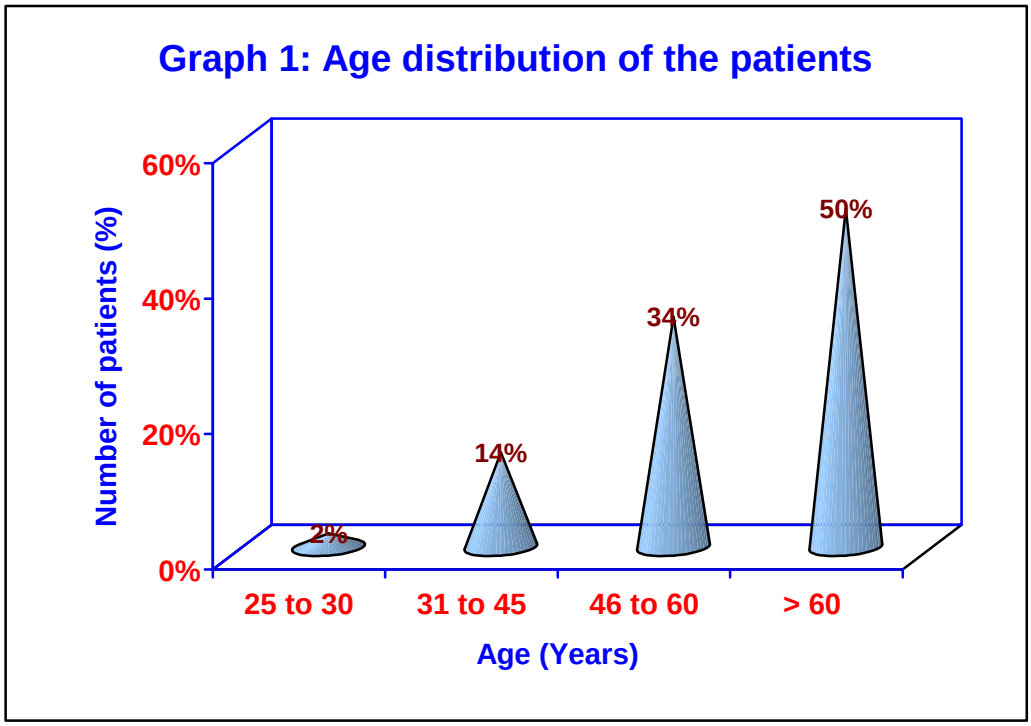
Chi Square Test is used to determine the relationship between ocular findings with duration of renal dialysis in diabetic end stage kidney diseases.

RESULTS

The present study was conducted in the Department of Ophthalmology, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum on patients with diabetes mellitus who are on renal haemodialysis during the period of January 2008 to December 2008. In this study, 50 patients with diabetes mellitus undergoing hemodialysis were studied and observations and findings were recorded and tabulated as below.

Table 2: Age distribution of the patients

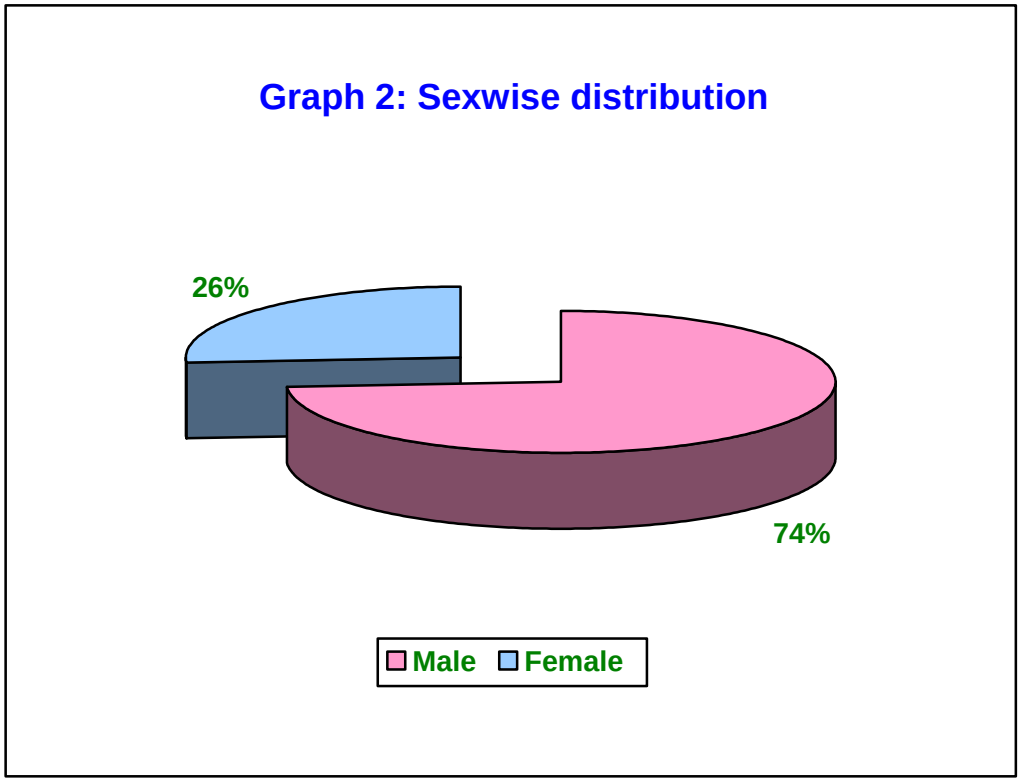
Age (Years)	Patients	
	Number	**Percentage**
25 to 30	01	2%
31 to 45	07	14%
46 to 60	17	34%
≥ 60	25	50%
Total	**50**	**100%**



In the present study age ranged from 28 to 69 years. Fifty percent (50%) of the patients were in the age group of more than 60 years followed by 34% in 46 to 60 years and 14% in 31 to 45 years. Two percent (2%) of the patients belonged to the age group of 25 to 30 years.

Table 3: Sex distribution

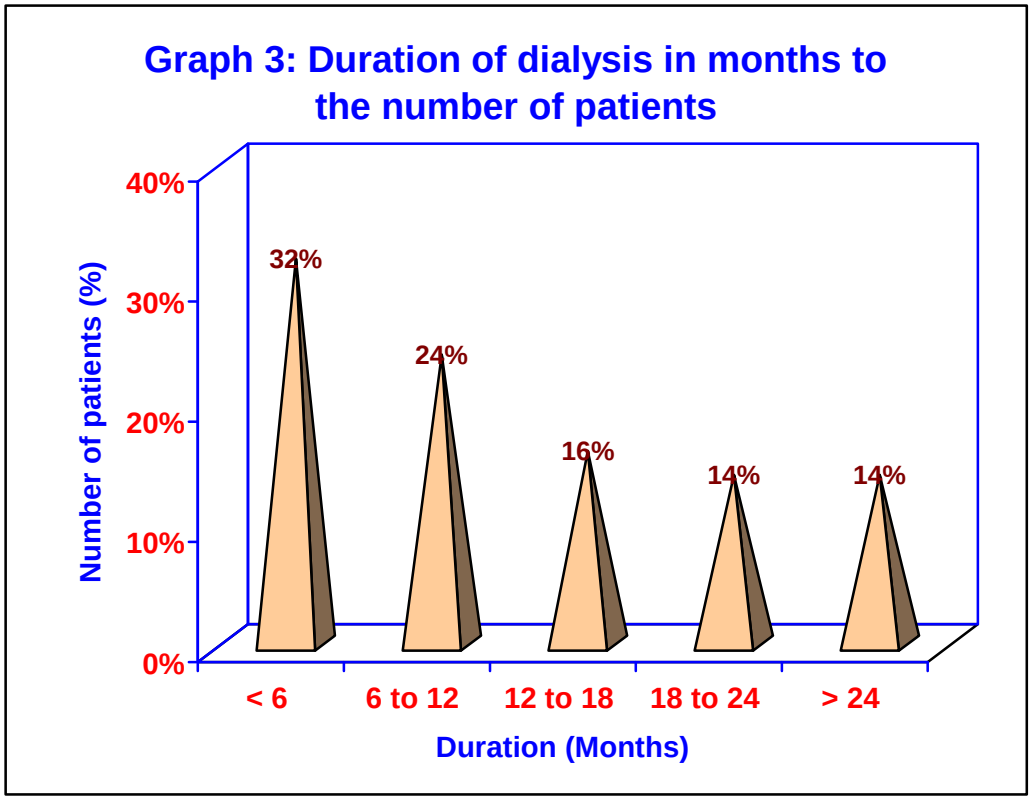
Sex	Patients	
	Number	**Percentage**
Males	37	74%
Female	13	26%
Total	**50**	**100%**



In the present study male preponderance was seen. There were 74% of males and 26% of females with male to female ratio of 2.84:1.

Table 4: Duration of dialysis in months to the number of patients

Duration of dialysis	Patients	
	Number	**Percentage**
Less than six month	16	32%
6 to 12 months	12	24%
12 to 18 months	8	16%
18 to 24 months	7	14%
More than 24 months	7	14%
Total	**50**	**100%**



In this study 14% of patients had duration of dialysis more than two years and 32% of the patients had duration of less than six months. Remaining 24% patients had duration between six months to 12 months and 16% of patients had 12 months to 18 months.

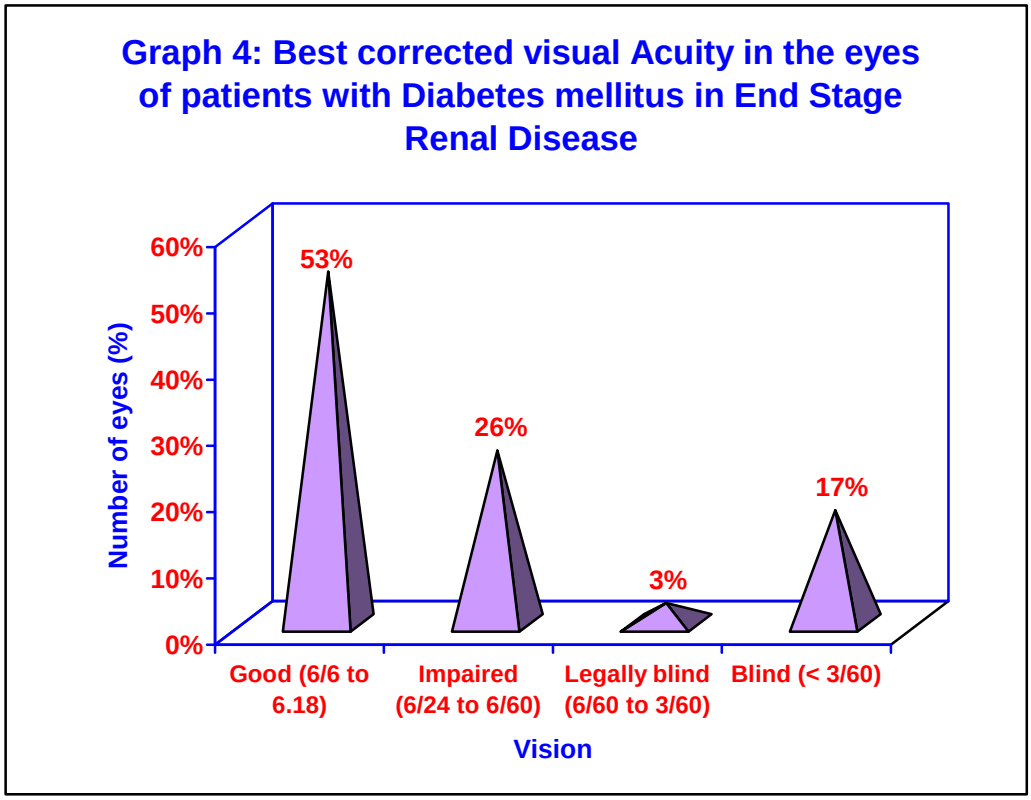
Table 5: Duration of vision loss to duration of Diabetes Mellitus in end stage kidney disease

Duration of Diabetes mellitus	Duration (Years) of vision loss in number of eyes				
	No. loss	0 to 1	1 to 2	2 – 3	> 3
0 to 4 years	04	26	6	00	00
5 to 9 years	02	16	10	04	04
10 to 14 years	00	04	00	04	02
More than 15 years	00	00	12	00	06

The duration of diabetes mellitus ranged from one year to 20 years and duration of vision loss ranged from one week to ten years. Twenty six (26) eyes had duration of vision loss within a year with duration of diabetes upto four years, 16 eyes had vision loss with diabetic duration of five to nine years and 12 eyes had vision loss between one to two years with diabetic duration of more than 15 years.

Table 6: Best corrected visual Acuity in the eyes of patients with Diabetes mellitus in End Stage Renal Disease.

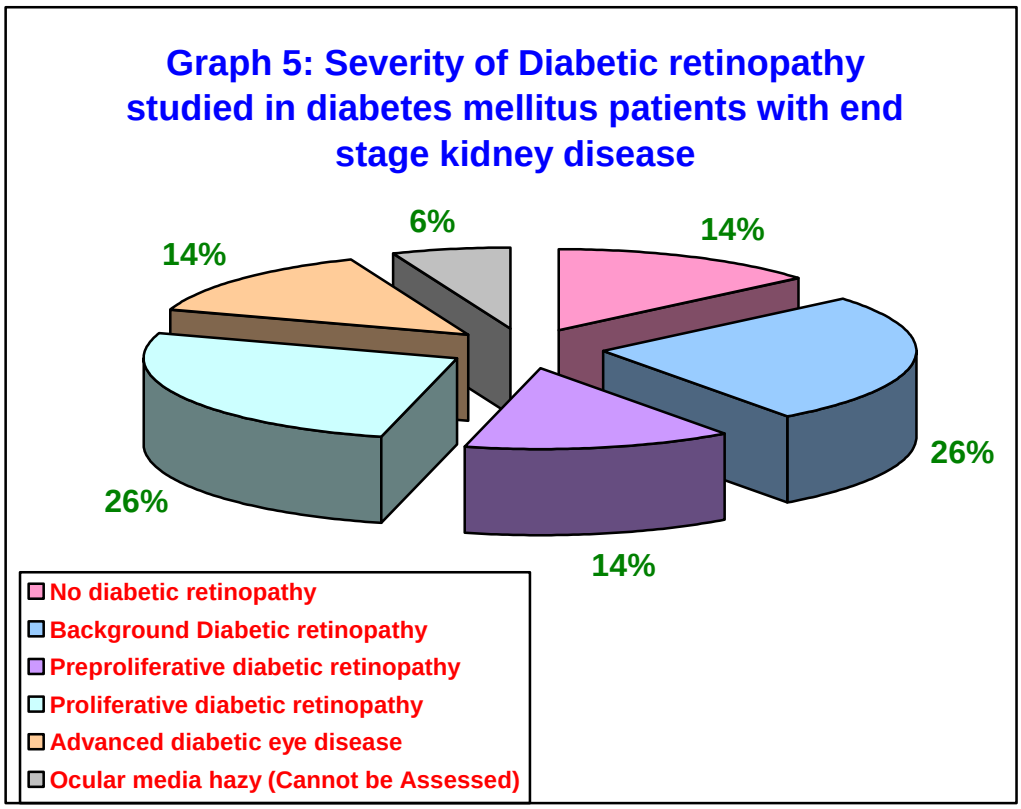
WHO criteria	BCVA	Total Eyes (%)
Good Vision	6/6 – 6/18	53%
Impaired vision	6/24 – 6/60	26%
Legally blind	6/60 – 3/60	3%
Blind	< 3/60	18%



Blurring of vision (Decrease in good vision) was the most important symptom complained by patients. Patients with decreased vision < 6/24 were about (47%). Most of them were of gradual onset and remaining patients were having vision of 6/6 to 6/18 in 53%.

Table 7: Severity of Diabetic retinopathy studied in diabetes mellitus patients with end stage kidney disease

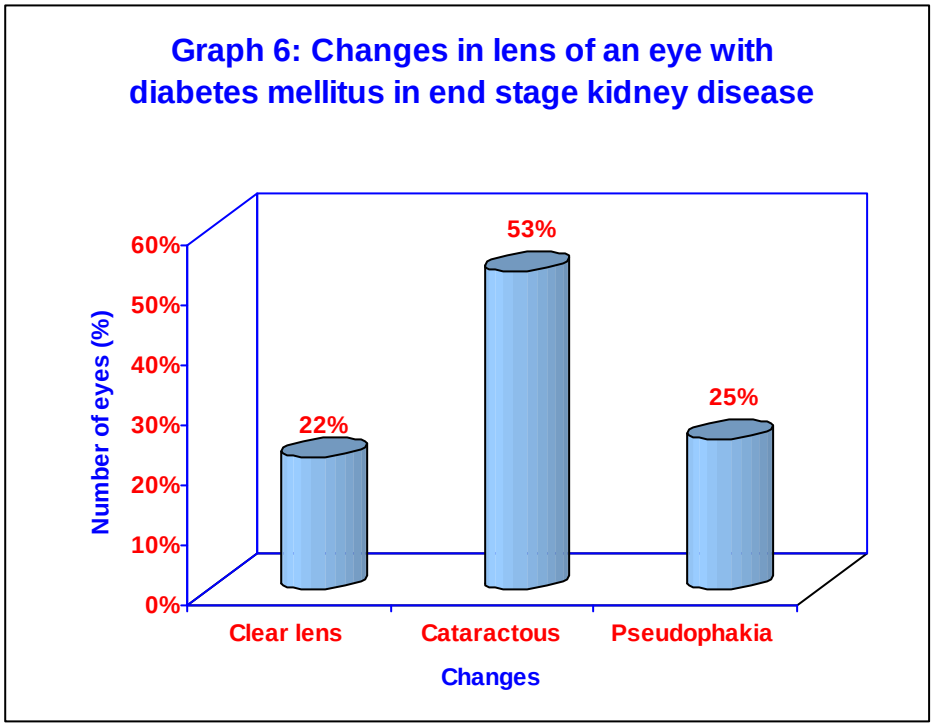
Severity of diabetic retinopathy	Total eyes (%)
No diabetic retinopathy	14%
Background diabetic retinopathy	26%
Preproliferative diabetic retinopathy	14%
Proliferative diabetic retinopathy	26%
Advanced Diabetic eye Disease	14%
Ocular Media Hazy (cannot be assessed)	6%



In our study out of 100 eyes, 80% of eyes had diabetic retinopathy in one or other form, some of these were associated with other symptoms which had close correlation to diabetic retinopathy.

Table 8: Changes in lens of an eye with diabetes mellitus in end stage kidney disease

Type of Lens	Total eyes (%)
Clear lens	22%
Cataractous - All stages of cataract	53%
Pseudophakia	25%



In patients with diabetes mellitus having end stage kidney disease the cataractous lens (Grade II NS – Grade IV NS) and posterior subcapsular cataract was present in 53%. In the remaining, 25% of patients had undergone cataract surgery with pseudophakia and 22% patients had clear lens.

Table 9: Ocular changes with duration of diabetes mellitus seen in end stage kidney disease group of patients.

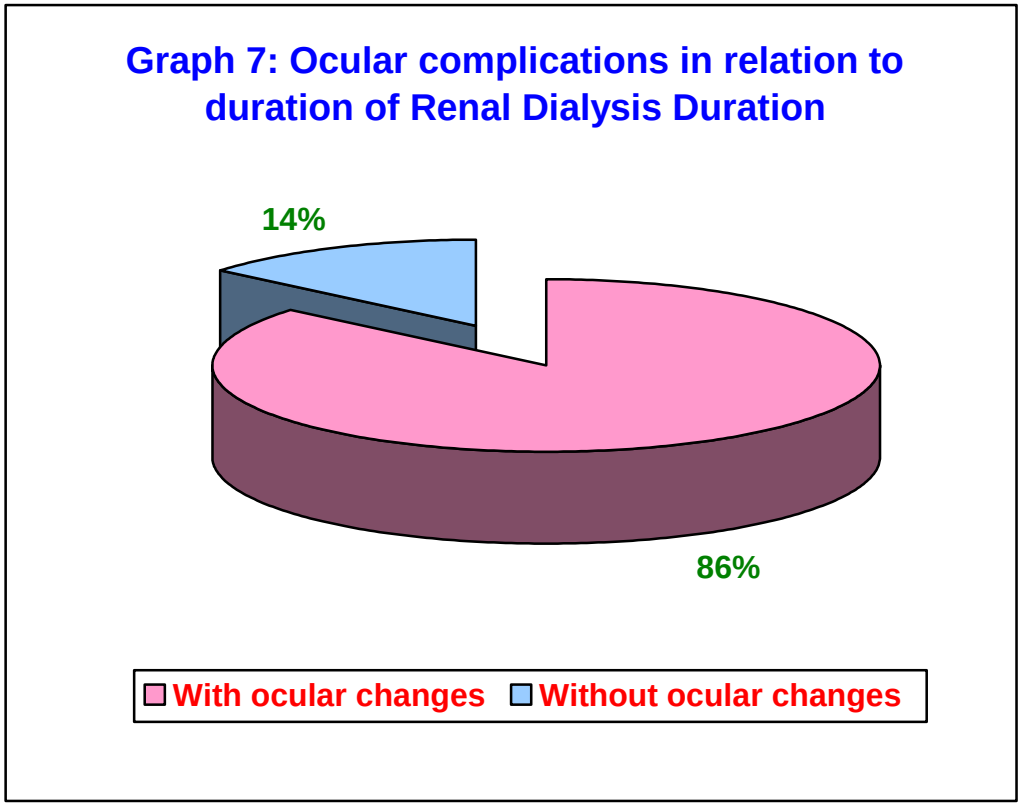
Ocular findings	Duration of diabetes mellitus (Years)				
	0 – 4	**5 – 9**	**10 – 14**	**> 15**	**%**
Diabetic retinopathy	6	20	10	12	48%
Hypertensive retinopathy	10	2	-	-	12%
Maculopathy (DM / HTN)	2	3	-	-	5%
Retinal Detachment	2	-	-	2	4%
Vitreous Hemorrhage	-	2	-	2	4%
Papilledema	2	-	-	-	2%
Glaucoma suspect	2	-	-	-	2%
Age related macular degeneration	2	-	-	-	2%
Cataract	-	5	2	2	9%
Normal	10	2	-	-	12%

In the present study diabetic retinopathy was seen commonly among the patients (48%) with diabetes mellitus having end stage kidney disease followed by 12% with hypertensive retinopathy. The other ocular findings noted were cataract in nine percent of patients, maculopathy in five percent, four percent each had retinal detachment and vitreous haemorrhage, and two percent each had papilledema, glaucoma, age related macular degeneration. In 12% of patients no ocular findings were recorded.

Table 10: Ocular complications in relation to duration of Renal Dialysis Duration

Duration of Renal Dialysis	Number of Eyes with ocular changes	No of eyes without ocular changes
Less than one year	58 (80.5%)	14 (19.5%)
More than one year	28 (100%)	0 (0%)
Total	86%	14%

x^2 with Yate's correction = 4.818; Df=1 p<0.050

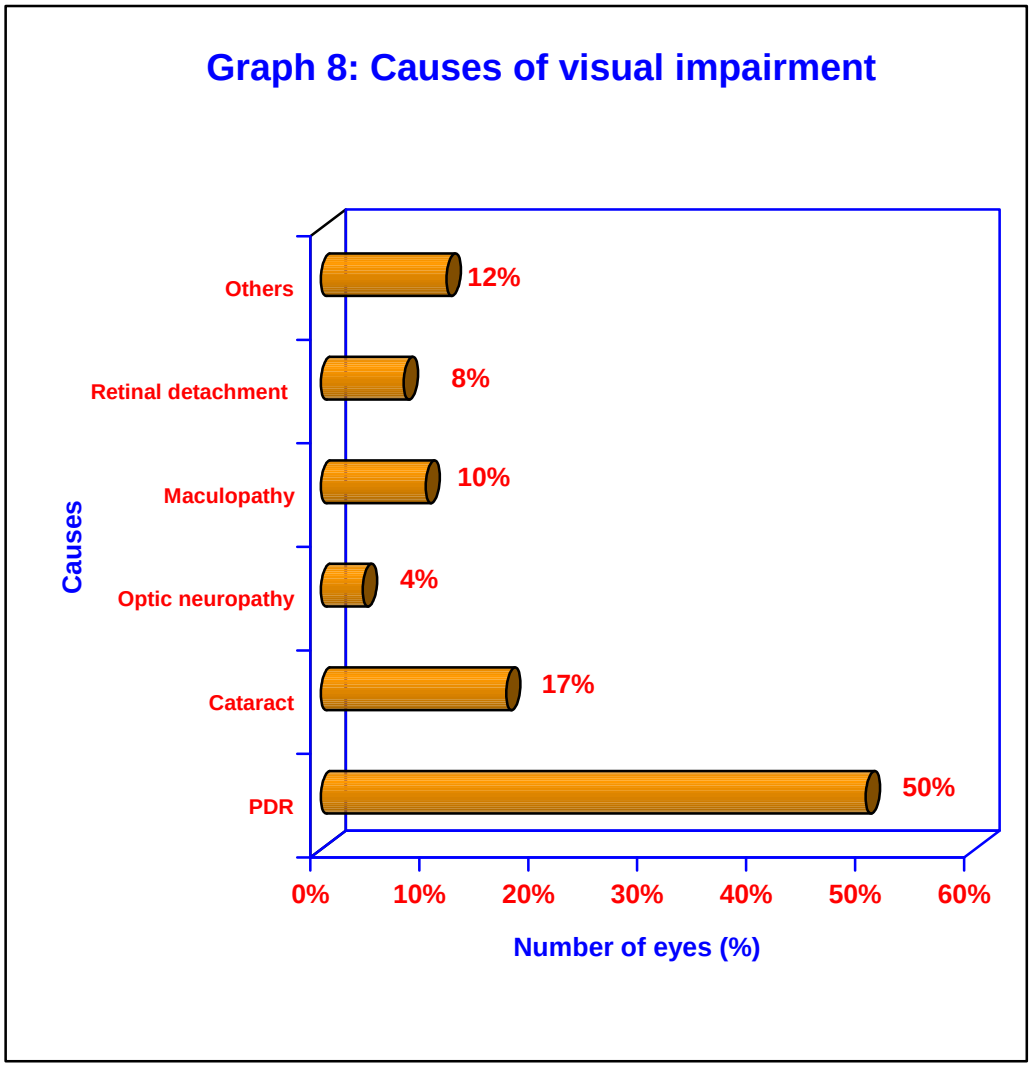


From above table, we conclude that duration of dialysis within (less than one year) had almost 4.14:1 is the ratio of number of eyes with ocular changes and number of eyes without ocular changes. But after one year duration this ratio

increased to 28:1 indicating six fold increase in complications. These finding were statistically significant (p=<0.05).

Table 11: Causes of visual impairment

Causes	Patients	
	Number	**Percentage**
Proliferative diabetic retinopathy	26	50.0%
Cataract	09	17.0%
Optic neuropathy	02	3.84%
Maculopathy	05	9.61%
Retinal detachment	04	7.60%
Others	06	11.53%



In the present study proliferative diabetic retinopathy was the commonest (50%) cause of visual impairment. The other causes of visual impairment were cataract (17%), optic neuropathy (3.84%), maculopathy (9.61%) and retinal detachment (7.60%). The other causes like age related macular degeneration and vitreous haemorrhage contributed 11.53% as causes of visual impairment.

DISCUSSION

The present study was conducted in the Department of Ophthalmology, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum on patients with diabetes mellitus who are on renal haemodialysis during the period of January 2008 to December 2008. In this study, 50 patients with diabetes mellitus, diagnosed to have chronic renal failure undergoing hemodialysis were included in the study. Patients who are not willing to undergo procedures and patients in coma were excluded in the study.

Diabetes mellitus justifiably known as ‘devil’ or silent killer engenders spectrum of maladies, affecting almost every tissue and cell in the human body. Diabetic retinopathy, once was seventeenth cause of blindness has rapidly ascended as third position, while diabetic nephropathy remains most common cause of end stage kidney disease.

These ocular complications like retinopathy which are microvascular complications are innocuous in onset progressively destructive in their course and are remediable only to a point. Unfortunately, most often they are symptomatically evident, only after considerable damage has occurred and restoration of anatomical and physiological function of normal is impossible.

Over the years, voluminous information has accumulated on the pathogenesis of diabetes complications like retinopathy. Many clinical trials and researches have yielded fruitful results. These results are however not being

effectively transferred between ophthalmologist, nephrologists and physicians, so as to benefit the patients.

In the present study age ranged from 28 to 69 years. Fifty percent (50%) of the patients were in the age group of more than 60 years followed by 34% in 46 to 60 years and 14% in 31 to 45 years. Age group more than or equal to 60 years is more prone for metabolic disorder like diabetes mellitus which leads to diabetic nephropathy and deteriorates to end stage of chronic renal failure were on renal dialysis.

Similar findings were reported by authors in various studies.[4] The study showed that incidence of end stage renal disease increases with advancing age of patient.

In the present study male preponderance was seen. There were 74% of males and 26% of females. Similar findings were reported in a study that is overall male: female ratio in chronic renal failure was 2.8:1 which was similar to worldwide data.[49]

This study documented patients with increased age have diabetes mellitus, which leads to diabetic nephropathy and then chronic renal failure with other associated factors like, hypertension, glomerulonephritis and polycystic kidney diseases. These risk factors were in elderly males leading to chronic renal failure and then patients for renal dialysis.

Arteriolar hyalinosis which occurs as a physiological change with advancement of age and its association with hypertension leads to capillary

closure downstream and pathological changes in retinal vasculature and renal vasculature. This is enhanced in diabetes mellitus.[4,25] Hence this study confirms close relationship between renal dialysis, diabetes mellitus and life span of patients in chronic renal failure. This also shows ocular diabetic changes which leads to ocular complications. The same ocular findings were seen in this study group.

In this study 14% of patients had duration of dialysis more than two years and 32% of the patients had duration of less than six months. Remaining 24% patients had duration between six months to 12 months and 16% of patients had 12 months to 18 months.

It was observed that as the duration of dialysis increased, group of patients undergoing dialysis was declined. This could be attributed to patient's poor compliance, low socioeconomic status, uncontrolled diabetes mellitus, hypertension, anemia and due to secondary infections and mortality.[50]

In this study duration of diabetes mellitus ranged from one year to 20 years and duration of visual loss ranged from one week to ten years. Twenty six (26%) eyes had duration of visual loss within year with duration of diabetes upto four years as this group has more patients.

In the present study blurring of vision (Decrease in good vision) was the most important symptom complained by patients. Patients with decreased vision < 6/24 were about (47%). Most of them were of gradual onset and remaining patients were having vision of 6/6 to 6/18 in 53%. Similar findings were reported in other study.[4]

In this study out of 100 eyes, 80% of eyes had diabetic retinopathy in one or other form which was closely associated with diabetes mellitus. Visual loss increases with increase in duration of diabetes mellitus and this was more with patients undergoing renal dialysis.

Similar findings have been observed by various studies[4] in the literature. The studies inferred that incidence of diabetic retinopathy along with duration of diabetes mellitus increases. If patient has diabetes mellitus and is undergoing renal dialysis, the association for diabetic retinopathy was 49%. Severity of retinopathy increases with nephropathy.

In this study, patients with diabetes mellitus having end stage kidney disease, the cataractous lens (Grade II NS – Grade IV NS) and posterior subcapsular cataract was present in 53%. In the remaining, 25% of patients had undergone cataract surgery with pseudophakia and 22% patients had clear lens.

This study shows with advancing of age visual loss was compounded with the cataractous changes in lens and diabetic retinopathy. Some of the patients underwent intraocular implant surgeries and further studies are required to see whether diabetic retinopathy progressed with intraocular lens implantation.

In the present study diabetic retinopathy was seen commonly among the patients (48%) with diabetes mellitus having end stage kidney disease followed by 12% with hypertensive retinopathy. Thirteen percent (13%) of the diabetic retinopathy patients had maculopathy, vitreous haemorrhage, retinal detachment. These complications were more with end stage renal disease and these required close followup of the patients with ophthalmologist in preventing the

complications. Two percent of the patients had papilledema in hypertensive group because of the accelerated hypertension. There were two percent of glaucoma suspect which required further follow-up and treatment. Based on previous reports, most common cause of renal failure is diabetes mellitus, followed by hypertension. Similar findings have been reported in another hospital based study[51] conducted to evaluate ocular findings in patients with chronic renal failure.

In the present study PDR was the commonest (50%) cause of visual impairment. The other causes of visual impairment were cataract (17%), optic neuropathy (3.84%), maculopathy (9.61%) and retinal detachment (7.60%). The other causes like ARMD and vitreous haemorrhage contributed 11.53% as causes of visual impairment. A study[51] confirms similar findings in the literature.

Patient in diabetes mellitus with renal dialysis is known to aggravate the retinopathy especially, vitreous hemorrhage, retinal detachment and clinically significant macular edema an effect that may be mediated through the increase in blood pressure, fibrinogen levels, raised lipoproteins.

Severity of diabetic retinopathy is seen due to unique histological structure and metabolic activity of retina, which is susceptible to noxious stimuli resulting from hypertensive and uremic changes of diabetic nephropathy in chronic renal failure in renal dialysis.

Ocular complications are still not reduced inspite of newer advances of treatment of diabetic retinopathy and end stage renal disease. This is due to longitivity of patients with chronic renal failure and advancing stages of the

disease. Thus it requires a thorough biochemical investigations, renal profile and management of diabetic retinopathy to prevent its complications.

Patients on renal dialysis have life expectancy less than three to five years. In Indian scenario its still reduced, due to low socioeconomic status, irregular medications, mental and physical instability, poor compliance, improper care taking, protein malnutrition and lack of knowledge. So patients are in irregular periods of renal dialysis, due to which it deteriorates the life of patient. Patients are reduced in numbers.

Early referral of patient with diabetic end stage kidney disease may bring to surface a retinal lesion, ophthalmologist's intervention and appropriate management of which, may prevent loss of vision.

Care of diabetic patients is a demanding task. It requires intense attention to multiple details. In addition to members of the dialysis team representatives of other specialties (for example vascular surgery, neurologist and utmost ophthalmologist) are needed. Existence of a diabetic team from all sub-specialties should work under the coordination of nephrologists.

Patients should be educated and told the importance of eyes and kidneys. Patients who are on chronic renal failure on renal dialysis with diabetes mellitus are told the importance of ocular examination; with detailed ophthalmic test whichever are necessary. They should be screened and detected and properly treated with all possibilities. It should be done with dedication of patient and ophthalmologist and preserve the vision in order to do his routine duties independently.

CONCLUSION

The present study was conducted in the Department of Ophthalmology, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum on patients with diabetes mellitus who are on renal haemodialysis during the period of January 2008 to December 2008. In this study, 50 patients with diabetes mellitus, diagnosed to have chronic renal failure undergoing hemodialysis were studied and following conclusions may be drawn.

- Fifty percent (50%) of the patients were in the age group of more than 60 years.

- In the present study male preponderance was seen. There were 74% of males and 26% of females with male to female ratio of 2.84:1.

- Thirty two percent (32%) of the patients had duration of renal dialysis less than six months.

- Twenty six (26%) eyes had duration of vision loss within a year with duration of diabetes upto four years.

- Blurring of vision (Decrease in good vision) was the most important symptom noted among the patients. Patients with decreased vision < 6/24 were about (47%). Most of them were of gradual onset and remaining patients were having vision of 6/6 to 6/18 in 53%.

- Eighty percent 80% of eyes had diabetic retinopathy in one or other form.

- Overall ocular changes seen in the patients were diabetic retinopathy (48%), hypertensive retinopathy (12%) and cataract (9%).

- Proliferative diabetic retinopathy was the commonest (50%) cause of visual impairment. The other causes of visual impairment were cataract (17%), optic neuropathy (3.84%), maculopathy (9.61%) and retinal detachment (7.60%).

- The duration of dialysis within less than one year had almost 4.14:1 is the ratio of number of eyes with ocular changes and number of eyes without ocular changes. But after one year duration this ratio increased to 28:1 indicating six fold increase in complications ($p=<0.05$).

SUMMARY

Diabetes mellitus is a clinical syndrome characterized by hyperglycaemia due to absolute or relative deficiency of insulin. Now in modern era, diabetes mellitus is a burning issue and its incidence is increasing day by day. Its long term complication leads to microvascular complications like neuropathy, retinopathy, and nephropathy. Diabetes affects vasculature in retina and kidneys.

Present study was undertaken to find ocular changes and complications associated with diabetic end stage kidney diseases.

The present one year cross-sectional study was conducted in the Department of Ophthalmology, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum during the period of January 2008 to December 2008 on 50 patients with diabetes mellitus and undergoing renal haemodialysis. The patients were subjected to general physical examination and systemic examination. Ocular examination was carried out to assess best corrected visual acuity, intraocular pressure and detailed examination of anterior and posterior segment.

In the present study male preponderance was seen. There were 74% of males and 26% of females with male to female ratio of 2.84:1. Fifty percent (50%) of the patients were in the age group of > 60 years. Thirty two (32%) of patients had duration of renal dialysis less than six months. Twenty six (26%) eyes had duration of vision loss within a year with duration of diabetes upto four years.

Blurring of vision (Decrease in good vision) was the most important symptom complained by patients. Patients with decreased vision < 6/24 were about (47%). Most of them were of gradual onset and remaining patients were having vision of 6/6 to 6/18 in 53%. Eighty percent 80% of eyes had diabetic retinopathy in one or other form. Overall ocular changes seen in the patients were diabetic retinopathy (48%), hypertensive retinopathy (12%) and cataract (9%).

Most of them were of gradual onset and remaining patients were having vision of 6/6 to 6/18 in 53%. Eighty percent 80% of eyes had diabetic retinopathy in one or other form. Overall ocular changes seen in the patients were diabetic retinopathy (48%), hypertensive retinopathy (12%) and cataract (9%). Proliferative diabetic retinopathy was the commonest (50%) cause of visual impairment.

The study may be concluded that patients with diabetic end stage kidney diseases are at high risk of ocular morbidities. Timely screening and treatment may help to reduce the ocular morbidities in this group.

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ANNEXURE I - CONSENT FORM

You are being asked to participate in a Cross-sectional study entitled "One year cross-sectional studies to determine relationship between ocular changes, visual outcome and complications in diabetic end stage kidney diseases" conducted by Dr. Nagbhushan Chougale, Post Graduate Student in M. S. Ophthalmology, Jawaharlal Nehru Medical College, Belgaum. Before you decide to participate it is important for you to understand why the trial is being done and what it will involve.

I Mr/Mrs/Ms. _____ have been asked to participate in research study entitled "One year cross-sectional studies to determine relationship between ocular changes, visual outcome and complications in diabetic end stage kidney diseases" conducted by Dr. Nagbhushan Chougale, Post Graduate Student in M.S. Ophthalmology, Jawaharlal Nehru Medical College, Belgaum. You are requested to enroll yourself to participate in this study as you are eligible for participating in the study.

Purpose of study

The purpose of research is to determine relationship between ocular changes and visual outcome and complications in diabetic end stage kidney diseases in patients with diabetes mellitus. Here we are going to look for ocular problems and complications in diabetic end stage kidney diseases with visual outcome of patients.

Procedure involved

If you agree to participate in this study, you will be asked to give detailed history of the disease you have and willing to undergo necessary investigations that may be required. As per the study design there will be no follow-ups.

Risks and Benefits

As such there are no major risks involved, however some discomfort may occur during the process of investigations and the risks involved with the end stage kidney diseases like patients may go for chronic renal failure, diabetic coma, for which all precautions will be taken. As such minimal risk is involved in the evaluating such patients mentioned above.

If you agree to enroll in the study, you will be helpful in determining the stages/progression duration of diabetes and its effect and in visual outcome. Your participation may benefit you and others suffering from same ailment in future. No financial incentives are promised for being a part of study.

Alternatives

Your decision whether to participate or not to participate in this study will not affect the quality of treatment you receive and will be treated according to the existing protocol. Further you may withdraw from the study at any time.

Costs for participating in this research

There will not be any extra cost incurred by you. You will however have to pay for the investigations which are the part of the existing management

protocol for this ailment. There is no commitment for any reimbursement or any other compensation.

Privacy and confidentiality

Your participation in this study is purely voluntary. You may withdraw your participation from the trial at any time. Your privacy is guaranteed. However, your medical records can be directly accessed and reviewed by authorized individuals or by ethics committee. Records, which could reveal your identity, will be kept confidential. Personal data will remain anonymous if data is being published or written as a dissertation.

Authorization to publish results

When the results of the research are published or discussed, in a conference no information will be displayed that would disclose your identity. Any information that is obtained in connection with this study and that can be identified with you will remain confidential.

Compensation

In the event of injury related to the study, treatment will be made available through KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum. There is no compensation or payment for such medical treatment by law. The doctors and the staff will provide facilities and medical attention.

Questions

If you have any questions about the research you may contact;

1. Investigator, Dr. Nagbhushan Chougale, Post Graduate Student, Department of Ophthalmology. Jawaharlal Nehru Medical College, Belgaum Contact No. 98867 45920
2. Guide, Dr. S. B. Patil $_{MS}$, Professor, Department of Ophthalmology. Jawaharlal Nehru Medical College, Belgaum Contact No. 94482 78549
3. Dr. V. D. Patil $_{MD\ DCH}$, Principal, Jawaharlal Nehru Medical College, Belgaum and Chairman, Institutional Ethics Committee Contact No. 0831-2471350.

Consent for participation in research trial

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

Subject Name: _____
Signature or the left thumb print of subject _____
Name of the Witness: _____
Signature of the Witness: _____
Investigator Name: _____
Signature of Investigator: _____
Date: Place:

ANNEXURE II - PROFOMA

Serial No. :

Name :

Address : Age : Sex :

Tel. No (if any):

K.L.E.S. Hospital I.P. No : O.P.D. No. :

DOA. : / / D.O.D. : / /

HISTORY

1. H/O visual loss :

Duration

YES / NO

RE/LE/BE

Corrected with glasses

For Distance/ Near

Sudden/ Gradual

Decrease/ Complete loss

Progressive

2. H/O Floaters : YES / NO
3. H/O Pain : YES / NO
4. H/O Redness : YES / NO
5. H/O Discharge : YES / NO
6. H/O Photophobia : YES / NO
7. H/O Ocular surgery / Procedure : YES / NO
8. Ocular History : YES / NO

   Myopia : YES/ NO

   Glaucoma surgery : YES/ NO

   Cataract surgery : YES/ NO

   RE/ LE/ BE

H/o Diabetes Mellitus

1. Duration of diabetes :
2. Diagnosis of diabetes : Type I IDDM/Type II NIDDM.
3. Blood sugars : RBS : mg %
   FBS : mg % (Normal : 60 - 110 mg %)
   PPBS : mg % (Normal: upto 140 mg%)
4. Glycosylated haemoglobin : % (Normal: 6.2 - 8.3 %)
5. H/O Treatment : YES/ NO
   Duration
   - Diet YES/ NO
   - Oral hypoglycaemic drugs YES/ NO
   - Insulin YES/ NO
   - Regular YES/ NO

H/O Associated Hypertension YES/ NO

1. Duration of hypertension :
2. Last blood pressure recording : / mm of Hg.
3. H/O Treatment : YES/ NO
   Duration
   - Diet : YES/ NO
   - Anti-hypertensives : YES/ NO
   - Regular : YES/ NO

Medical history on admission

1. since
2. since
3. since
4. since

Past history

Family history

Diabetes Mellitus	:	YES/ NO
Hypertension	:	YES/NO
Ocular Disease	:	YES/NO

Personal history

Smoking	:	YES NO/ STOPPED SINCE
Alcohol	:	YES- NO/ STOPPED SINCE
Tobacco	:	YES/ NO/ STOPPED SINCE
Diabetic diet	:	YES/ NO

General physical examination

Mental state	:	Conscious/ Drowsy/ Unconscious
Vital Parameters	:	B.P.: / mm of Hg.
		Pulse : /minute, regular/irregular
		Temperature: Febrile/ Afebrile
		Respiration: cycles/ min., regular/ irregular
		Generalized/ Facial/ Pedal/Absent
Oedema	:	YES NO
Icterus	:	YES NO
Cyanosis	:	YES NO
Clubbing	:	YES NO
Lymphadenopathy	:	YES NO
Pallor:		

SYSTEMIC EXAMINATION

C.V.S.	:
R.S.	:
C.N.S.	:
P.A.	:

OCULAR EXAMINATION

Head posture :

Facial symmetry :

Visual axes :

Extra - ocular movements :

Vision

	R.E.	**L.E.**	**B.E.**
Vision : (Snellen's)			
P.M. :			
With glasses :			
Near vision :			
Near vision: (with glasses)			
Colour vision :			

Refraction

	O.D.							
	Sphere	**Cylinder**	**Axis**	**Vision**	**Sphere**	**Cylinder**	**Axis**	**Vision**
Distance								
Near								

Adnexa : O.D. O.S.

Conjunctiva :

Cornea :

Anterior chamber :

Iris :

I Pupil :

Lens :

Intraocular pressure :

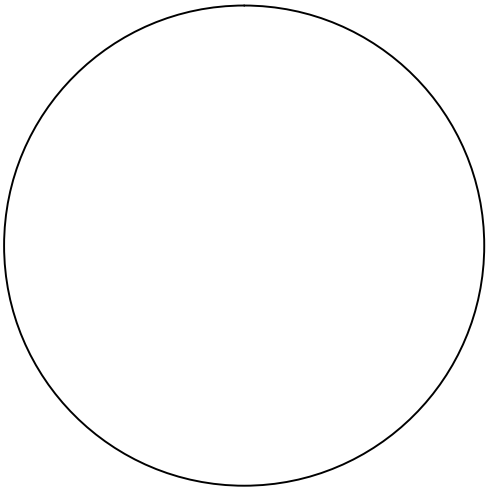
(with gms. Weight) mm. of Hg. mm. of Hg

FUNDUS EXAMINATION

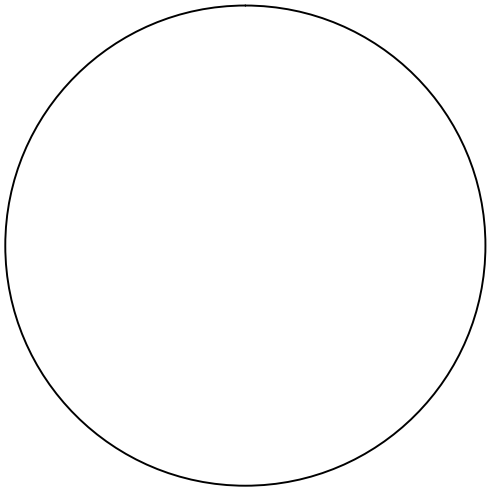
	O.D.	**O.S.**
Glow :		
Media :		
Disc. : ▪ Shape: ▪ Size: ▪ Colour: ▪ Margins: ▪ Cup: ▪ Cup: Disc ratio: ▪ Neovascularization (NVD):		
Vessels : 1. Arteries : ▪ Narrowing: ▪ Generalised: ▪ Focal: ▪ Segmental: ▪ Sheathing: ▪ Sclerosis:		
2. Veins ▪ Dilatation: ▪ Venous tortuosity: ▪ Venous beading/ looping/ knotting: ▪ Sheathing:		
3. Arteriovenous crossing changes:		
4. A: V ratio:		
Background : Hemorrhages : ▪ Superficial : ▪ Deep : ▪ Pre- retinal : ▪ Vitreous :		

Exudates : ▪ Hard exudates: ▪ Discrete : ▪ Confluent : ▪ Soft exudates :		
Microaneurysms :		
Neovascularization (NVE) :		
IRMA :		
Proliferative changes :		
Retinal detachment :		
Macula : Microaneurysms :		
Hemorrhages : ▪ Superficial : ▪ Deep : ▪ Pre- retinal : ▪ Vitreous :		
Exudates : ▪ Hard exudates : ▪ Discrete : ▪ Confluent : ▪ Circinate :		
Soft exudates :		
Neovascularization :		
IRMA :		
Macular oedema :		

Mapping of the fundus lesions



R.E



L.E

FUNDUS FLUORESCEIN ANGIOGRAPHY :

RADIOLOGICAL INVESTIGATIONS: (X-RAY KUB / USG / IVP)

MISCELLANEOUS INVESTIGATIONS :

DIAGNOSIS

1. Diabetes : Type 1 IDDM / Type 2 NIDDM

2. Diabetic

Retinopathy :	Normal	
	Background diabetic retinopathy	
	Pre- proliferative retinopathy	
	Proliferative retinopathy	
	Maculopathy	Oedematous
		Exudative
		Ischemic

3. Nephropathy :

Normal	
Hypertrophy - hyperfiltration stage	
Incipient nephropathy	
Stage of microalbuminuria	
Overt diabetic nephropathy	
End stage renal disease	

4. Miscellaneous :

Hypertensive retinopathy
Neuropathy
Cardiovascular disease

INVESTIGATIONS

A. HEMATOLOGICAL:		**NORMAL**
Blood Urea:	mg%	10- 40 mg%
Serum Creatinine:	mg%	0.5- 1.4mg%
Serum Cholesterol:	mg%	1 50- 250 mg%
Serum Electrolytes: Sodium:	mEq/L	127- 147 mEq/L
Potassium:	mEq/L	3.0-5.0 mEq/L
Chlorides:	mEq/L	60- 100 mEq/L
Haemoglobin:	gml%	12.5- 15gm %
TLC: DLC : Neutrophils: Lymphocytes: Eosinophils: Basophils: Monocytes:	Cells/cu. mm. % % % % %	5,000-10,000 cells/cumm 50 - 70% 20 - 35% 2 - 8% 0 - 1% 0 - 2%
ESR:	mm/hour	0- 20 mm at the end of 1 hour
B. URINE : Sugar : Albumin : Microalbuminuria: (24-hour specimen) 24 hour protein or Protein: Creatinine ratio: 24-hour Creatinine clearance Microscopy : WBC : RBC : Epithelial cells : Culture :	 mg/ day mg/ day ml/ min cells/ HPF cells/ HPF cells/ HPF	 Absent Absent 2.5-17 mg/day <300 mg/ day 105 - 140 ml/ min

ANNEXURE III – PHOTOGRAPHS

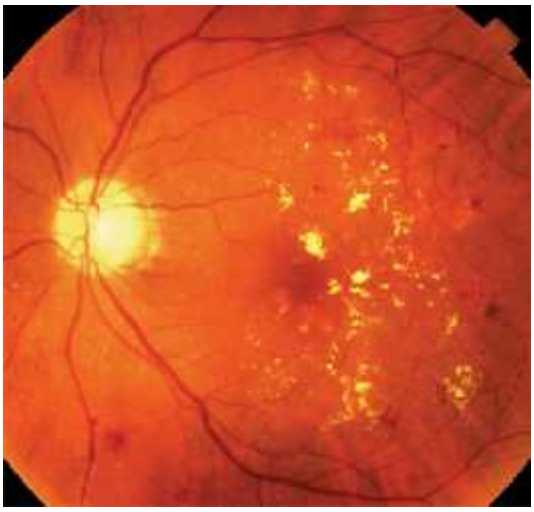


Figure 1: Background diabetic retinopathy

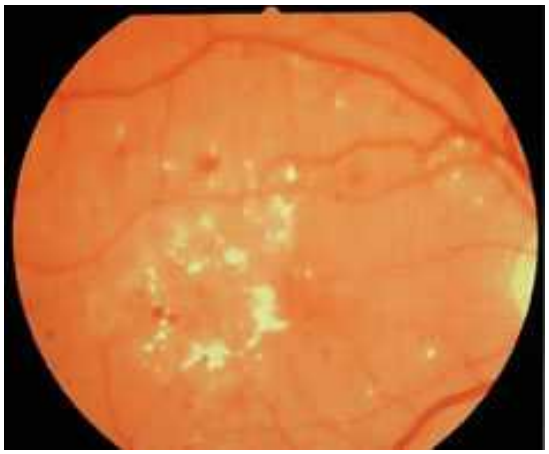


Figure 2: Diabetic maculopathy

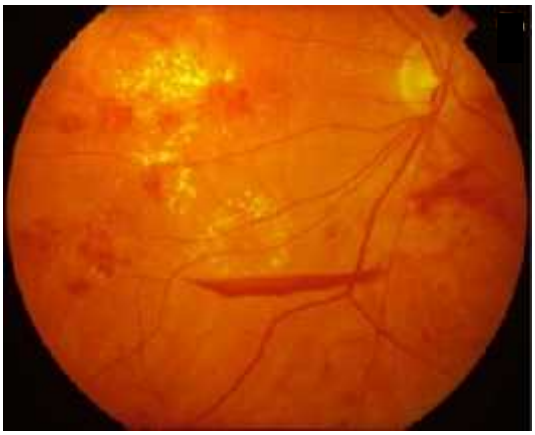


Figure 3: Preproliferative diabetic retinopathy

Figure 4: Proliferative diabetic retinopathy

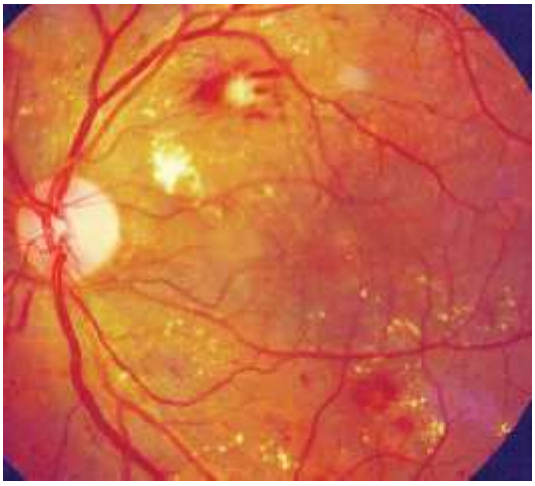


Figure 5: Advanced diabetic disease

Figure 6: Tractional retinal detachment

ANNEXURE IV - MASTER CHART

				History																						General Physical Examination			Ocular Examination										
				Diabetes				Vision								HTN		Renal Dialysis			Family		Personal						Vision		Pin hole		Refraction				Conjunctiva		Cor
								Visual Loss						Ocular Surgery																									
						Rx		Duration		BCVA		Onset																					Distance		Near				
Sl. No.	IP / OP No.	Gender	Age (Years)	Duration (Years)	Diagnosis	Oral	Insulin	Right	Left	Right	Left	Right	Left	Right	Left	Duration (Years)	Treatment	Duration	Frequency	Other	Diabetes mellitus	Ocular Disease	Smoking	Alcohol	Tobacco	BP (mm Hg)	Oedema	Pallor	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left	Right
1	579337	Ml	60	6	ND	+	+	2Y	2Y	6/12	6/12	G	G	CAT	CAT	4	+	1Y	3D/W	-	-	-	-	-	-	130/82	-	-	6/12P	6/12P	6/12	6/12	6/12	6/12	NR6	NR6	N	N	N
2	579431	Ml	49	7	ND	+	+	2Y	2Y	6/9	6/9	G	G	-	CAT	3	+	1.5Y	2D/W	-	-	-	-	+	-	130/92	-	+	6/24	6/36	6/12	6/9	6/9	6/9	NR6	NR6	N	N	N
3	1058524	Ml	69	6	ND	+	+	2Y	2Y	6/12	6/9	G	G	CAT	CAT	5	+	3M	2D/W	-	-	-	-	+	+	140/100	+	+	6/12P	6/12P	6/12	6/12	6/12	6/9	NR6	NR6	N	N	N
4	767879	Ml	60	8	ND	+	+	6M	6M	6/12	6/12	G	G	CAT	CAT	5	+	1.5Y	3D/W	-	-	-	-	-	-	140/92	-	-	6/12P	6/12P	6/12	6/12	6/12	6/12	NR6	NR6	N	N	N
5	325981	Ml	60	8	ND	+	+	2Y	2Y	6/9P	6/9P	G	G	CAT	CAT	8	+	1Y2M	3D/W	-	-	-	-	-	-	150/100	-	+	6/18	6/18	6/12	6/12	6/9P	6/9P	NR6	NR6	N	N	N
6	582121	Ml	45	5	ND	+	+	6M	6M	6/36	6/36	G	G	-	-	5	-	4M	2D/W	-	-	-	-	-	-	130/92	-	+	6/60	6/60	6/36	6/36	6/60	6/60	NR8	NR8	N	N	N
7	585112	F	61	12	ND	+	+	3Y	3Y	6/18	CFIMT	G	G	-	-	2	+	1.5Y	3D/W	-	-	-	-	-	-	120/80	+	+	6/18	CF1MT	6/12	CF1MT	6/12	-	NR10	-	N	N	N
8	705515	Ml	60	16	ND	+	+	2Y	2Y	6/12	6/12	G	G	-	-	10	+	1Y	3D/W	-	-	-	+	+	-	130/96	+	+	6/18	6/18	6/12	6/12	6/12	6/12	NR10	NR10	N	N	N
9	922063	Ml	60	20	ND	+	+	2Y	2Y	6/12	6/12	G	G	-	-	-	-	2Y	3D/W	-	-	-	-	-	-	130/96	+	-	CF3MT	CF3MT	6/18	6/18	6/12	6/12	NR10	NR10	N	N	N
10	578487	Ml	42	3	ND	+	-	2Y	2Y	6/9	6/9	G	G	-	-	6	+	4M	1D/W	-	-	-	-	-	-	140/80	-	+	6/18	6/12	6/9	6/9	6/9	6/9	NR6	NR6	N	N	N
11	578230	Ml	61	6	ND	+	+	4Y	4Y	6/9P	6/9P	G	G	CAT	CAT	3	+	1Y	2D/W	-	-	-	-	-	-	140/80	-	+	6/12P	6/12P	6/9P	6/9	6/9	6/9	NR6	NR6	N	N	N
12	917166	Ml	60	17	ND	+	+	10Y	10Y	6/24P	6/24P	G	G	-	-	1	+	1Y	2D/W	-	-	-	-	-	-	140/80	-	+	6/60	6/60	6/24	6/24	6/24P	6/24P	NR6	NR6	N	N	N
13	1107705	F	57	6	ND	-	-	6M	6M	6/12	6/12	G	G	-	-	3	+	2M	1D/W	-	-	-	-	-	-	130/96	-	+	6/36	6/36	6/12	6/12P	6/12	6/12	NR6	NR6	N	N	N
14	1058524	Ml	60	2	ND	+	-	2Y	2Y	6/12	6/12	G	G	-	-	1	+	6M	1D/W	-	-	-	-	-	-	130/88	+	-	6/24	6/24	6/12	6/12	6/12	6/12	NR6	NR6	N	N	N
15	837727	Ml	60	4	ND	+	+	1W	1W	CFCF	CFCF	S	S	-	-	7	+	2Y	3D/W	-	-	-	+	+	+	170/110	+	+	CFCF	CFCF	-	-	-	-	-	-	N	N	N
16	986554	F	55	18	ND	-	+	1.5Y	1.5Y	-	-	G	G	-	-	7	-	2Y	3D/W	-	-	-	-	-	-	130/90	+	+	6/24P	CF2MT	6/18P	-	-	-	-	-	N	N	N
17	589348	Ml	64	14	ND	+	+	2.5Y	2.5Y	6/12P	6/12P	G	G	CAT	CAT	12	+	1.5Y	2D/W	-	-	-	-	-	-	170/110	-	+	6/12P	6/12P	6/12	6/12	6/12	6/12	NR6	NR6	N	N	N
18	848838	Ml	56	9	ND	+	+	1Y	1Y	6/12	6/12	G	G	-	-	5	-	2M	1/DW	-	+	-	-	-	-	130/92	-	+	6/24	6/36	6/12	6/12P	6/12	6/12P	NR6	NR6	N	N	N
19	1059289	Ml	41	7	ND	+	+	6M	6M	6/6P	6/6P	G	G	-	-	-	-	1M	1D/W	-	-	-	+	-	-	120/80	-	+	6/9	6/9	6/6P	6/6P	6/6P	6/6P	NR6	NR6	N	N	N
20	580173	Ml	62	12	ND	+	+	1Y	1Y	6/12	6/12	G	G	-	-	10	+	3Y	2D/W	-	-	-	-	-	-	150/90	+	+	6/24	6/24	6/12	6/12	6/12	6/12	NR6	NR6	N	N	N
21	768912	F	53	5	ND	-	-	1Y	1Y	6/6P	6/6P	G	G	-	-	-	-	6M	2D/W	-	-	-	-	-	-	120/80	-	-	6/9	6/9	6/6P	6/6P	6/6	6/6	NR6	NR6	N	N	N
22	897163	Ml	50	2	ND	+	-	1Y	1Y	6/18	6/18	G	G	-	-	5	+	8M	2D/W	-	-	-	+	+	+	140/100	-	+	6/16	6/36	6/24P	6/24P	6/18	6/18	NR6	NR6	N	N	N
23	590129	F	62	1	ND	+	+	2Y	2Y	6/18	6/36	G	G	CATSX	CATSX	12	+	2Y	3D/W	-	+	-	-	-	-	128/80	+	+	6/60	6/60	6/18P	6/36	6/18	6/36	NR10	NR10	N	N	N
24	848739	F	52	8	ND	+	+	2Y	2Y	-	-	G	G	-	-	5	+	1Y	3D/W	-	+	-	-	-	-	140/110	+	+	6/36	CF3MT	6/24	6/60	-	-	-	-	PTY	PTY	N
25	880782	Ml	55	6	ND	+	-	5Y	5Y	6/18	6/18	G	G	CATSX	CATSX	2	-	3M	2D/W	-	-	-	-	-	-	140/100	-	+	6/36	6/36	6/24	6/24	6/18P	6/18P	NR6	NR6	N	N	N
26	578772	F	60	3	ND	+	+	6M	6M	6/9	6/9	G	G	-	-	6M	-	6M	2D/W	-	+	-	-	-	-	130/90	-	-	6/12P	6/12P	6/9	6/9	6/9	6/9	NR6	NR6	GRIIPTY	GRIIPTY	N
27	848812	F	45	15	ND	+	+	6M	6M	HMCF	HMCF	G	G	-	-	2	+	10M	3D/W	-	-	-	-	-	-	130/80	-	+	HMCF	HMCF	HMCF	HMCF	HMCF	HMCF	-	-	N	N	N
28	1080979	Ml	68	6	ND	+	-	6M	6M	6/12	6/12	G	G	-	-	6	+	1.5Y	2D/W	-	-	-	-	-	-	130/90	-	+	6/24	6/24	6/12	6/12	6/12	6/12	NR12	NR12	PTY	PTY	N
29	395715	F	65	15	ND	+	+	2Y	6Y	CF3MT	CF3MT	G	G	CATSX	CATSX	15	+	2Y	3D/W	-	+	-	-	-	-	130/90	+	+	CF3MT	6/60	6/60	6/36P	6/60	6/36P	-	-	N	N	N
30	3244092	Ml	55	18	ND	+	+	2Y	2Y	PLPR	PLPR	S	S	CATSX	CATSX	18	+	1M	2D/W	-	+	+	+	+	-	130/92	+	+	PL PR	PL PR	-	-	-	-	-	-	N	N	N
31	720462	Ml	60	8	ND	+	+	8M	8M	CF2 MT	CF2 MT	G	G	CATSX	CATSX	10	+	1.5	2D/W	-	-	-	-	-	-	130/90	+	+	CF2MT	CF2MT	-	-	-	-	-	-	N	N	N
32	580111	Ml	65	20	ND	+	+	6M	6M	6/18	6/18	G	G	CATSX	CATSX	20	+	1.5Y	3D/W	-	+	-	-	-	-	130/90	+	-	6/18P	6/18P	6/18	6/18	6/18	6/18	NR6	NR6	N	N	N
33	579575	Ml	60	3	ND	+	+	2Y	2Y	6/9	6/9	G	G	-	-	6M	+	4M	2D/W	-	+	-	-	-	+	120/80	+	+	6/12	6/12	6/9	6/9	6/9	6/9	NR6	NR6	N	N	N

		Ocular examination				Fundus Examination																	Investigations					Visual Outcome	
	hea	Lens		IOP		Glow		Media		Disc		CD Ratio		Vessels		Macula		Background		Diagnosis			Haematological						
Sl. No.	Left	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left	FFA	Blood Urea (mg/dL)	Sr. Creatinine (mg/dL)	Haemoglobin (%)	ESR (mm/hr)	RBS (mg%)	Ocular changes	Treatment
1	N	PCIOL	PCIOL	17.3	17.3	+	+	CL	CL	N	N	0.3	0.3	N	N	N	N	PRP	PRP	PDR PRP	PDR PRP	+	135	11.5	9.5	18	162	PDR PRP	CAT SX PRP
2	N	GRIINS	PCIOL	17.3	17.3	+	+	H	CL	-	N	-	0.3	-	N	-	N	-	PDR	CAT	PDR PRP	-	36	1.8	8	20	129	RE CAT LE PDR	CAT SX PRP
3	N	PCIOL	PCIOL	17.3	17.3	+	+	CL	CL	N	N	0.3	N	ANVD	ANVD	N	N	BDR	BDR	BDR	BDR	-	162	4.6	4.8	12	180	BDR	CAT SX
4	N	PCIOL	PCIOL	20.6	20.6	+	+	CL	CL	N	N	0.4	0.4	ANVD	ANVD	N	N	PPDR	PPDR	PPDR	PPDR	-	56	11.8	7.1	12	160	BDR	CAT SX
5	N	PCIOL	PCIOL	20.6	18.2	+	+	CL	CL	N	N	0.4	0.4	ANVD	ANVD	N	N	PDR	PDR	PDR PRP	PDR PRP	-	42	11.1	11.8	18	200	PDR PRP	CAT SX
6	N	GRIIINS	GRIINS	20.6	20.6	+	+	H	H	-	-	-	-	-	-	-	-	-	-	CAT	CAT	-	92	5.6	11	10	125	CAT	-
7	N	GRINS	GRIIINS WITH PSC	20.4	20.4	+	+	H	H	-	-	-	-	-	-	-	-	-	-	CAT	CAT	-	122	8.2	7.3	20	123	CAT	-
8	N	GRINS	GRINS	18.4	18.4	+	+	CL	CL	N	N	0.3	0.3	ANVD	ANVD	CSME	CSME	PDR PRP	PDR PRP	PDR PRP	PDR PRP	+	84	9.8	8.2	20	106	CAT PDR	PRP
9	N	GRINS	GRINS	16.4	16.4	+	+	CL	CL	N	N	0.4	0.4	ANVD	ANVD	N	N	PPDR	PPDR	PPDR	PPDR	-	104	8.6	11	26	140	PPDR	-
10	N	GRINS	GRINS	20.4	20.4	+	+	CL	CL	N	N	0.3	1.3	ANVD	ANVD	N	N	N	N	BDR HR	BDR HR	-	88	2.6	12	8	128	BDRC HR	-
11	N	PCIOL	PCI102	17.3	17.3	+	+	CL	CL	N	N	0.3	0.3	ANVD	ANVD	CSME	CSME	NVD	NVD	PDR PRP	PDR PRP	-	30	1.8	14.1	14	140	PDRPRP	CAT SX
12	N	GRIIINS	GRIIINS WITH PSC	17.3	17.3	+	+	H	H	-	-	-	-	-	-	-	-	-	-	CAT	CAT	+	26	0.9	9	11	120	CAT	PRP
13	N	GRINS	GRINS	20.4	20.4	+	+	CL	CL	N	N	0.3	0.3	ANVD	ANVD	N	N	BDR	BDR	BDR	BDR	-	96	4.8	8	26	150	BDR	-
14	N	GRINS	GRINS	14.6	14.6	+	+	CL	CL	N	N	0.3	0.3	N	N	N	N	BDR	BDR	BDR	BDR	-	49	2.6	12	11	136	BDR	-
15	N	GRINS	GRINS	8	12	+	+	CL	CL	Pap	Pap	-	-	AN	AN	N	N	RD	RD	RD	RD	-	49	2.9	4.8	12	188	RD	-
16	N	GRIINS	GRINS	17.3	17.3	+	+	H	H	N	N	0.4	0.4	AN	AN	CSME	CSME	PDR	PDR	PDR PRP	PDR PRP	-	56	4.4	6.9	22	200	CAT PDR	-
17	N	PCIOL	PCI102	17.3	17.3	+	+	CL	CL	N	N	0.5	0.5	ANVD	ANVD	N	N	PDR	PDR	PDR PRP	PDR	+	164	12.2	8.5	16	98	PDP	PRP CAT SX
18	N	GRII NS	GRIINS	17.3	17.3	+	+	CL	CL	N	N	0.3	0.3	AN	AN	N	N	BDR	BDR	BDR	BDR	-	89	6.4	8.8	11	150	BDR	-
19	N	CL	CL	14.6	14.6	+	+	CL	CL	N	N	0.3	0.3	N	N	N	N	BDR	BDR	BDR	BDR	-	104	3.6	1.4	10	110	BDR	-
20	N	GRII NS	GRIINS	17.3	17.3	+	+	CL	CL	N	N	0.5	0.5	AN	AN	N	N	PPDR	PPDR	PPDR	PPDR	-	56	2.9	9.4	8	132	PPDR	-
21	N	GRINS	GRINS	17.3	17.3	+	+	CL	CL	N	N	0.3	0.3	ANVD	ANVD	N	N	BDR	BDR	BDR	BDR	-	69	2.2	8	6	298	BDR	-
22	N	GRIINS	GRIINS	17.3	17.3	+	+	CL	CL	N	N	0.3	0.3	AN	AN	N	N	GRII HTR	GRII HTR	GRIIHTR	GRIIHTR	-	99	6.4	6.8	11	86	GRIIHTR	-
23	N	PCIOL	PCIOL	17.3	17.3	+	+	CL	CL	N	N	0.3	0.3	ANVD	ANVD	CSME	N	NVE	NVE	PDR	PDR	-	49	2.8	9.4	18	138	PDR	-
24	N	GRIINS	GRIINS	17.3	20.6	+	+	H	H	N	N	0.4	0.4	ANVD	ANVD	N	N	NVE	NVE	PDR	PDR	+	186	14.4	6.8	19	230	PDR	-
25	N	PCIOL	PCIOL	20.6	20.6	+	+	CL	CL	PALP	PALP	0.6	0.5	ANVD	ANVD	N	N	PDPR GIV	PDPR GRIV	PPDR	PPDR	-	40	1.6	12.8	10	102	PPDR	-
26	N	GRIINS	GRIINS	17.3	17.3	+	+	CL	CL	N	N	0.3	0.3	ANVD	ANVD	N	N	BDR	BDR	BDR	BDR	-	59	1.8	12	20	102	BDR	-
27	N	GRIINS	GRIINS	20.4	20.4	+	+	H	H	-	-	-	-	-	-	-	-	VH	VH	ADR VH	ADR VH	-	89	5.6	13.6	16	130	PPDR VH	-
28	N	GRINSC	GRINS.PSC	17.3	17.3	+	+	CL	CL	N	N	0.3	0.3	ANVD	ANVD	N	N	BDR	BDR	BDR	BDR		12	0.8	14.6	12	108	BDR	-
29	N	PCIOL	PCIOL	17.3	17.3	+	+	CL	CL	N	N	0.3	0.3	ANVD	ANVD	N	N	PDR LASERS	PDR LASERS	PDR	PDR	+	104	9	8.8	14	230	PDR	LASER
30	N	PCIOL	PCIOL	10.0	12.0	+	+	CL	CL	-	-	-	-	-	-	-	-	RD	RD	RD	RD	-	99	6.4	6.8	11	280	RD	-
31	N	PCIOL	PCIOL	14	14	+	+	H	H	-	-	-	-	-	-	-	-	VH	VH	PDR VH	PDR VH	+	68	2.8	12.6	14	180	VHPDR	-
32	N	PCIOL	PCIOL	17.3	17.3	+	+	CL	CL	N	N	0.4	0.4	ANVD	ANVD	N	N	PPDR	PPDR	PPDR	PPDR	-	99	4.8	13	4	180	PPDR	-
33	N	GRINS	GRINS	14.3	14.3	+	+	CL	CL	N	N	0.3	0.3	ANVD	ANVD	N	N	BDR	BDR	BDR	BDR	-	56	1.8	9.4	16	190	BDR	-

Sl. No.	IP / OP No.	Gender	Age (Years)	History																																Ocular Examination										
				Diabetes				Vision								HTN		Renal Dialysis			Family		Personal			General Physical Examination				Vision		Pin hole		Refraction				Conjunctiva		Cor
						Rx		Visual Loss						Ocular Surgery																				Distance		Near				
								Duration		BCVA		Onset																													
				Duration (Years)	Diagnosis	Oral	Insulin	Right	Left	Right	Left	Right	Left	Right	Left	Duration (Years)	Treatment	Duration	Frequency	Other	Diabetes mellitus	Ocular Disease	Smoking	Alcohol	Tobacco	BP (mm Hg)	Oedema	Pallor	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left	Right
34	636033	F	62	5	ND	+	+	3Y	3Y	6/12	6/12	G	G	-	-	6	+	6M	2D/W	-	-	-	-	-	-	120/80	+	+	6/18	6/18	6/12P	6/12P	6/12P	6/12P	NR6	NR6	N	N	N
35	958732	Ml	71	6	ND	-	+	-	-	6/9	6/9	-	-	-	-	-	-	1M	1D/W	-	+	-	-	-	-	120/80	-	+	6/12	6/12	6/9	6/9	6/9	6/9P	NR6	NR6	N	N	N
36	1143042	Ml	48	1	ND	-	+	1Y	1Y	6/24P	6/24P	G	G	-	-	-	-	3M	2D/W	-	-	-	+	+	+	144/88	-	+	6/60	6/60	6/24	6/24	6/24	6/24	NR6	NR6	N	N	N
37	954366	Ml	28	2	ND	+	-	-	-	6/24	6/24	-	-	-	-	-	-	1M	1D/W	-	-	-	+	+	-	120/80	-	-	6/36	6/36	6/24	6/24	6/24	6/24	NR6	NR6	N	N	N
38	116174	Ml	70	7	ND	+	+	2.5Y	2.5Y	-	-	G	G	-	-	4	+	2M	2D/W	-	+	-	-	-	+	130/98	-	-	CFCF	CFCF	-	-	-	-	-	-	N	N	N
39	1180217	Ml	48	3	ND	-	+	-	-	6/12	6/12	-	-	-	-	-	-	6M	1/W	-	-	-	+	-	-	120/80	-	-	6/18	6/12P	6/12	6/12	6/12	6/12	NR6	NR6	N	N	N
40	1021510	Ml	53	4	ND	-	+	1Y	1Y	6/24	6/24	G	G	-	-	2	+	8M	2D/W	-	+	-	-	+	-	140/98	-	-	6/36	6/36	6/24	6/24	6/24	6/24	NR10	NR10	N	N	N
41	750764	F	38	1	ND	+	-	-	-	6/9	6/9	-	-	-	-	-	-	2M	1D/W	-	-	-	-	-	-	130/98	-	+	6/12	6/12	6/9	6/9	6/9	6/9	NR6	NR6	N	N	N
42	1189592	Ml	54	3	ND	+	-	6M	6M	6/18	6/18	G	G	-	-	5	+	8M	2D/W	-	-	-	+	-	+	140/90	+	+	6/24	6/24	6/18	6/18	6/18	6/18	NR12	NR12	N	N	MO
43	579337	Ml	60	10	ND	+	+	5Y	5Y	CF3MT	CF3MT	G	G	+	+	10	+	1Y	2D/W	-	+	-	-	-	+	140/100	-	+	CF3MT	CF3MT	CF3MT	CF3MT	CF3MT	CF3MT	NR36	NR36	N	N	N
44	920443	Ml	63	4	ND	+	+	1Y	1Y	6/36	6/36	G	G	-	-	6	+	4M	3/W	-	+	-	+	+	+	130/90	+	+	6/60	6/60	6/36	6/36	6/36	6/36	NR10	NR10	N	N	N
45	740225	Ml	58	2	ND	+	+	6M	6M	6/12	6/12	G	G	-	-	7	+	10M	2/W	-	-	-	-	-	-	140/90	-	-	6/18	6/18	6/12	6/12	6/12	6/12	NR6	NR6	N	N	N
46	339700	Ml	50	5	ND	+	+	6M	3M	CF1MT	6/60	G	G	-	-	3	+	1Y	2/W	-	-	-	-	-	-	150/80	-	-	CF3MT	CF3MT	-	6/60	-	6/60	NR36	NR36	N	N	N
47	582121	Ml	28	3	ND	+	-	6M	6M	6/18	6/18	G	G	-	-	3	+	3M	1D/W	-	-	-	-	+	-	130/80	-	-	6/24	6/36	6/18	6/18	6/18	6/18	NR6	NR6	N	N	N
48	832012	Ml	63	2	ND	+	-	3M	3M	6/9	6/9	G	G	CAT	CAT	1	+	6M	1D/W	-	-	-	-	-	-	169/90	-	-	6/12	6/12	6/9	6/9	6/9	6/9	NR6	NR6	N	N	N
49	1018460	F	48	3	ND	-	+	1Y	1Y	6/8	6/8	G	G	-	-	-	-	10M	2/W	-	-	-	+	-	+	120/70	-	-	6/9	6/9	6/8	6/8	6/8	6/8	NR6	NR6	N	N	N
50	494027	F	48	10	ND	+	+	1Y	1Y	6/12	6/12	G	G	-	-	5	+	1Y	1D/W	-	-	-	-	-	-	140/90	-	+	6/18	6/12	6/12	6/12	6/12	6/12	NR6	NR6	N	N	N

		Ocular examination				Fundus Examination																	Investigations					Visual Outcome	
	hea	Lens		IOP		Glow		Media		Disc		CD Ratio		Vessels		Macula		Background		Diagnosis			Haematological						
Sl. No.	Left	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left	FFA	Blood Urea (mg/dL)	Sr. Creatinine (mg/dL)	Haemoglobin (%)	ESR (mm/hr)	RBS (mg%)	Ocular changes	Treatment
34	N	GRINS	GRINS	17.3	20.6	+	+	CL	CL	N	N	0.3	0.3	ANVD	ANVD	N	N	GRII HTR	GRII HTR	GRII HTR	GRII HTR	-	88	2.6	12	14	180	GRIIHTR	-
35	N	GRINS	GRINS	14.6	14.6	+	+	CL	CL	N	N	0.3	0.3	N	N	N	N	N	N	-	-	-	104	8.6	11	26	171	-	-
36	N	GRINS	GRINS	17.3	17.3	+	+	CL	CL	N	N	0.3	0.3	ANVD	ANVD	N	N	BDR	BDR	BDR	BDR	-	69	4.8	8	26	130	BDR	-
37	N	CL	CL	20.4	20.4	+	+	CL	CL	N	N	0.3	0.3	N	N	N	N	N	N	-	-	-	40	5	12	20	120	-	-
38	N	GRIINS PSC	GRIINS PSC	20.6	20.6	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	94	5.2	9.8	20	120	CAT	-
39	N	CL	CL	14.6	17.3	+	+	CL	CL	N	N	0.2	0.2	N	N	N	N	N	N	N	N	-	75	8.8	11	13	167	-	-
40	N	CL	CL	17.3	17.3	+	+	CL	CL	N	N	0.3	0.3	N	N	N	N	N	N	GRIIHTR	GRIIHTR	-	70	5.9	9	11	102	GRIIHTR	-
41	N	CL	CL	14.6	14.6	+	+	CL	CL	N	N	0.3	0.3	N	N	N	N	N	N	N	N	-	99	6.9	7	24	130	-	-
42	N	CL	CL	17.3	17.3	+	+	CL	CL	N	N	0.3	0.3	ANVD	ANVD	ARMD	ARMD	N	N	ARMD	ARMD	-	79	5.8	9.2	20	123	ARMD	-
43	N	GRIINS	GRIINS	17.3	14.6	+	+	H	H	N	N	0.3	0.3	ANVD	ANVD	N	N	PDR	PDR	PDR	PDR	-	68	4.9	10	12	169	PDR	-
44	N	CL	CL	17.3	17.3	+	+	CL	CL	N	N	0.3	0.3	ANVD	ANVD	N	N	N	N	N	N	-	87	11	10.8	15	160	-	-
45	N	GRINS	GRINS	17.3	17.3	+	+	CL	CL	N	N	0.3	0.3	ANVD	ANVD	N	N	GRII HTR	GRII HTR	GRIIHTR	GRIIHTR	-	90	18	110	21	130	GRIIHTR	-
46	N	CL	CL	17.3	17.3	+	+	CL	CL	N	N	0.3	0.3	ANVD	ANVD	N	N	PPDR	PPDR	PPDR	PPDR	-	110	13	10.1	13	140	PPDR	-
47	N	CL	CL	14.6	14.6	+	+	CL	CL	N	N	0.3	0.3	ANVD	ANVD	N	N	BDR HTR	BDR HTR	BDR HTR	BDR HTR	-	66	5.6	11.2	22	188	BDR HTR	CAT SX
48	N	CL	CL	17.3	14.6	+	+	CL	CL	N	N	0.3	0.3	ANVD	ANVD	N	N	N	N	N	N	-	70	2.1	10.2	18	138	-	-
49	N	CL	CL	17.3	17.3	+	+	CL	CL	N	N	0.3	0.3	ANVD	ANVD	N	N	BDR CSMC	BDR CSMC	BDR CSMC	BDR CSMC	-	88	4.1	10.3	11	206	BDRE CSMC	-
50	N	GR I NS	GR I NS	17.3	17.3	+	+	CL	CL	N	N	0.3	0.3	ANVD	ANVD	N	N	PPDR	PPDR	PPDR	PPDR	-	108	6.5	7.8	12	210	PPDR	-

ANNEXURE IV

KEY TO MASTER CHART

-	-	Absent
/W	-	Per week
+	-	Present
AN	-	Arterial narrowing
ANVD	-	Arterial narrowing venous dilatation
ARMD	-	Age related macular degeneration
BCVA	-	Best corrected visual acuity
BDR	-	Background diabetic retinopathy
CAT	-	Cataract
CATSX	-	Cataract surgery
CD ratio	-	cup disc ratio
CF	-	Counting finger
CFCF	-	Counting finger close to face
CSME	-	Clinically significant macular oedema
D/W	-	Day per week
ERD	-	Exudative retinal detachment
ESR	-	Erythrocyte sedimentation rate
F	-	Female
FFA	-	Fundus fluoroscein angiography
G	-	Gradual
GR	-	Grade

HMCF	-	Hand movements close to face
HTN	-	Hypertension
HTR	-	Hypertensive retinopathy
IOP	-	Intra ocular pressure
IP. No.	-	In patients number
M	-	Month
Ml	-	Male
mg	-	Milligram
mg/dL	-	Milligram per deciliter
mm Hg	-	Millimeters of mercury
MT	-	Meter
N	-	Normal
ND	-	Non insulin dependent diabetes mellitus
NR	-	Near vision
NS	-	Nucleosclerosis cataract
NVE	-	Neovascularization elsewhere
OP. No.	-	Outpatients number
Pap	-	Papilloedema
PCIOL	-	Posterior capsule intraocular lens
PDR	-	Proliferative diabetic retinopathy
PLPR	-	Perception of light projection of rays
PPDR	-	Preproliferative diabetic retinopathy
PRP	-	Pan retinal photocoagulation
PSC	-	Posterior subcapsular cataract

PTY	-	Pterygium
RBS	-	Random blood sugar
RD	-	Retinal detachement
Rx	-	Treatment
Sl. No.	-	Serial number
Sr	-	Serum
VH	-	Vitreous haemorrhage
Y	-	Year