A Dissertation on

ASSOCIATION BETWEEN DIABETIC RETINOPATHY AND THE NEUTROPHIL LYMPHOCYTE RATIO, PLATELET LYMPHOCYTE RATIO, MONOCYTE LYMPHOCYTE RATIO.

Dissertation Submitted to

THE TAMILNADU Dr. M.G.R. MEDICAL UNIVERSITY

CHENNAI - 600 032

With partial fulfillment of the regulations

for the award of the degree of

M.D. GENERAL MEDICINE

BRANCH-I

COIMBATORE MEDICAL COLLEGE

COIMBATORE

MAY 2018

CERTIFICATE

Certified that this is the bonafide dissertation done by **Dr.KIRUTHIKA J** and submitted in partial fulfillment of the requirements for the Degree of **M.D., General Medicine**, Branch I of **The Tamilnadu Dr. M.G.R. Medical University, Chennai.**

Date:

Guide, Professor & Chief
Medical Unit I

Date:

Professor & Head
Department of Medicine

Date:

Dean
Coimbatore Medical College
Coimbatore

DECLARATION

I solemnly declare that the dissertation titled **"Association between Diabetic retinopathy and the Neutrophil lymphocyte ratio, Platelet lymphocyte ratio, Monocyte lymphocyte ratio"** was done by me from JULY 2016 to JUNE 2017 under the guidance and supervision of Professor **Dr. KUMAR NATARAJAN. M.D.,**

This dissertation is submitted to **The Tamilnadu Dr.M.G.R. Medical University** towards the partial fulfilment of the requirement for the award of MD Degree in General Medicine (Branch I).

Place: Coimbatore **Dr. KIRUTHIKA J**

Date:

ACKNOWLEDGEMENT

I wish to express my sincere thanks to our respected **Dean Dr. B.ASHOKAN, M.S**,**Mch** for having allowed me to conduct this study in our hospital.

I express my heartfelt thanks and deep gratitude to the Head of the Department of Medicine Prof. **Dr. KUMAR NATARAJAN, M.D**. for his generous help and guidance in the course of the study.

I owe a great debt of gratitude to our respected Professor and unit chief Prof. **Dr. KUMAR NATARAJAN, M.D** without whose help and advice this work would not have been possible.

I sincerely thank all professors and Asst. Professors - **Dr. P. VISHNURAM, MD, Dr.N. KARUPPUSAMY,M.D, Dr.A.AKILA, M.D, Dr.SANGEETHA M.D**, for their guidance and kind help.

I also extend my gratitude to Prof. **Dr.M.HEMANANDHINI,MS, DO.,** Department of ophthalmology for her support and expert guidance.

I am extremely grateful to **Dr. MANIMEGALAI, M.D** (Bio), HOD, Department of Biochemistry, for their valuable help and cooperation and allowing me to use institutional facilities.

My sincere thanks to all my friends and post-graduate colleagues for their whole hearted support and companionship during my studies.

I thank all my **PATIENTS**, who formed the backbone of this study without whom this study would not have been possible.

Lastly, I am ever grateful to the **ALMIGHTY GOD** for always showering His blessings on me and my family.

DATE: **Dr. KIRUTHIKA J**

PLACE:

CERTIFICATE – II

This is to certify that this dissertation work titled "**Association between Diabetic retinopathy and the Neutrophil lymphocyte ratio, Platelet lymphocyte ratio, Monocyte lymphocyte ratio"** of the candidate DR.KIRUTHIKA J with registration Number 201511303 for the award of M.D in the branch of General Medicine I personally verified the urkund.com website for the purpose of plagiarism Check. I found that the uploaded thesis file contains from introduction to conclusion pages and result shows 3% (three percentage) of plagiarism in the dissertation.

Guide & Supervisor sign with Seal.

Coimbatore Medical College

COIMBATORE, TAMILNADU, INDIA - 641 014

(Affiliated to The Tamilnadu Dr. MGR Medical University, Chennai)

ETHICS COMMITTEE

CERTIFICATE

Name of the Candidate : DR. KIRUTHIKA. J.

Course : M.D. GENERAL MEDICINE

Period of Study : ONE YEAR

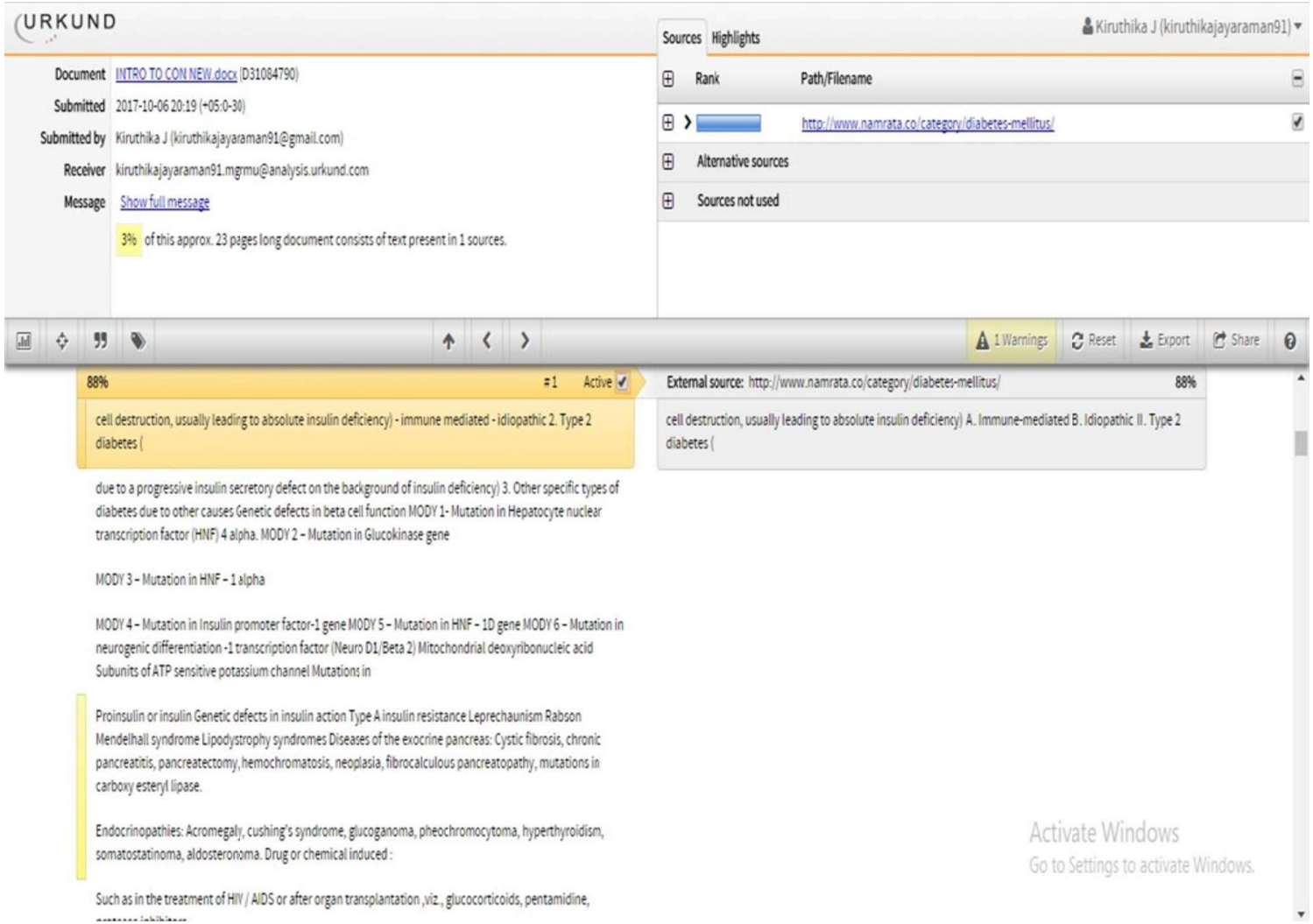
College : COIMBATORE MEDICAL COLLEGE.

Dissertation Topic : ASSOCIATION BETWEEN DIABETIC RETINOPATHY AND THE NEUTROPHIL - LYMPHOCYTE RATIO, PLATELET LYMPHOCYTE RATIO, MONOCYTE-LYMPHOCYTE RATIO

The Ethics Committee, Coimbatore Medical College has decided to inform that your Dissertation Proposal is accepted / ~~Not~~ accepted and you are permitted / ~~Not~~ ~~permitted~~ to proceed with the above Study.

Member Secretary
Ethics Committee

22.4.16


URKUND
Kiruthika J (kiruthikajayaraman91)
Sources
Highlights
Document INTRO TO CON NEW.docx (D31084790)
Submitted 2017-10-06 20:19 (+05:0-30)
Submitted by Kiruthika J (kiruthikajayaraman91@gmail.com)
Receiver kiruthikajayaraman91.mgrmu@analysis.urkund.com
Message Show full message
3% of this approx. 23 pages long document consists of text present in 1 sources.
Rank
Path/Filename
http://www.namrata.co/category/diabetes-mellitus/
Alternative sources
Sources not used
1 Warnings
Reset
Export
Share
88%
#1
Active
External source: http://www.namrata.co/category/diabetes-mellitus/
88%
cell destruction, usually leading to absolute insulin deficiency) - immune mediated - idiopathic 2. Type 2 diabetes (
cell destruction, usually leading to absolute insulin deficiency) A. Immune-mediated B. Idiopathic II. Type 2 diabetes (
due to a progressive insulin secretory defect on the background of insulin deficiency) 3. Other specific types of diabetes due to other causes Genetic defects in beta cell function MODY 1- Mutation in Hepatocyte nuclear transcription factor (HNF) 4 alpha. MODY 2 – Mutation in Glucokinase gene
MODY 3 – Mutation in HNF – 1 alpha
MODY 4 – Mutation in Insulin promoter factor-1 gene MODY 5 – Mutation in HNF – 1D gene MODY 6 – Mutation in neurogenic differentiation -1 transcription factor (Neuro D1/Beta 2) Mitochondrial deoxyribonucleic acid Subunits of ATP sensitive potassium channel Mutations in
Proinsulin or insulin Genetic defects in insulin action Type A insulin resistance Leprechaunism Rabson Mendelhall syndrome Lipodystrophy syndromes Diseases of the exocrine pancreas: Cystic fibrosis, chronic pancreatitis, pancreatectomy, hemochromatosis, neoplasia, fibrocalculous pancreatopathy, mutations in carboxy esteryl lipase.
Endocrinopathies: Acromegaly, cushing's syndrome, glucoganoma, pheochromocytoma, hyperthyroidism, somatostatinoma, aldosteronoma. Drug or chemical induced :
Such as in the treatment of HIV / AIDS or after organ transplantation ,viz., glucocorticoids, pentamidine,
Activate Windows
Go to Settings to activate Windows.

URKUND

Urkund Analysis Result

Analysed Document:	INTRO TO CON NEW.docx (D31084790)
Submitted:	10/6/2017 4:49:00 PM
Submitted By:	kiruthikajayaraman91@gmail.com
Significance:	3 %

Sources included in the report:

http://www.namrata.co/category/diabetes-mellitus/

Instances where selected sources appear:

7

LIST OF ABBREVIATIONS

AGEs	–	Advanced Glycation End Products
anti- GAD	–	anti-Glutamic acid decarboxylase
BMI	–	Body mass index
CRP	–	C- reactive protein
CVD	–	Cardiovascular disease
DR	–	Diabetic retinopathy
ER	–	Endoplasmic reticulum
ETDRS	–	Early treatment of diabetic retinopathy study
GDM	–	Gestational diabetes mellitus
HLA	–	Human leucocyte antigen
IAA	–	Islet Autoantibody
ICA	–	Islet cell cytoplasmic autoantibodies
ICMR	–	Indian Council of Medical Research
IDPP	–	Indian Diabetic Prevention Programme
IFG	–	Impaired Fasting Glycemia
IGT	–	Impaired Glucose Tolerance
iNos	–	Inducible nitric oxide synthase
IRMA	–	Intraretinal Microvascular Abnormality
IRS	–	Insulin Receptor Substrate
LADA	–	Latent autoimmune diabetes of Adults
MODY	–	Maturity onset Diabetes of Young

NAD	–	Nicotinamide adenine dinucleotide
NADH	–	Nicotinamide adenine dinucleotide hydrate
NKK	–	NF-KB Kinase
NLR	–	Neutrophil Lymphocyte Ratio
NPDR	–	Non Proliferative Diabetic Retinopathy
OGTT	–	Oral Glucose Tolerance Test
PAI	–	Plasminogen Activator Inhibitor
PDR	–	Proliferative Diabetic Retinopathy
PKC	–	Protein Kinase C
PLR	–	Platelet lymphocyte ratio
ROS	–	Reactive Oxygen Species
T1DM	–	Type 1 Diabetes mellitus
T2DM	–	Type 2 Diabetes mellitus
TGF	–	Transforming Growth factor
TNF	–	Tumour Necrosis Factor
VEGF	–	Vascular Endothelial Growth Factor
WHO	–	World Health Organisation

CONTENTS

LIST OF TABLES

LIST OF CHARTS

LIST OF FIGURES

INTRODUCTION

Diabetes mellitus is a condition in which there is a chronically raised blood glucose concentration. It is caused by an absolute or relative lack of the hormone insulin, i.e. insulin is not being produced from the pancreas or there is insufficient production of insulin or impaired insulin action for the body's needs.

The two main types of diabetes are Type 1 which presents mainly in childhood and early adult life and accounts for about 20% of cases in Europe and North America. It is thought to be caused by autoimmune destruction of insulin producing islet cells of pancreas.

Type 2 Diabetes usually starts in middle age or in the elderly. It is more common accounting for 80% of cases. It is due to either impaired insulin secretion or resistance to the action of insulin at its targets cells. Most of these patients are obese.

One of the most important clinical features of diabetes is its association with chronic tissue complications that occurs after several years of diabetes and affect both small blood vessel (microangiopathy) in the eye, kidney and nerves and large vessels. The frequency of arterial disease (atherosclerosis or microangiopathy) is also markedly increased. Microangiopathy is thought to be related to the duration and severity of hyperglycemia.

Diabetic retinopathy is a serious complication of diabetes mellitus and it is considered as a major cause of blindness in working population. Its pathogenesis is complicated and it is related to many factors, but many groups have described the role of inflammatory markers in the development of diabetic retinopathy.

The WBC and its subtypes Neutrophil lymphocyte ratio, Monocyte lymphocyte ratio and platelet lymphocyte ratio are all novel markers of inflammation. Till date, only few articles have studied the relationship between the occurrence of diabetic microvascular complication and the markers of inflammation.

AIM OF STUDY

The aim of my study is to evaluate the association between Diabetic retinopathy and the Neutrophil – Lymphocyte ratio, Monocyte – Lymphocyte Ratio and the Platelet – Lymphocyte Ratio.

REVIEW OF LITERATURE

DIABETES MELLLITUS

Diabetes mellitus is a metabolic disorder involving carbohydrate, protein and fat metabolism resulting from absolute or relative insulin deficiency and resulting in chronic hyperglycemia manifesting with its microvascular and macrovascular complications. In fact diabetes can have a long variable asymptomatic period of 5 years to 15 years and may be diagnosed for the first time because of its comorbities or complications.

The long term effects of diabetes include damage, dysfunction and failure of various other organs which includes progressive development of retinopathy with potential blindness, nephropathy that may lead to renal failure, neuropathy with risk of foot ulcers, amputation, charcot joints and features of autonomic dysfunction including sexual dysfunction. People with diabetes are at increased risk of macrovascular complications like cardiovascular, peripheral vascular and cerebrovascular diseases.

EPIDEMIOLOGY

According to the data collected by World Health Organisation (WHO) in 2016, it is estimated that around 422 million of adults are living with diabetes mellitus. It is mainly due to increase in risk factors for type 2 diabetes mellitus notably sedentary lifestyle, obesity and increased longevity.

TYPE 1 DIABETES

Type 1 diabetes may present at any age, but most typically presents in early life with peak incidence around the time of puberty. Its incidence varies from 50 -100 fold around the world, with the highest among the Northern Europe and in individuals of European extraction. Both the sexes are equally affected in childhood, but men are more commonly affected in early adult life. This distinction between type 1 and type 2 varies in later life and thus true life incidence is unkown. According to DIAMOND study, Finland has the maximum number of patients with Diabetes.

TYPE 2 DIABETES

The World Health Organisation estimated that 9% of the World's population suffered from Diabetes in 2014, over 90% of them had type 2 Diabetes. Moreover type 2 diabetes caused 5 million deaths per year , mostly from cardiovascular disease, and type 2 diabetes is expected to become 7th leading cause of death globally by 2030. Type 2 diabetes is strongly associated with obesity and as such the major burden is now in the middle income and developing countries where urbanization and recent affluence has rapidly changed the lifestyle.

The large population of the Western pacific contributed most to the absolute numbers, while the % prevalence is highest in the Middle east and North Africa. The larger number of diabetics are in the 40-59

age groups (132 million in 2010) which are expected to rise further. By 2030, there will be more diabetic population in the 60 to 79 age groups (196 million).

GESTATIONAL DIABETES

GDM is common in many population including Asian Indians. Pregnant women should be tested for GDM at 24 weeks to 28 weeks of gestation. Gestational diabetes is a prediabetic state with an increased risk of development of the disorder in subsequent pregnancies, in 60 to 90%. It is also known that women with GDM have a high risk upto 30% of developing diabetes within 7 – 10 years of index pregnancy.

PREVALENCE IN INDIA

The prevalence of diabetes in India in 1970s was 2.3% in urban and 1.5% in rural areas as shown by study conducted by ICMR. In 2000s the prevalence gradually increased. India which has a large pool of pre diabetics shows rapid conversion of these high risk subjects to diabetes. The Indian Diabetic Prevention Programme – 1 (IDPP – 1) has shown an annual incidence of approximately 18% among subjects with IGT.

National studies or population based studies on diabetic complications are sparse in India. A few population based studies indicate that the prevalence of retinopathy to be 27% and overt nephropathy is 2.2%. Peripheral vascular disease is prevalent in 6.3%, peripheral neuropathy in 25% and coronary artery disease is seen in 21%.

The major contributory factors for the prevalence of the complications are: delayed diagnosis of diabetes, inadequate control of diabetes, hypertension and lack of awareness about the disease among majority of the public.

Diabetic retinopathy is one of the most common complication and leading cause of preventable blindness among the working population. It is estimated that around 93 million have diabetic retinopathy of whom 17 million (18%) have proliferative diabetic retinopathy, 21 million (23%) have diabetic macular edema, and 28 million (20%) have vision threatening diabetic retinopathy.

WHO CRITERIA:

Criteria for Diabetes diagnosis: 4 options

- Fasting plasma glucose ≥ 126 mg/dl (7.0mmol/L)

  Fasting is defined as no caloric intake for ≥ 8 hours.

- 2 hour post prandial glucose ≥ 200mg/dl (11.1mmol/L) during OGTT (75g)

  Using a glucose load containing the equivalent of 75g anhydrous glucose dissolved in water.

- HbA1C ≥ 6.5% (48mmol/L)
- Random plasma glucose ≥ 200mg/dl (11.1 mmol/L) with symptoms of hyperglycemia.[26]

CLINICAL CLASSIFICATION

Classicaly, the clinical presentation of Diabetes was the basis of its classification into insulin dependent and non insulin dependent diabetes. Insulin dependent diabetes term was used to refer an "early onset diabetes (affecting children and adolescents and adults < 30 years of age", affected patients are lean and thin presenting with classical osmotic symptoms (polyuria, polydipsia, weight loss) and are ketosis prone and requiring insulin i.e.,insulin was needed to prevent ketosis for their survival.

Similarly, non insulin dependent diabetes refers to " adult onset diabetes (>40 years age)", in overweight / obese individuals who were not insulin requiring but were insulin resistant and could be controlled on diet, exercise and medications in combination or alone. However at the turn of the twenty first century this nomenclature was replaced and diabetes was classified into type 1 and type 2 diabetes, this indicated a paradigm shift in the basis of classification from a clinical basis to pathogenetic basis.

PATHOGENIC CLASSIFICATION

Type 1 diabetes mellitus referring to immune destruction of pancreatic islets etiology and type 2 diabetes referring to non immune etiology were enunciated.

Diabetes can be classified into four clinical categories:

1. Type 1 diabetes (due to beta cell destruction, usually leading to absolute insulin deficiency)
   - immune mediated
   - idiopathic
2. Type 2 diabetes (due to a progressive insulin secretory defect on the background of insulin deficiency)
3. Other specific types of diabetes due to other causes

   Genetic defects in beta cell function

   MODY 1- Mutation in Hepatocyte nuclear transcription factor (HNF) 4 alpha.

   MODY 2 – Mutation in Glucokinase gene

   MODY 3 – Mutation in HNF – 1 alpha

   MODY 4 – Mutation in Insulin promoter factor-1 gene

   MODY 5 – Mutation in HNF – 1D gene

   MODY 6 – Mutation in neurogenic differentiation -1 transcription factor (Neuro D1/Beta 2)

   Mitochondrial deoxyribonucleic acid

   Subunits of ATP sensitive potassium channel

   Mutations in Proinsulin or insulin

Genetic defects in insulin action

Type A insulin resistance

Leprechaunism

Rabson Mendelhall syndrome

Lipodystrophy syndromes

Diseases of the exocrine pancreas:

Cystic fibrosis, chronic pancreatitis, pancreatectomy, hemochromatosis, neoplasia, fibrocalculous pancreatopathy, mutations in carboxy esteryl lipase.

Endocrinopathies:

Acromegaly, cushing's syndrome, glucoganoma, pheochromocytoma, hyperthyroidism, somatostatinoma, aldosteronoma.

Drug or chemical induced :

Such as in the treatment of HIV / AIDS or after organ transplantation ,viz., glucocorticoids, pentamidine, protease inhibitors, nicotinic acid, diazoxide, epinephrine, beta adrenergic agonists, thiazides, hydantoin, asparaginase, antipsychotics, etc.,

Infections:

Congenital rubella, cytomegalovirus, coxsackie virus

Uncommon forms of immune mediated diabetes:

Stiff person syndrome, insulin receptor antibodies

Other genetic syndromes sometimes associated with diabetes: Wolfram's syndrome, Down's syndrome, Klinefelter's syndrome, Turner's

syndrome, Friedrich's ataxia, Hunting's chorea, Laurence moon biedl syndrome, myotonic dystrophy, porphyria, Prader willi syndrome.

4. Gestational diabetes mellitus

ETIOLOGY AND RISK FACTORS:

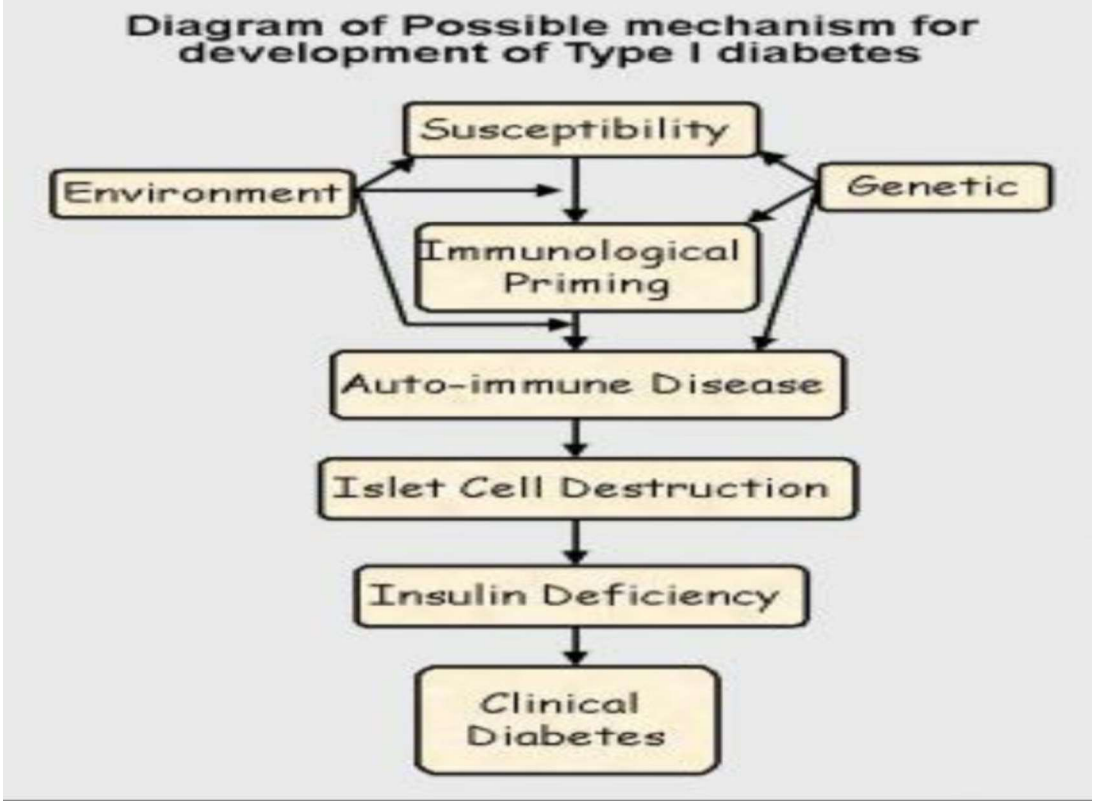
Diabetes both type 1 or type 2 has equally strong genetic and environmental risk factors an interaction of which leads to clinical expression of the disease. The genetic suscepitibilty for type 1 is associated with certain Human leucocyte antigen (HLA) combinations DR3, DR4 and the environmental insults are rather ill defined. Possibilty of some aspects of diet and viral infections trigerring an autoimmune exposure causing specific destruction of beta cells of pancreas has been proposed.

Type 2 Diabetes mellitus has a more complex etiopathology. Though it has strong genetic basis as shown by its hereditary nature, the major suscepitibilty genes have not yet been identified. Racial predisposition as seen in Asian population is also common . The environmental factors showing strong association with diabetes are increasing age, family history of diabetes, obesity, unhealthy diet, physical inacitivity, insulin resistance, adverse intrauterine, environmental and stress factors.

PATHOPHYSIOLOGY

In Type 1 diabetes there is autoimmune destruction pancreatic β islet cells following interaction between environmental and genetic factors. The major antibodies detected are insulin autoantibody, glutamic acid decarboxylase autoantibody, insulinoma associated autoantigen 2 autoantibody and zinc transporter 8 autoantibody. Indeed, immunological studies revealed the essential involvement of the adaptive immune system in the pathogenesis of T1DM. It is found that CD8+ T cells are the most predominant in the insulitis lesion, followed by CD68+ macrophages, CD4+ T cells, CD20+ B lymphocytes and CD138+ plasma cells.

Figure 1. Pathophysiology of Type 1 DM

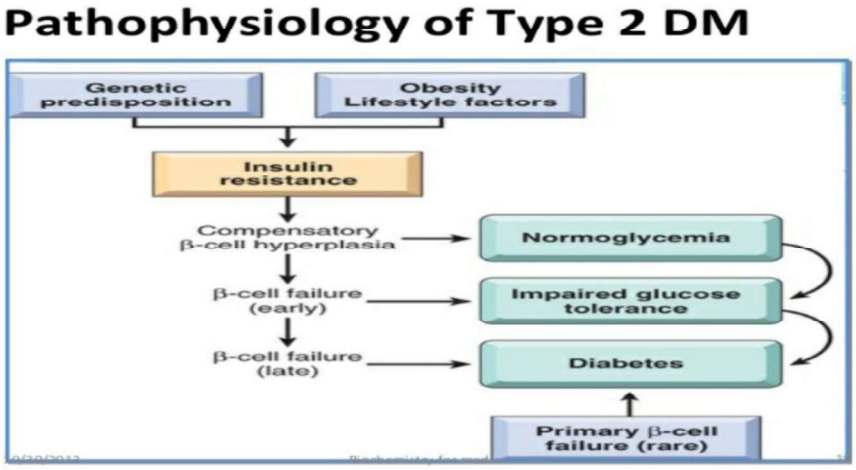


The pathophysiology of type 2 diabetes includes impaired insulin secretion, impaired insulin action, insulin resistance and impaired incretin effect on the beta cell function and non suppression of the action of alpha cells with rising blood glucose levels. In the last two decades the role of adipokines as regulators of beta cell function and insulin sensitivity has been demonstrated in number of studies.

Type 2 Diabetes is a life style disorder and an interaction of genetic and environmental factors precipitates the metabolic abnormalities existing in prediabetic subjects to the clinical stage of diabetes. There is a long asymptomatic pre-diabetic stage before the development of diabetes. These stages are easily identifiable by OGTT.

For the development of diabetes both the basic pathophysiological defects ,i.e., insulin resistance and beta cell secretory defect have to coexist.

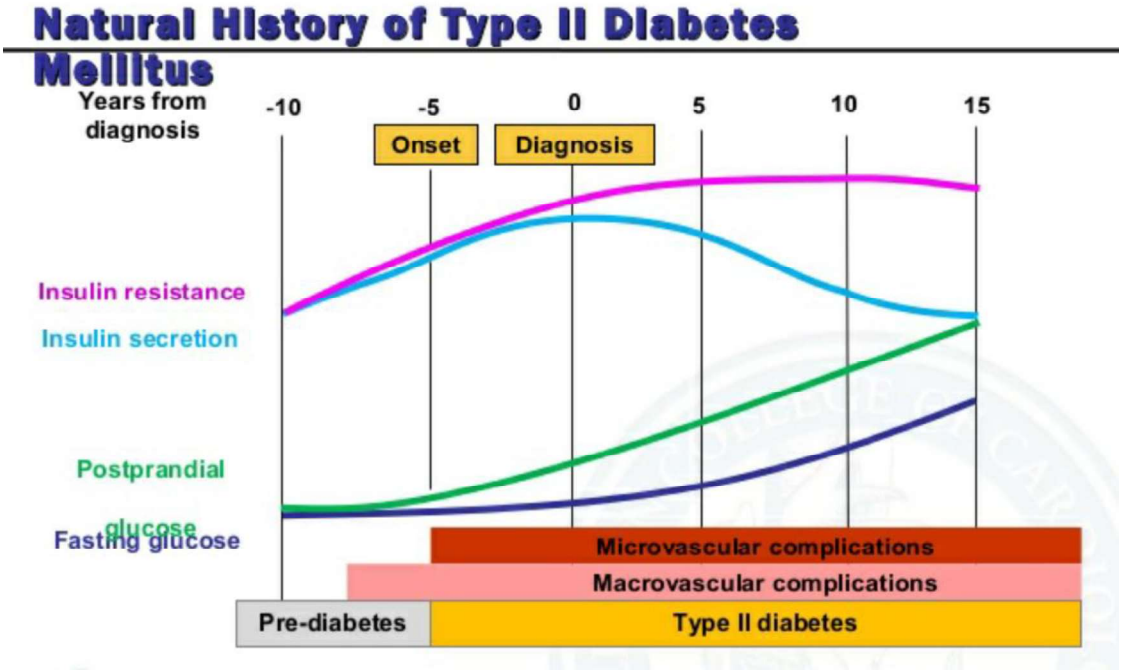
Figure 2



PRE DIABETES

The definition of IGT has been stable. The American Diabetes Association recommends the normal cut off for fasting plasma glucose as <100mg/dl. Both IGT and IFG have heterogenous pathogenesis and hence may have different rates of progression to diabetes. People with combined IFG and IGT have approximately double the rate of conversion to diabetes than those with any one of the abnormalities. Both the states are associated with insulin resistance and other cardiovascular risk factors such as dyslipidemia and hypertension. IGT is shown to be stronger predictor than IFG.

Figure 3



CLINICAL FEATURES

The clinical features depend upon the type of Diabetes, the stage in the natural history of diabetes and on the presence of its attendant complications or comorbidities. Type 1 diabetes constitutes <5% of all diabetes while Type 2 diabetes contributes to 95% of diabetes in the world including in India. Type 1 diabetes results in near total destruction of beta cells of islets of Langerhans in the pancreas resulting in absolute insulin deficiency resulting in hyperglycemia which presents with osmotic symptoms like polyuria, polydipsia and unexplained weight loss and with diabetic ketoacidosis and intercurrent infections.

Type 2 Diabetes due to environmental and genetic factors result in insulin resistance (relative insulin deficiency). Hyperinsulinemia in initial stages keeps fasting plasma glucose normal but in response to glucose load, post prandial hyperglycemia occurs. During the period of worsening insulin resistance there will be loss of first phase insulin release followed by hyperglycemia in both fasting and post prandial state. This continued hyperglycemia will result in both microvascular and macrovascular complication after a variable period of asymptomatic phase.

LATENT AUTOIMMUNE DIABETES OF ADULTS (LADA)

It is a peculiar type of diabetes of adults wherein patients harbor autoantibodies to islet cells as seen in type 1 diabetes, but it occurs in adults and is phenotypically similar to type 2 diabetes i.e., somewhere

between type 1 and type 2 diabetes. Age of onset ≥ 30years, no insulin requirement for at least 6 months after diagnosis and presence of one or more of the antibodies (anti-GAD, IAA OR ICA) are the criteria for diagnosis of LADA. Latent autoimmune diabetes of adults in turn has been classified into LADA type 1 and LADA type 2.

The LADA type 1 has two or more antibodies present in high titres and has a phenotype closer to one described for classical type 1 diabetes. On the contrary, LADA type 2 has only one antibody present in low titres and the phenotype is similar to that for type 2 diabetes.

MODY

Maturity onset diabetes of Young is diabetes with a monogenic inheritance pattern. It has a autosomal dominant inheritance and has early age of onset and the genetic defect results in diminished insulin secretion. Any person with diabetes in three successive generations with the age of diabetes < 25 years without any classical features of insulin resistance should be suspected to have MODY.

Diabetes mellitus can come to our notice with one or more of the following clinical features:

- Asymptomatically diagnosed on routine screening in health camps or preventive health check ups.
- Noticing ants in the toilet after urination because of melituria-sweet urine

- Unexplained weight loss despite normal appetite
- Recurrent bacterial skin infection - boils, carbuncles, cellulitis
- Recurrent urinary tract infections
- Recurrent or difficult to treat fungal infections of skin and its appendages – tinea corporis / pedis / cruris / candidial intertrigo or paronychia.
- Chronic vaginal discharge or vulval pruritis in females and recurrent balanoposthitis in males.
- Tuberculosis – diabetics with uncontrolled hyperglycemia have a greater predisposition to develop tuberculosis
- Polyuria and polydipsia
- Overt renal failure or microalbuminuria (diabetic nephropathy)
- Diabetic neuropathy – symmetrical peripheral neuropathy or other variants Impotence, loss of libido, dyspareunia and loss of sudomotor functions secondary to autonomic dysfunction
- Vision disturbances – rapidly changing glasses because of osmotic changes in the lens secondary to glycemic fluctuations, early onset cataract, secondary glaucoma and diabetic retinopathy.
- Atherosclerotic vascular disease – coronary, cerebral or peripheral vascular disease
- Acute complications – diabetic ketoacidosis and non ketotic hyperosmolar state.

RISK FACTORS TO SCREEN

Risk factors for diabetes which mandates screening in asymptomatic adult individual:

Over weight (BMI ≥23kg/m2) with any one of the following features:

Physical inactivity

Diabetes in first degree relative

History of gestational diabetes mellitus or gave birth to a baby weighing >4kg

Hypertension (BP – 140/90mmHg)

High density Lipoprotein cholesterol <35mg/dl

Serum triglycerides >250mg/dl

High risk ethic groups like pima Indians or races

Pre diabetes

Women with polycystic ovarian syndrome

Clinical conditions associated with insulin resistance – severe obesity, acanthosis nigricans

History of cardiovascular disease and age >45 years

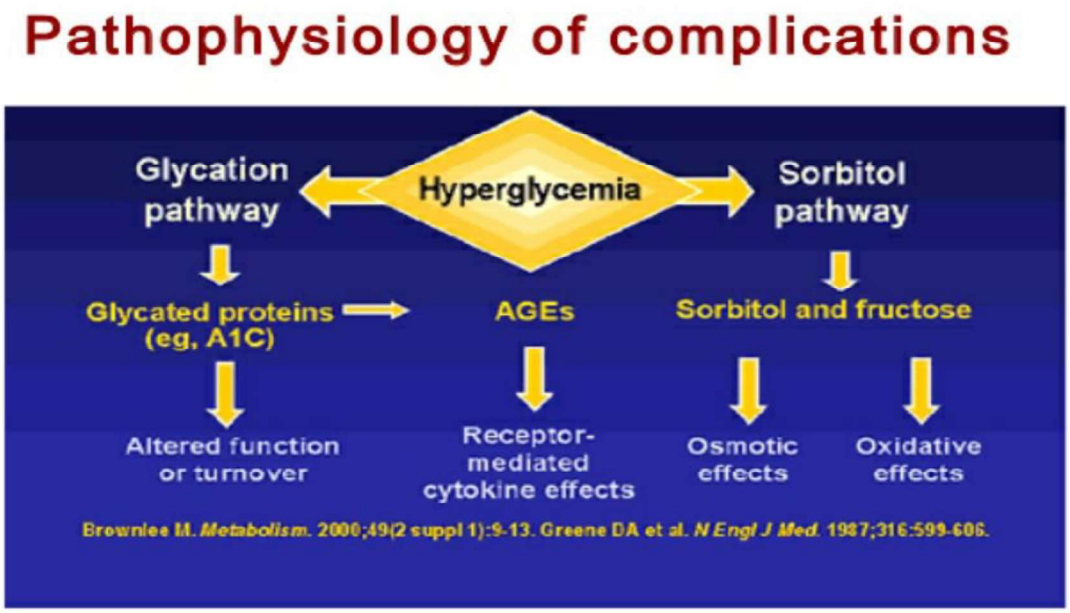
COMPLICATIONS

Unlike the microvascular disease, which starts with the onset of diabetes, the macrovascular disease antedates the development of overt diabetes by several years. Around 75% to 80% of all diabetic patients will die prematurely of cardiovascular (macrovascular) disease, particularly coronary heart disease. Diabetic foot problems (gangrene, large non healing infected ulcers) are the commonest cause of non traumatic lower limb amputation. In one Indian study done at Chennai, the prevalence of coronary heart disease was 21.4% among diabetic patients, 14.9% among impaired glucose tolerance subjects and 11% among non diabetic patients. The prevalence of peripheral arterial disease in the same population was 6.3%.

There is a close relationship existing between prediabetes, Diabetes and macrovscular disease throughout life and the substantial body of evidence supports the concept that increased morbidity and mortality due to cardiovascular disease is associated with abnormalities in glucose metabolism across the entire continuum of glucose intolerance ranging from normal to clinical diabetes. While the interplay between diabetes and cardiovascular disease has been recognized for many decades, recent data analysis of the existing studies has helped to redefine several aspects of the relationship with relevance to clinical practice.

Meta analysis and systemic reviews have confirmed that DM increases CVD risk by around two fold on an average and this risk is subject to wide variation being lowest in the newly diagnosed and highest in those with existing vascular disease, proteinuria or renal disease.

Figure 4



The effects of diabetes on pathogenesis of atherosclerosis is due to endothelial dysfunction, oxidative stress, activation of polyol pathways, metabolic factors, coagulation and inflammatory factors and vascular related factors.

Chronic microvascular complications of diabetes mellitus are retinopathy, neuropathy, and nephropathy. Three fourth of cases develop retinopathy after more than 15 years of diabetes, half the diabetics have neuropathy and one third have nephropathy in larger population study in

US. Poor glycemic control, long duration of diabetes and systolic blood pressure are risk factors for microvascular complications.

Risk of chronic complication in type 1 and 2 diabetes results from chronic hyperglycemia. It has been conclusively demonstrated in type 1 and type 2 diabetes microvascular complications can be prevented or delayed if chronic hyperglycemia is reduced. Other incompletely defined factors may moderately reduce development of complications. For instance, some individuals never develop nephropathy or retinopathy despite long standing diabetes though they may have similar glycemic control to patients with microvascular complications suggesting genetic suscepitibilty for developing particular compications.

There is now strong correlation between the occurrence and severity of microvascular complications in both type 1 and type 2 with duration and degree of hyperglycemia. Glucose appears to damage tissues by acute reversible changes in metabolism (e.g. sorbitol accumulation, increased NADH/NAD+ ratio, decreased myoinositol, early glycation) and by cumulative, irreversible alterations in stable macromolecules forming advanced end glycation products. Genetic susceptibility and other accelerating factors such as hypertension and hyperlipidemia, smoking also play a role.

Hyperglycemia causes increase in intracellular glucose in insulin independent tissue like nerves, lens, retina, glomerulus. In these tissues glucose is converted by aldose reductase to sugar alcohol, sorbitol. In

many tissues it is subsequently oxidixed to fructose with the help of sorbitol dehydrogenase with NAD+ as cofactor. This sorbitol does not cross the cell membrane easily and gets accumulated intracellularly. It causes damage to the tissues through its osmotic effects, by increasing NADH/NAD+ ratio inducing pseudohypoxia and by depleting intracellular myoinositol.

Myoinositol is structurally related to glucose and it helps in activating Na+ - K+- ATPase for maintaining nerve conduction. Its depletion leads to impaired nerve function in diabetes.

In other tissues hyperglycemia leads to de novo synthesis of diacylglycerol and activation of the enzyme protein kinase C. Protein kinse c pathway is a family of serine threonine kinase that change the transcription of genes for fibronectin, type 4 collagen, contractile proteins and extracellular matrix protein in endothelial cells and neurons.

This enzyme is implicated in several process causing diabetic complications such as increased capillary permeability and contractility, blood flow, cellular proliferation, basement membrane thickening. Protein kinase c mediates TGF-β1, angiotensin 2 and vascular endothelial growth factor and modulates mitogen activated protein kinase which mediates sclerosis. Inhibitors of PKC – β like ruboxistuarin mesylate that reduce the direct cellular actions of AGES, VEGF, endothelin-1 reduce oxidized lipids and oxidant production are being studied in clinical trials in DM for retinopathy and neuropathy.

Next is the Hexosamine pathway where Fructose 6 phosphate, a substrate for O linked glycosylation and proteoglycan production is generated through the hexosamine pathway when hyperglycemia increase the flux. Hexosamine may alter function by glycosylation of proteins such as endothelial nitric oxide synthase or by changes in gene expression of TGF-β or plasminogen activator inhibitor-1 (PAI-1).

With chronic hyperglycemia Amadori products in long lived molecules like collagen and DNA combine to form cross linked irreversible structures called advanced end glycation products (AGE). Early non enzymatic glycation products are reversible as hyperglycemia continues intermediate poorly reversible products are formed and later irreversible AGEs are formed. There is a correlation between serum levels of AGEs and the level of glycemia; these products accumulate as the glomerular filtration rate declines.

AGE accumulation leads to binding of LDL and other proteins to collagen in blood vessel walls predisposing to atherosclerosis and disruption of structure and impaired enzymatic turn over of matrix proteins leading to basement membrane permeability and thickening. It also causes endothelial cells to release cytokines and growth factors for cell proliferation.

DIABETIC RETINOPATHY:

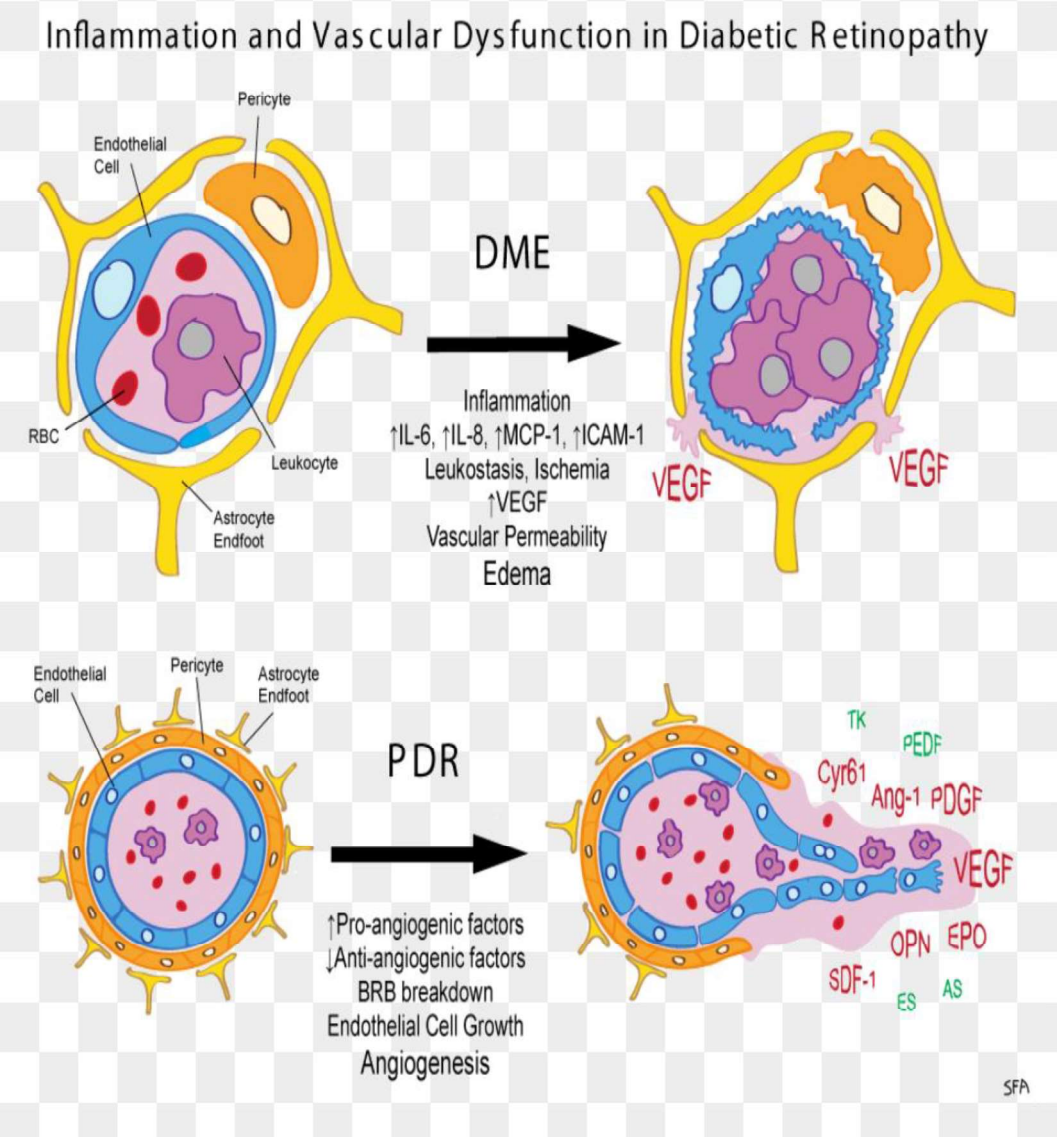
Diabetic retinopathy is a disorder of the retinal vessels that eventually develops to some degree in nearly all patients with long standing diabetes mellitus. A recent study in South India in urban population estimates prevalence of DM in adult population as high as 28% and the prevalence of DR in diabetics as 18%. Risk factors for diabetic retinopathy are age at diagnosis of diabetes, duration, poor control of diabetes, pregnancy, hypertension, nephropathy, hyperlipidemia, obesity, anemia, smoking.

Hyperglycemia causes intracellular accumulation of sorbitol , free radical injury, accumulation of glycated end products, disruption of ion channel, protein kinase c activation all of which in turn leads to direct effect on retinal cells, capillary wall damage and hematological and rheological changes that leads to intra retinal hemorrhages, edema, exudates, microvascular occlusion progressing to new vessel formation in iris and retina resulting in unresolved vitreous hemorrhage, retinal detachment, neovscular glaucoma finally to blindness.

In diabetic retinopathy hemorrheological disturbances accompany and sometimes precede microangiopathy. Early abnormalities include increased capillary blood flow and pressure, increased blood viscosity, red cell aggregation and hypersensitivity of platelets to aggregating agents. This increased pressure causes tangential shear forces on

endothelium resulting in stimulation of basement membrane formation and leading to hyperfiltration of fluid out of the capillary. This later on leads to capillary thickening (sclerosis) limiting vasodilatation.

Figure 5



Growth factors:

Growth factors seem to play an important role in DM related complications and an increase is seen in their production by most of these proposed pathways. Vascular Endothelial Growth factor – A is increased locally in diabetic proliferative retinopathy and decreases after laser photocoagulation. Inhibition of angiotensin 2 also reduces VEGF, which could explain one of the beneficial effects of angiotensin 2 receptor blockers on microangiopathic diseases.

Monoclonal antibodies to VEGF like Ranizumab in experimental studies have shown improvement in proliferative diabetic retinopathy. An increase in transforming growth factor β in diabetic nephropathy stimulates basement membrane production of collagen and fibronectin by mesangial cells. Other growth factors like platelet derived growth facror, Epidermal growth factor, insulin like growth factor, growth hormone, basic fibroblast like growth factor, connective tissue growth factor and even insulin have been suggested to play a role in DM related like complications.

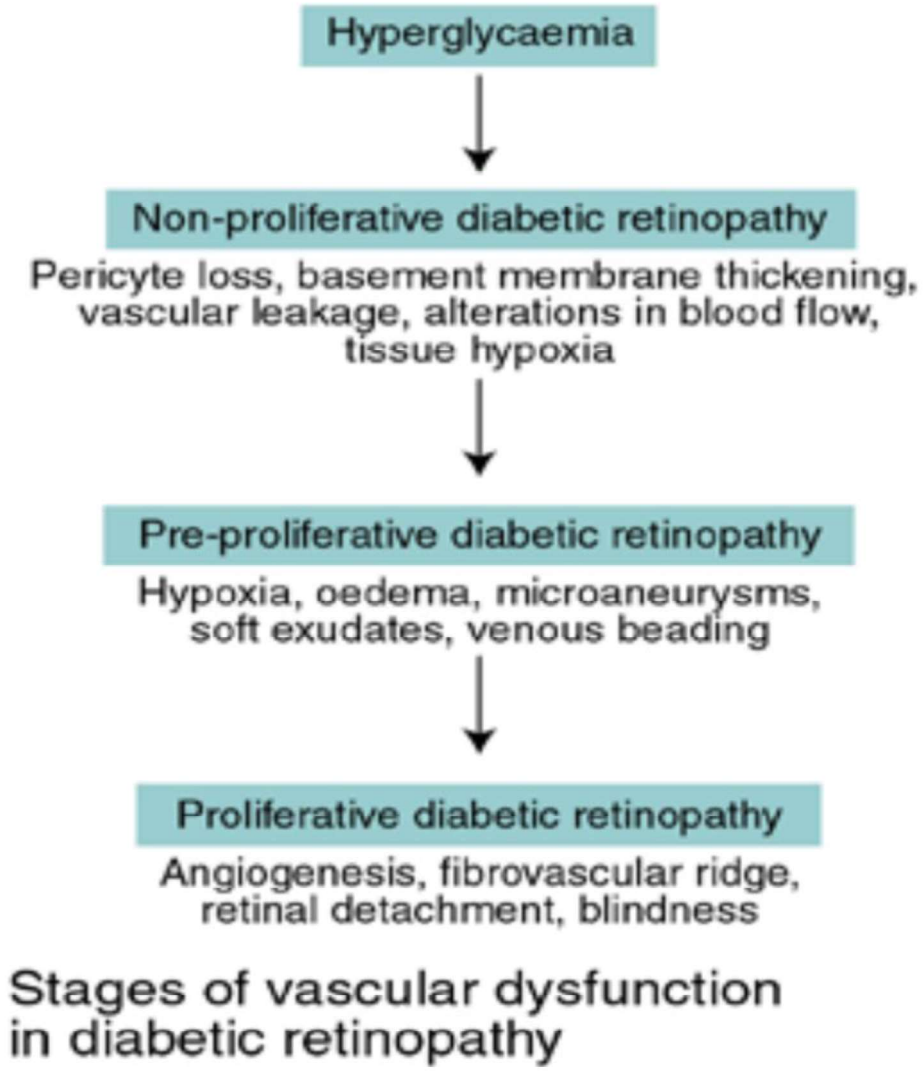
Angiotensin 2:

The renin angiotensin in the kidney is abnormally activated in diabetes. Angiotensin directly binds to receptors in renal cells and induces matrix deposition in mesangial and tubular cells through TGF-β1.

Angiotensin 2 stimulates VEGF production in mesangial cells and impairs glomerular structure and function. Similar changes are observed in retina.

STAGES OF DIABETIC RETINOPATHY:

Figure 6



Stages of vascular dysfunction in diabetic retinopathy

According to Early Treatment Diabetic Retinopathy Study (ETDRS), levels of diabetic retinopathy are

Figure 7

ABBREVIATED EARLY TREATMENT DIABETIC RETINOPATHY STUDY (ETDRS) CLASSIFICATION

CATEGORY	MANAGEMENT
NON-PROLIFERATIVE DIABETIC RETINOPATHY (NPDR)	
NO DR	Review in 12 months
VERY MILD •Microaneurysms only	Review most patients in 12 months
MILD •Any or all of: microaneurysms, retinal hemorrhages, exudates, cotton wool spots	Review range 6-12 months, depending on severity of signs, stability, systemic factors, and patient's personal circumstances
MODERATE •Severe retinal haemorrhages in 1-3 quadrants or mild IRMA •Significant venous beading in no more than 1 quadrant •Cotton wool spots	Review in approximately 6 months (PDR in up to 26%, high-risk PDR in up to 8% within a year)
SEVERE The 4-2-1 rule- •Severe retinal haemorrhages in all 4 quadrants •Significant venous beading in ≥2 quadrants •Moderate IRMA in ≥1 quadrants	Review in 4 months (PDR in up to 50%, high-risk PDR in up to 15% within a year)
VERY SEVERE •≥2 of the criteria for severe	Review in 2-3 months (High-risk PDR in up to 45% within a year)

NON PROLIFERATIVE DIABETIC RETINOPATHY

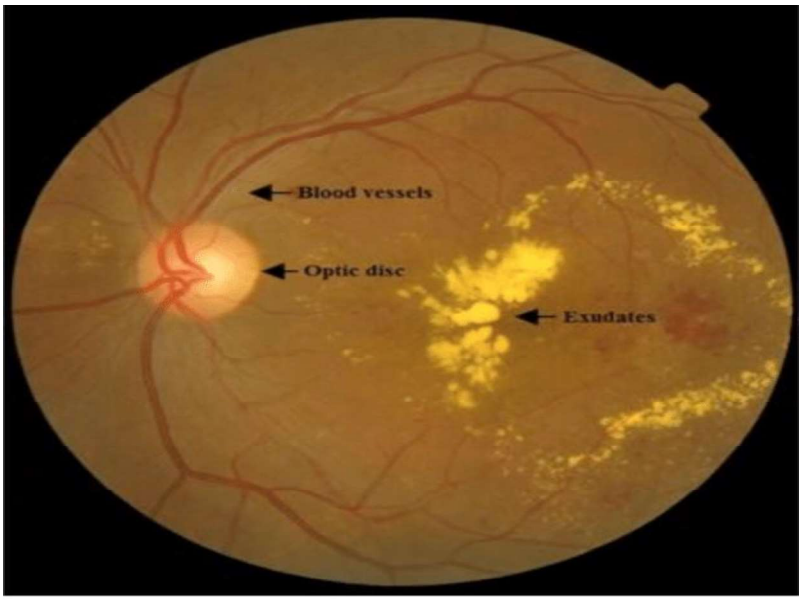


Figure 8

SEVERE PROLIFERATIVE DIABETIC RETINOPATHY

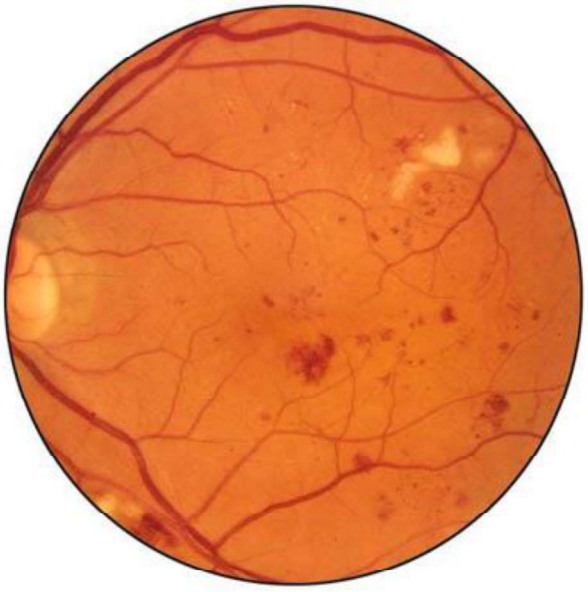


Figure 9

VERY SEVERE NON PROLIFERATIVE DIABETIC RETINOPATHY

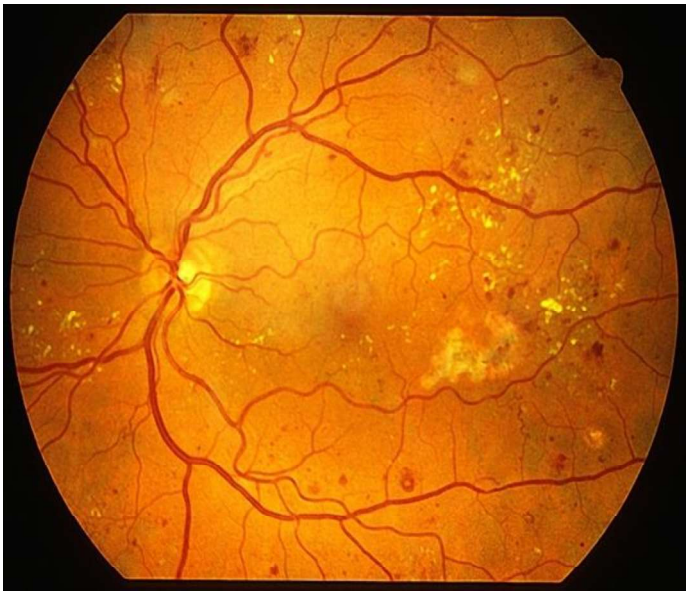


Figure 10

PROLIFERATIVE DIABETIC RETINOPATHY

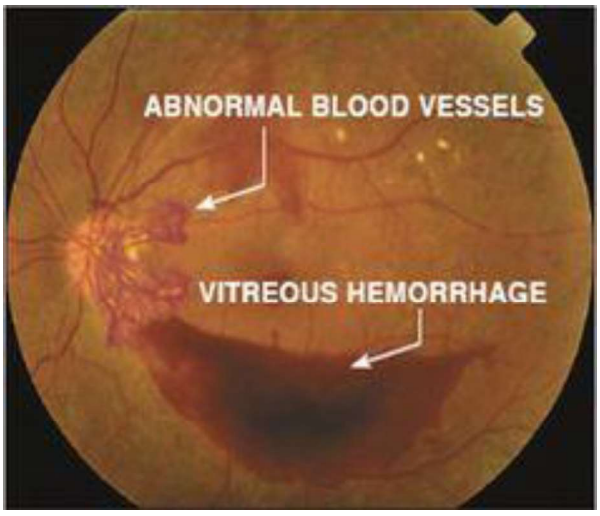


Figure 11

NPDR & PDR:

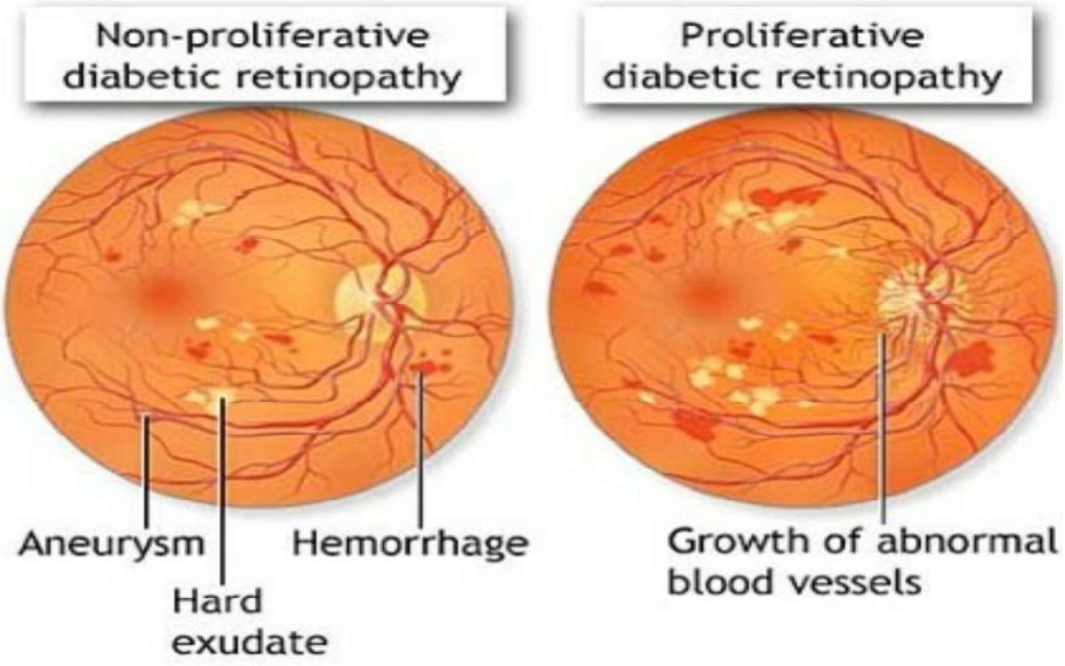


Figure 12

CLINICALLY SIGNIFICANT MACULAR EDEMA

(any one of the following)

- Thickening of the retina located 500µm or less from the centre of the macula.
- Hard exudates at 500µm or less from the centre of the macula with thickening of the adjacent retina.
- A zone of retinal thickening, one disc or larger in size, any portion of which is one disc diameter or less from the centre of macula.

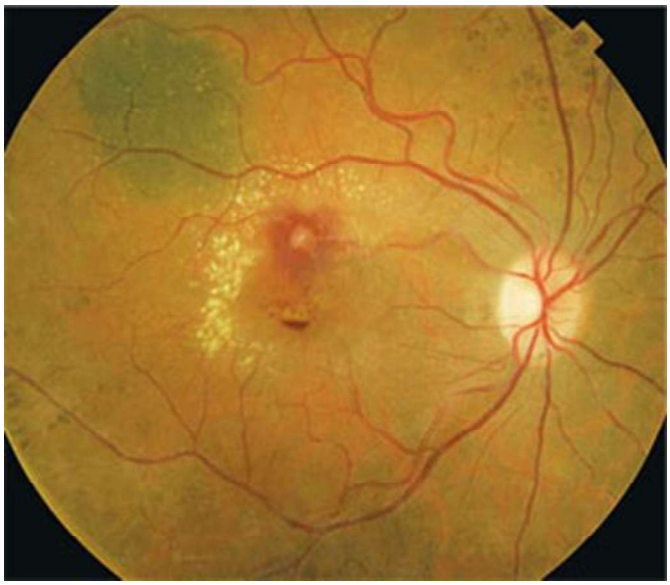


Figure 13

Diabetic eye disease primarily affects the retinal blood vessels, but diabetes also accelerates cataract formation. The lesions of diabetic retinopathy can be grouped into five categories according to the features seen on ophthalmoscopy- background, preproliferative and proliferative retinopathy, advanced diabetic eye disease and maculopathy.

BACKGROUND RETINOPATHY:

Background retinopathy is the first stage of retinopathy and is not associated with visual loss unless the macula becomes involved (maculopathy). Early subclinical abnormalities of the blood vessels are basement membrane thickening, loss of pericytes (contractile cells which control vessel caliber and flow) and increased blood flow and capillary permeability. Microaneursyms are the earliest clinical sign of retinopathy and appear as red dots. They are blind out pouchings of the capillaries

either at weakened points or a revascularization response to microvascular occlusion.

Hard exudates are off white / yellow flakes or plaques of plasma protein and lipid which have leaked from retinal blood vessels. They are more significant in the area of macula.

Various forms of intraretinal hemorrhage also occur in the background retinopathy (superficial flame shaped or deep dot and blot cluster hemorrhage). Cotton wool spots are whitish elevations of the nerve fibre layer due to intracellular accumulation of axoplasmic material in areas of microvascular occlusion.

PRE PROLIFERATIVE RETINOPATHY:

Preproliferative retinopathy is due to worsening retinal ischemia and carries a high risk of developing into sight threatening proliferative retinopathy. Early referral to a specialist ophthalmologist is required. Preproliferative changes include multiple cotton – wool spots (> 5), multiple hemorrhages, venous beading and intraretinal microvascular abnormalities (IRMAs, abnormally branched vessels in the retina, representing attempts to revascularise the ischaemic retina).

PROLIFERTIVE RETINOPATHY:

Proliferative retinopathy is marked by abnormal new vessels stimulated by growth factors released from the ischaemic retina. These new vessels grow forward towards the vitreous and overlie the retinal

vessels. Contraction of the vitreous gel causes hemorrhage into the vitreous or the space between the gel and the retina. New vessels on the optic disk are associated with the most severe retinal ischaemia and the worst visual prognosis but neovascularization also occurs elsewhere on the retina.

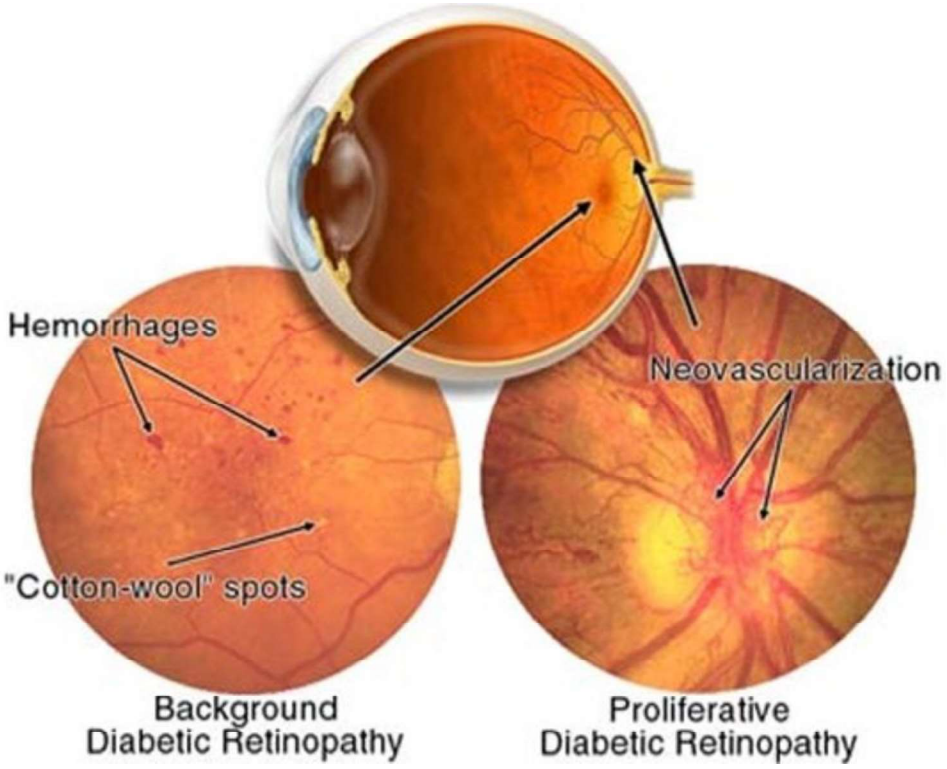


Figure 14

ADVANCED DIABETIC EYE DISEASE:

Advanced diabetic eye disease comprises retinal detachment or tears, with preretinal (boat shaped) or vitreous hemorrhages which occur when further vitreous contraction pulls on strong fibrous adhesions connecting the retina and vitreous. Sight can also be threatened by

glaucoma due to neovascular tissue on the iris (rubeosis iridis) spreading peripherally on the pupil and obstructing the drainage of aqueos humour.

MACULOPATHY:

Maculopathy is due to retinal edema and thickening close to macula thus threatening or causing loss of central vision. Focal or diffuse maculopathy are caused by microvascular leakage leading to formation of hard exudates in the area of macula. Ischemic maculpathy is associated with areas of capillary non perfusion and is difficult to detect. Hard exudates often occur in rings (circinate exudates) around the leaking area.

CATARACT:

Cataract is a common cause of blindness in diabetic patients. It is recognized as an opacity against the red fundal reflex when the eye is examined with an opthalmoscope at a distance of 30cm. Non enzymatic glycation of lens protein, especially alpha crystalline and subsequent cross linking probably contributes. Also sorbitol accumulation in the diabetic also could lead to osmotic swelling but the evidence for this mechanisms in human is less strong than in experimental diabetic cataracts in other species.

Diabetic retinopathy is the leading cause of blindness in the working population. The prevalence of retinopathy increases with duration of diabetes with few patients presenting with retinopathy in the first 5

years of diabetes and 80 – 100% developing some form of the complication after more than 20 years duration

Maculopathy is the most common in type 2 diabetes and can be associated with severe visual loss. Patients may present with acute onset cobwebs / floaters or complete obscuration of vision caused by vitreous hemorrhage from new vessels growing into the retina or optic disc. The vitreous hemorrhage may absorb spontaneously over the next few days / weeks but it is often complicated by recurrent attacks of fresh hemorrhage. The accompanying scar tissue may contract leading to retinal tearing resulting in combined rhegmatogenous retinal detachment. Patients with extensive retinal ischemia tend to develop neovascularization of the iris and the angle of anterior chamber leading to intractable glaucoma.

INFLAMMATION AND DIABETES:

Some studies defined a clear cut relation between systemic inflammation and insulin resistance in Type 2 diabetes mellitus suggesting that altered immune system plays a decisive role in the pathogenesis of DM. Due to increased delivery of glucose to adipose tissue in DM, endothelial cells in the fat pad may take up increasing amounts of glucose through their constitutive glucose transporters. Increased glucose uptake by endothelial cells in hyperglycemic conditions causes excess production of ROS in mitochondria, which inflicts oxidative damage and activates inflammatory signaling cascades inside endothelial cells.

Endothelial injury in the adipose tissue might attract inflammatory cells such as macrophages to this site and further exacerbate the local inflammation. Hyperglycemia also stimulates ROS production in adipocytes, which leads to increased production of proinflammatory cytokines.

Studies have proposed that hyperglycemia can lead to an excessive oxidation reaction in the tricarboxylic acid cycle leading to an increase in the generation of reactive oxygen species (ROS). As a result, mitochondrial function is impaired during the production of ROS. Studies have reported that leukocytes in subjects with diabetes mellitus generates more ROS, resulting in elevated oxidative DNA damage of lymphocytes in the hyperglycemic state.

Insulin exerts its action through binding to its receptor on the surface of insulin-responsive cells. The stimulated insulin receptor phosphorylates itself and several substrates, including members of the insulin receptor substrate (IRS) family, thus initiating downstream signaling events. The inhibition of signaling downstream of the insulin receptor is a primary mechanism through which inflammatory signaling leads to insulin resistance.

Exposure of cells to TNF-α or elevated levels of free fatty acids stimulates inhibitory phosphorylation of serine residues of IRS-1. This phosphorylation reduces both tyrosine phosphorylation of IRS-1 in

response to insulin and the ability of IRS-1 to associate with the insulin receptor and thereby inhibits downstream signaling and insulin action.

Hence, it has become clear that inflammatory signaling pathways can also become activated by metabolic stresses originating from inside the cell as well as by extracellular signaling molecules. It has been demonstrated that obesity overloads the functional capacity of the ER and that this ER stress leads to the activation of inflammatory signaling pathways and thus contributes to insulin resistance. Additionally, increased glucose metabolism can lead to a rise in mitochondrial production of ROS. ROS production is elevated in obesity, which causes enhanced activation of inflammatory pathways.

Several serine / threonine kinases are activated by inflammatory or stressful stimuli and contribute to inhibition of insulin signaling, including JNK, inhibitor of NF-κB kinase (NKK). Again, the activation of these kinases in obesity highlights the overlap of metabolic and immune pathways. Inflammatory cytokine stimulation can also lead to induction of iNOS. Overproduction of nitric oxide also appears to contribute to impairment of both muscle cell insulin action and β cell function in obesity. Deletion of iNOS prevents impairment of insulin signaling in muscle caused by a high-fat diet. Thus, induction of such proteins and iNOS represent two additional and potentially important mechanisms that contribute to cytokine-mediated insulin resistance. It is likely that

additional mechanisms linking inflammation with insulin resistance remain to be uncovered.

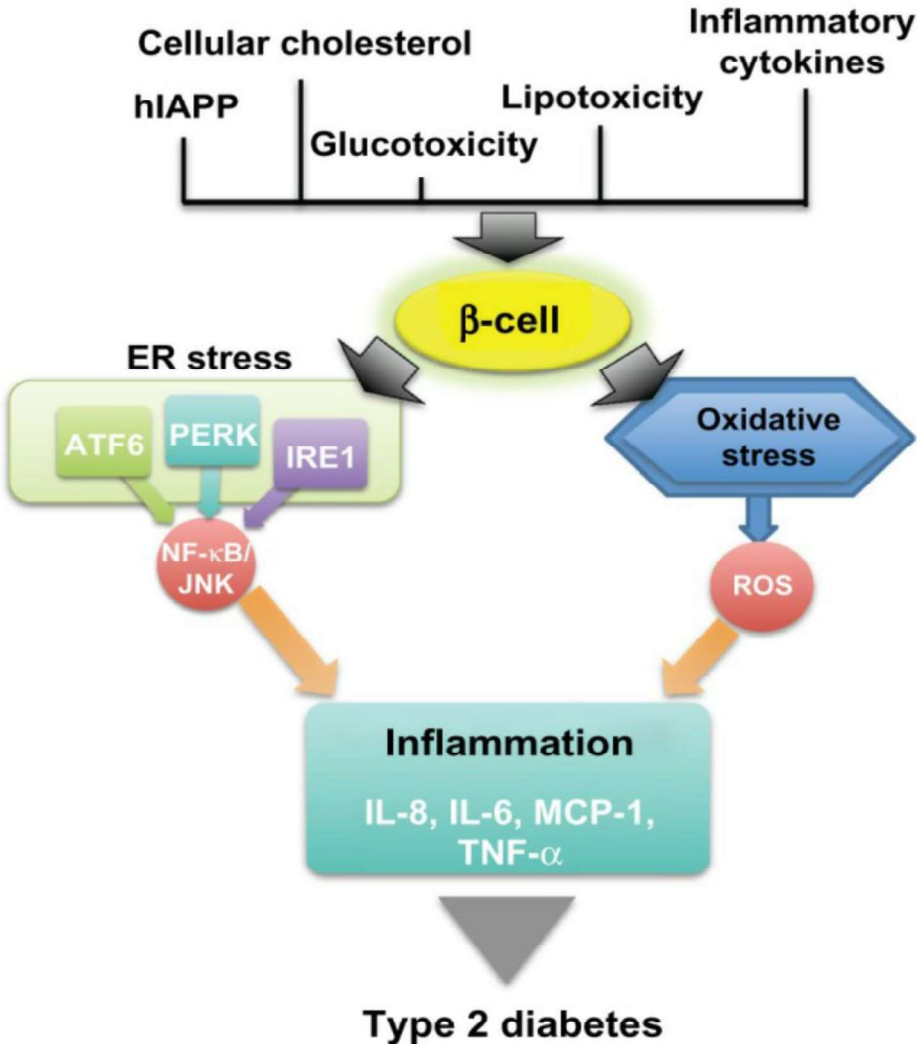


Figure 15. Inflammation and Diabetes

The role of lipids in metabolic disease is complex. As discussed above, hyperlipidemia leads to increased uptake of fatty acids by muscle cells and production of fatty acid metabolites that stimulate inflammatory state. In patients with diabetes, several studies explored connection

between systemic inflammation and vascular disease and found that chronic inflammation promotes the development and acceleration of microvascular and macrovascular complications.

Many inflammatory markers have been found to be related to DM, such as interleukin-1 (IL1), IL6, IL8, transforming growth factor beta 1, Tumor necrosis factor- alpha (TNF-α), and cytokines. However, their measurement is not used routinely as it is not easy to do it. Total white blood cell (TWBC) count is a crude but sensitive indicator of inflammation which can be done easily in laboratory routinely. It is a cost-effective investigation. Besides WBC counts, the Platelet Lymphocyte Ratio (PLR), Monocyte Lymphocyte Ratio (MLR), and Neutrophil Lymphocyte Ratio (NLR) are potential biomarkers reflecting inflammation and immune responses. Many studies have reported positive correlations of conventional inflammatory markers with the PLR and NLR.

NEUTROPHIL LYMPHOCYTE RATIO:

More importantly, a large number of studies found predictive effects of the PLR and NLR, particularly in DM[15 – 18]. The neutrophil-lymphocyte ratio (NLR) in complete blood count is studied in many diseases as an inflammatory marker and is used to predict the prognosis of diseases. Interestingly, NLR has been found to have a positive corelation with metabolic syndrome.

A study by Imtiaz *et al*. has suggested that chronic diseases such as hypertension and diabetes have a significant association with systemic inflammation, reflected by NLR.

Shiny *et al*. have shown that NLR is correlated with increasing severity of glucose intolerance and insulin resistance and can be used as a prognostic marker for macro- and micro-vascular complications in patients with glucose intolerance. Initially, NLR was recognized as a predictive marker in multiple types of cancer that might assist in patient stratification and individual risk . In this respect, NLR has emerged as a novel surrogate marker.

The immune response to various physiological challenges is characterized by increased neutrophil and decreased lymphocyte counts, and NLR is often recognized as an inflammatory marker to assess the severity of the disease. NLR represents a combination of two markers where neutrophils represent the active nonspecific inflammatory mediator initiating the first line of defense, whereas lymphocytes represent the regulatory or protective component of inflammation. But recently, multiple other studies have indicated that NLR might be a predictive marker for vascular diseases also. Recently, several studies have suggested that NLR could play a predictive role for assessing the development of microvascular complications of diabetes.

In a study, Ulu *et al*. [17] demonstrated NLR to be a quick and reliable prognostic marker for diabetic retinopathy and its severity.

A study conducted in geriatric population also suggested that increased NLR levels were in itself an independent predictor for microvascular complications of DM[36]. The exact molecular action leading to IR is not yet understood, but several studies have confirmed NLR is superior to other leukocyte parameters (e.g., neutrophil, lymphocyte, and total leukocyte counts) because of its better stability compared with the other parameters that can be altered by various physiological, pathological, and physical factors. Thus, as a simple clinical indicator of IR, NLR is more sensitive compared with the neutrophilic granulocyte count and CRP levels.

PLATELET LYMPHOCYTE RATIO:

Some angiogenesis factors such as vascular endothelial growth factor (VEGF) are key protein modulators expressed by platelets. Notably, high VEGF levels can stimulate the development of proliferative diabetic retinopathy (PDR)[38]. This would suggest that there is association between the PLR and DR progression. Data generated from research has supported a close association of systemic inflammatory processes with oxidative stress, leading to alterations of platelet and lymphocyte levels. Thus, the underlying mechanism of up-regulated PLR may also be based on the dysfunction of the inflammatory response.

MONOCYTE LYMPHOCYTE RATIO:

Monocytes are considered as a biomarker for inflammation because their activation leads to the synthesis of inflammatory cytokines. A previous report suggested that monocytes may be relevant to angiogenic processes in atherosclerosis[39]. Nevertheless, the mechanisms underlying the association between the MLR and DR should be investigated in future studies.

All the people with DM (type 1 or Type 2) are at risk. The longer the person has diabetes the higher the risk of developing DR. Early detection, education and research are the key to prevent visual impairment / blindness from DR. Ophthalmoscopy is the most commonly used technique to screen for DR. It is critical to identify patients who are in immediate need of treatment with laser photocoagulation.

Regular examination of the eyes in diabetic patients for early detection of retinopathy is essential and should include visual acuity measurement with a snellen chart and examination of the fundus through dilated pupils. When the retina cannot be seen because of cataract or hemorrhage, the patient should be referred to an ophthalmologist. Yearly examinations are recommended for those with no retinopathy, 6 monthly for those with background retinopathy and referral to an ophthalmologist for cataract , maculopthy, increasing hemorrhages. , proliferative and

preproliferative changes, marked fall in acuity, retinal detachment, vitreous hemorrhage and rubeosis iridis.

Blindness due to retinopathy can be caused by maculopathy, vitreous hemorrhage, retinal detachment and neovascular glaucoma but visual loss can now be largely prevented by laser photocoagulation and vitreoretinal surgery. Panretinal photocoagulation commonly with an argon laser is used to treat new vessels and preproliferative retinopathy. The whole retina is partially ablated except for the macula and papillomacular bundle which are essential for central vision. This concentrates the blood supply on the remaining retina and diminishes the ischaemic stimulus to new vessel formation. Established new vessels regress and further neovascularization is inhibited.

Laser photocoagulation is also used to treat maculopathy focal or grid (for diffuse or ischaemic maculopathy) treatment seals points of vascular leakage reducing edema and deposition of hard exudates. The 3 year risk of severe visual loss in maculopathy is reduced by over 50% with photocoagulation.

MATERIALS AND METHODS

Source of Data:

This study is done in patients who came to Coimbatore Medical College

Hospital outpatient department.

Study Period:

One year from June 2016 to July 2017.

Sample size:

150

Study Design:

Case control study

SELECTION CRITERIA:

- Inclusion criteria

Patients of both gender aged more than 18 years of age are selected.

- Exclusion criteria

Patients with the following comorbidities are excluded

- Hematological diseases

- Hepatic failure
- Renal failure
- Cardiac failure
- Any acute or chronic illness
- Alcohol abuse
- Hypertension
- On drugs that alter platelet function
- Pregnant women
- Patients not capable of giving consent
- Patients who are not willing to participate in the study.

TECHNIQUE:

This study involves 150 diabetes mellitus patients. They are divided into three groups.

Group A – 50 patients with diabetes mellitus as control subjects.

Group B – 50 diabetic patients with non - proliferative diabetic retinopathy.

Group C – 50 diabetic patients with proliferative diabetic retinopathy.

Cases and controls are selected on the basis of inclusion and exclusion criteria in the study.

Patients blood pressure, height and weight measurements, age, gender, accompanying disease history, smoking habits, treatment history will be recorded.

PLR, NLR, MLR AND DIABETIC RETINOPATHY DEFINITIONS:

They are calculated as ratios of platelets, neutrophils and monocytes to lymphocyte ratio.

Diabetes is diagnosed by WHO criteria.

Diabetic retinopathy:

- NPDR is identified by the presence of microaneursyms or intraretinal hemorrhages, hard and soft exudate.
- PDR is identified by the presence of neovascularisation of optic disc and / or elsewhere in fundus with or without vitreous hemorrhage.

INVESTIGATION:

Complete blood count – By using WBC, Neutrophil, Lymphocyte, Monocyte, Platelet - NLR, MLR, PLR can be calculated.

Biochemical tests like plasma glucose level, lipid profile and renal parameters, HbA1C are done.

After getting clearance from ethical committee of Coimbatore Medical college, study was done.

RESULTS AND ANALYSIS

The study population consisted of 150 patients who had fulfilled the inclusion and exclusion criteria and they are divided into three groups and all of them belong to type 2 diabetes mellitus.

Group A – 50 diabetic patients without retinopathy

Group B – 50 diabetic patients with non proliferative retinopathy

Group C – 50 diabetic patients with proliferative retinopathy

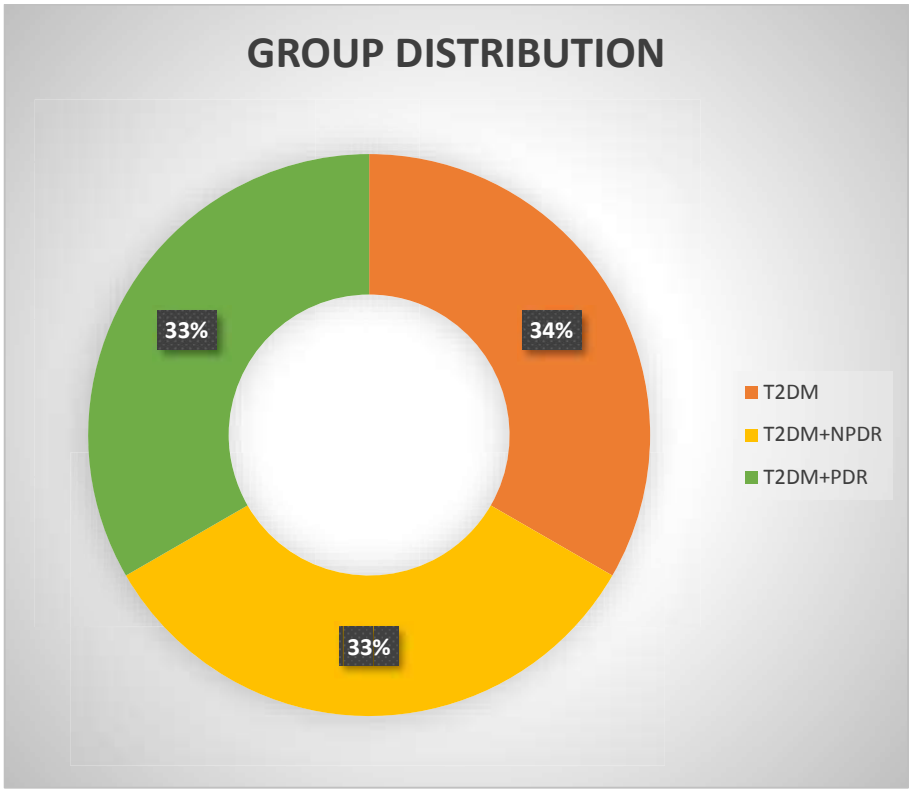
The baseline characteristics of all groups were analysed and are shown in the following tables and bar diagrams.

The mean value for each parameter like Age, Sex, Duration of DM, Blood pressure, Smoking, Lipid profile, Fasting blood sugar, Total count, Neutrophils, Lymphocytes, Monocyte, Platelet, NLR, MLR, PLR were calculated and compared between groups and co related with severity of diabetic retinopathy to find out the significance.

Table 1. Group wise distribution

GROUP	NO OF PATIENTS	PERCENTAGE
T2DM	50	33.33%
T2DM+NPDR	50	33.33%
T2DM+PDR	50	33.33%

Chart 1. Group wise distribution



The overall age distribution of the study population and age distribution in each group is shown in the below table and chart.

AGE DISTRIBUTION

Table 2. Age distribution in the study

AGE (IN YEARS)	NO OF PATIENTS	PERCENTAGE
< 50	56	37.30%
51-60	80	53.30%
> 60	14	9.40%

Chart 2. Age distribution in the study

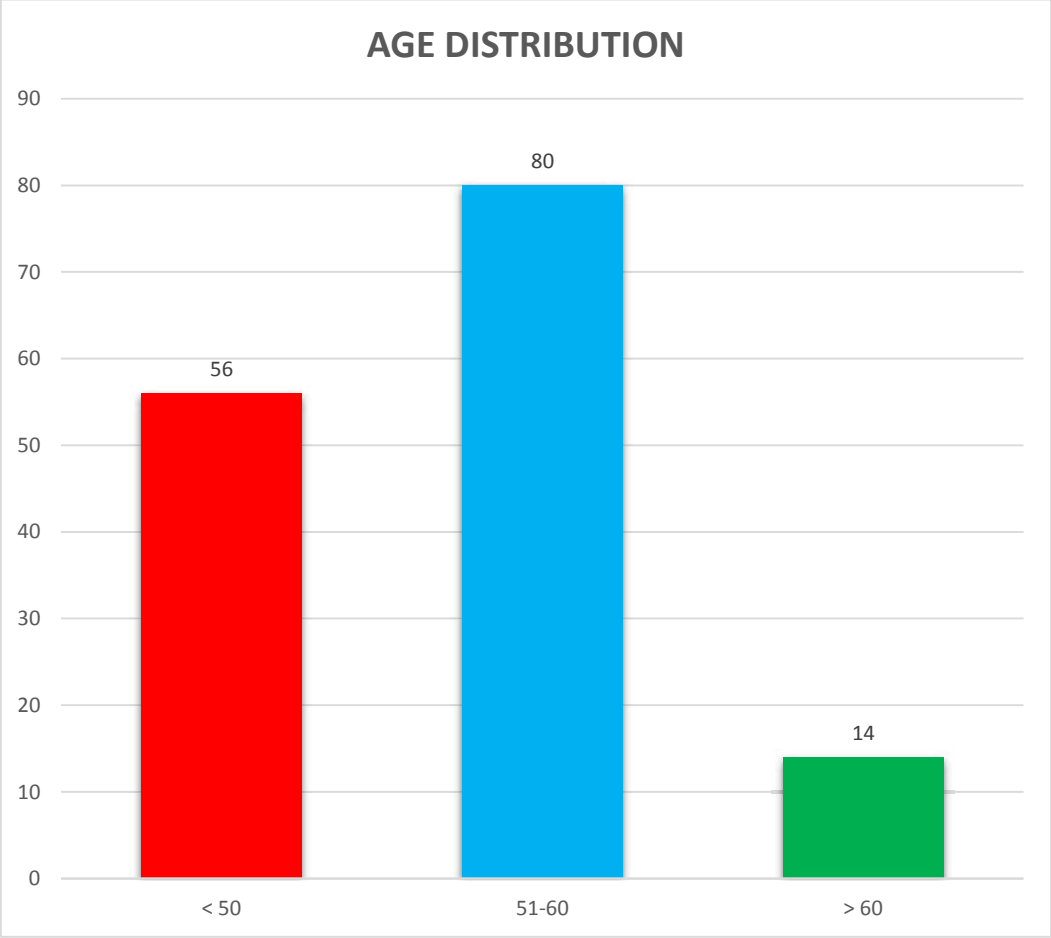


Table 3. Group wise Age distribution

	GROUP		
AGE (IN YEARS)	**T2DM**	**T2DM+NPDR**	**T2DM+PDR**
< 50	26	23	7
51-60	22	24	34
> 60	2	3	9

Chart 3. Group wise Age distribution

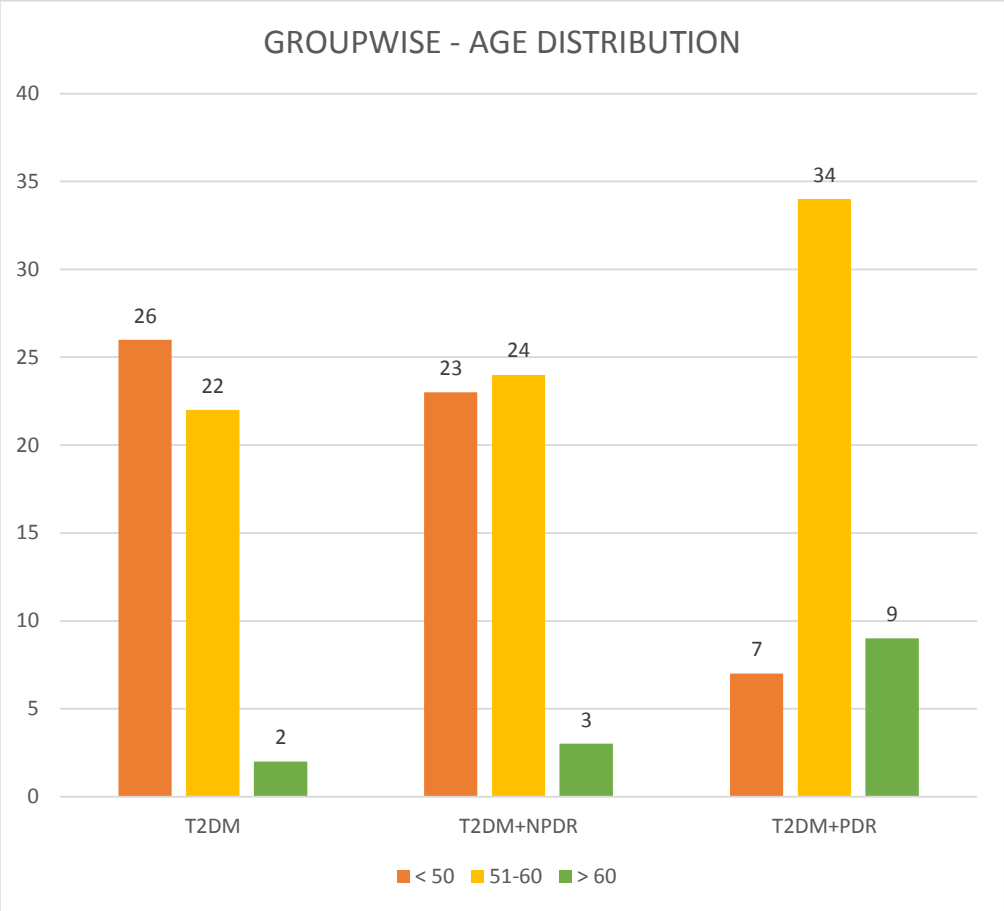


Table 4. Sex distribution in the study

SEX	NO OF PATIENTS	PERCENTAGE
MALE	75	50.00%
FEMALE	75	50.00%

Chart 4. Sex distribution in the study

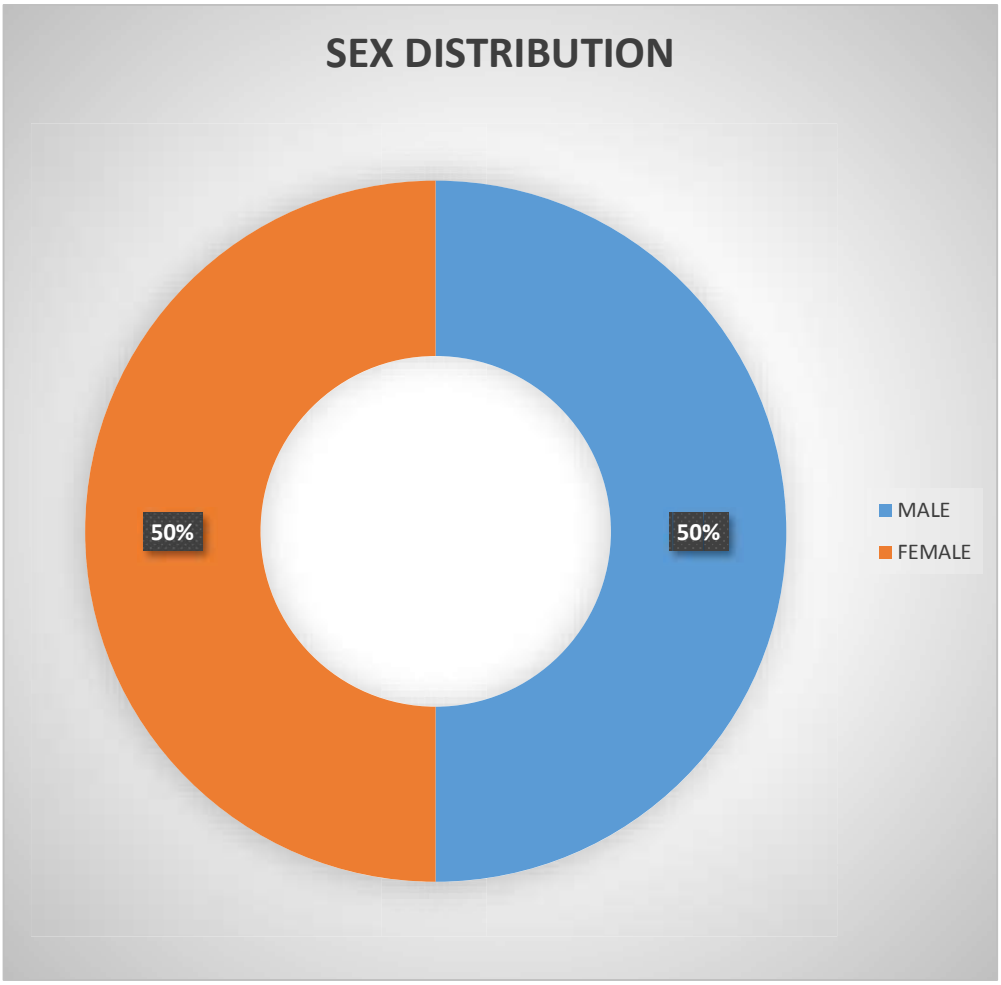


Table 5. Group wise sex distribution in the study

	GROUP		
SEX	**T2DM**	**T2DM+NPDR**	**T2DM+PDR**
MALE	21	29	25
FEMALE	29	21	25

Chart 5. Group wise sex distribution in the study

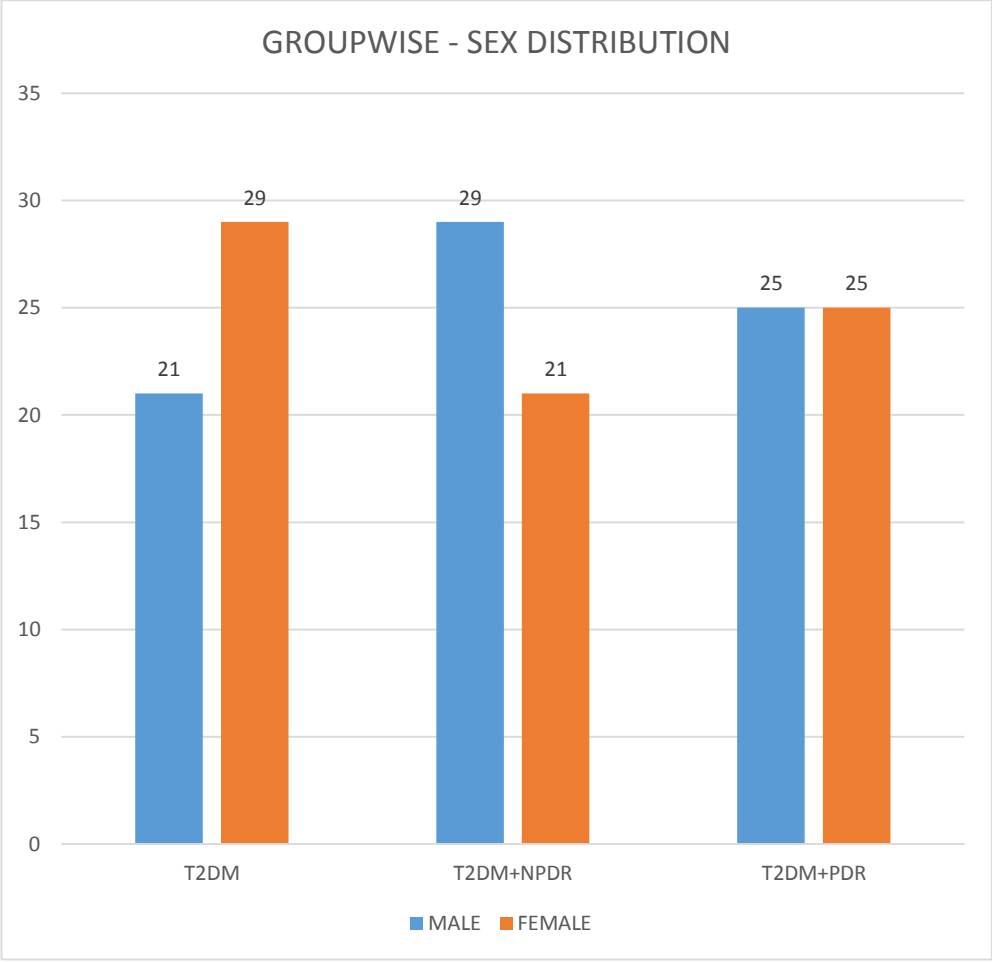


Table 6. Smoking distribution in the study

SMOKING	NO OF PATIENTS	PERCENTAGE
PRESENT	53	35.30%
ABSENT	97	64.70%

Chart 6. Smoking distribution in the study

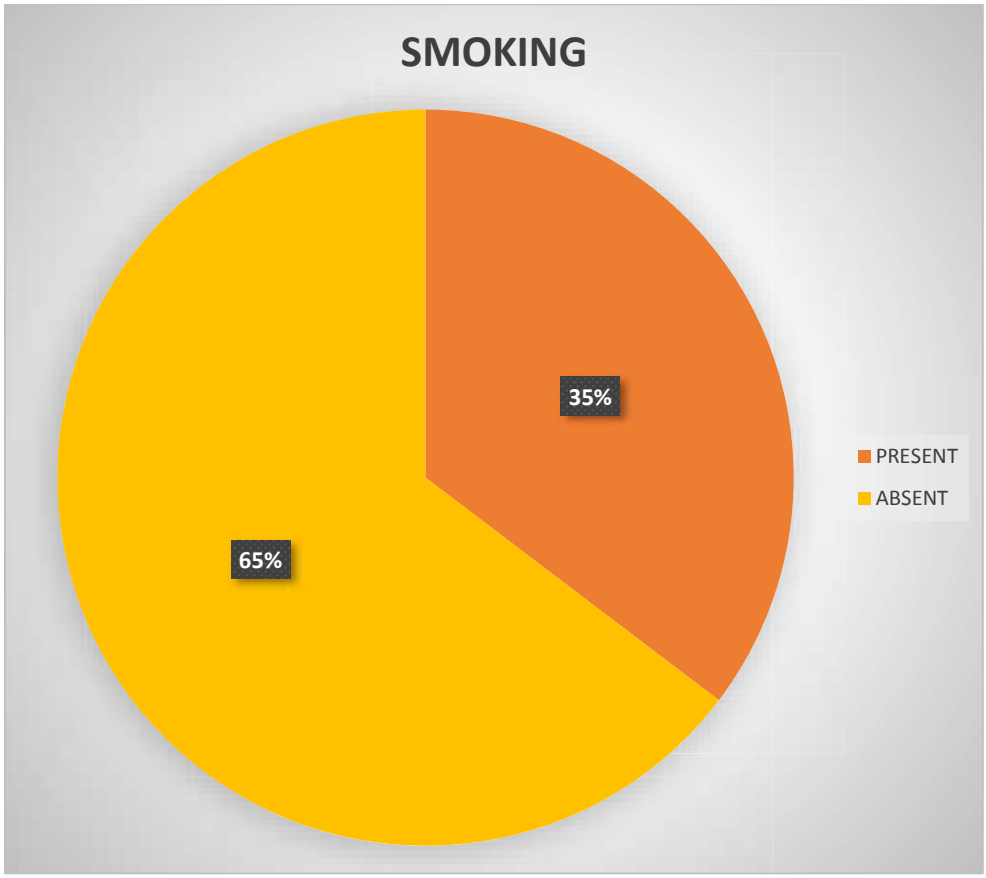


Table 7. Group wise smoking distribution in the study

	GROUP		
SMOKING	**T2DM**	**T2DM+NPDR**	**T2DM+PDR**
PRESENT	14	21	18
ABSENT	36	29	32

Chart 7. Group wise smoking distribution in the study

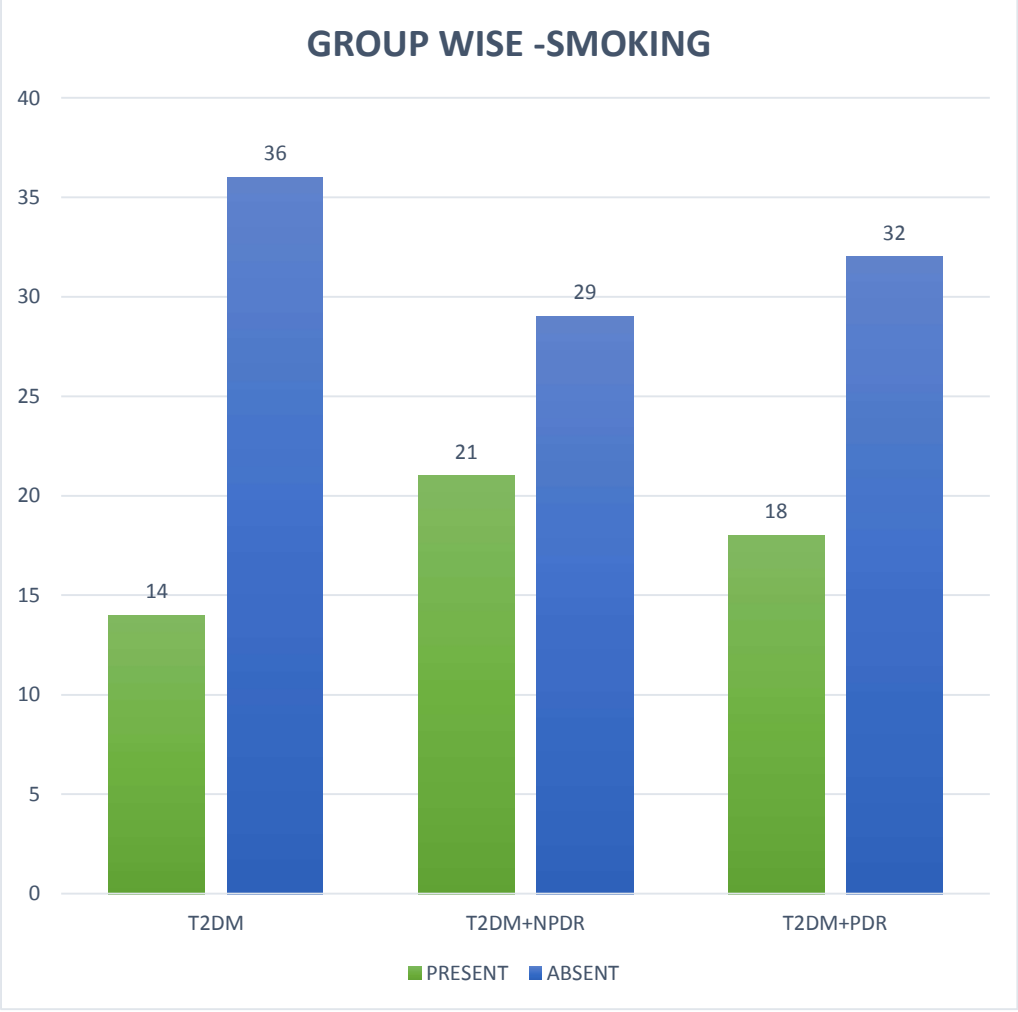


Table 8 . Duration of Diabetes mellitus

DURATION	NO OF PATIENTS	PERCENTAGE
< 5 YEARS	77	51.30%
5-10 YEARS	49	32.60%
> 10 YEARS	24	16.10%

Chart 8. Duration of diabetes mellitus

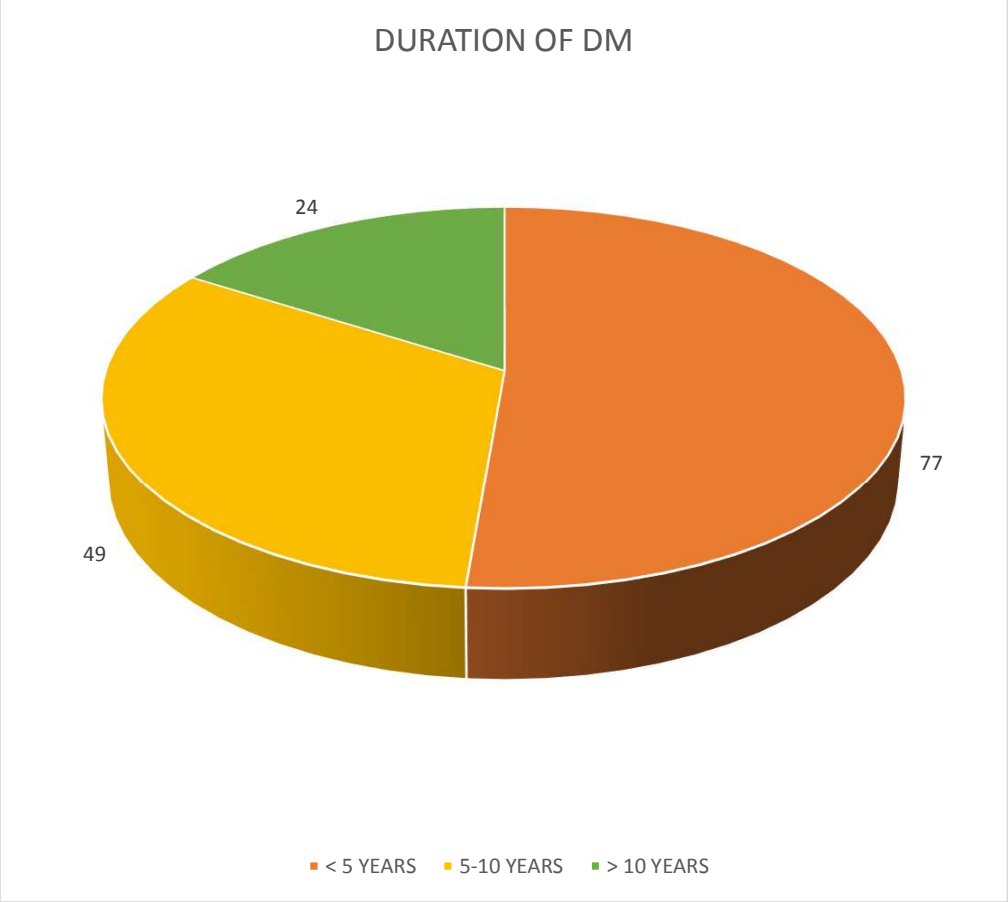


Table 9. Group wise duration of diabetes mellitus

	GROUP		
DURATION	**T2DM**	**T2DM+NPDR**	**T2DM+PDR**
< 5 YEARS	48	27	2
5-10 YEARS	2	23	24
> 10 YEARS	0	0	24

Chart 8. Group wise duration of diabetes mellitus

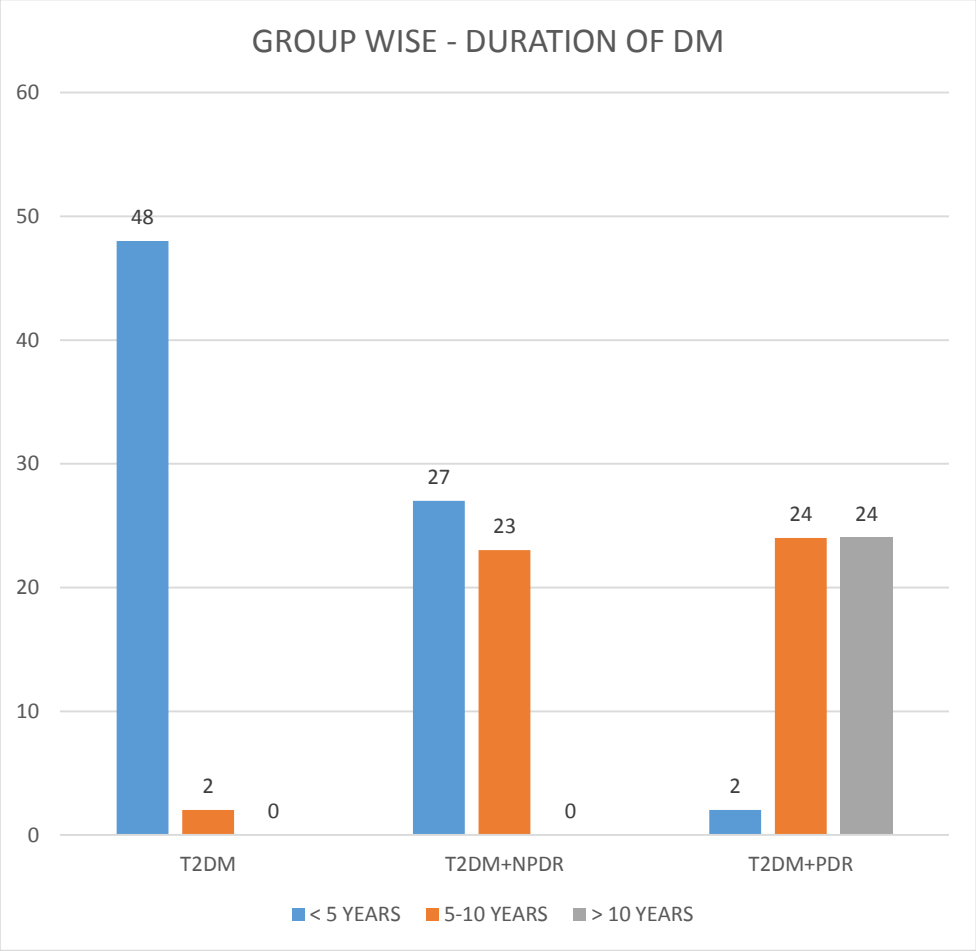


Table 10. Mean of Age, Systolic BP, Diastolic BP

GENERAL CHARECTERISTICS (N = 150)		
FACTOR	**MEAN**	**SD**
AGE (YRS)	52.92	6.99
SYSTOLIC BP	136.53	18.5
DIASTOLIC BP	87.07	13.87

Chart 10. Mean of Age, Systolic BP, Diastolic BP

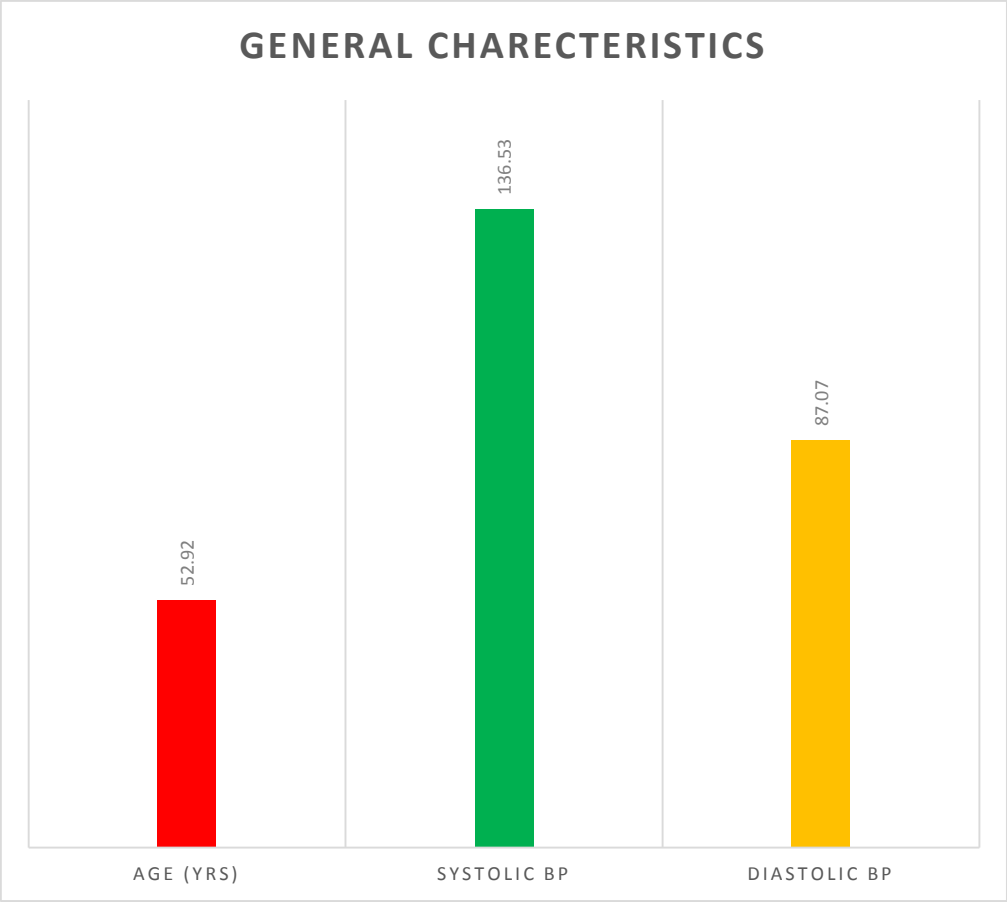


Table 11. Mean of Duration of DM, Fasting blood sugar,HbA1c

GENERAL CHARECTERISTICS (N = 150) – DM		
FACTOR	**MEAN**	**SD**
DURATION OF DM(YRS)	6.26	4.18
FBS	163.26	35.26
HBA1C	8.29	1.17

Chart 11. Mean of Duration of DM, Fasting blood sugar, HbA1c

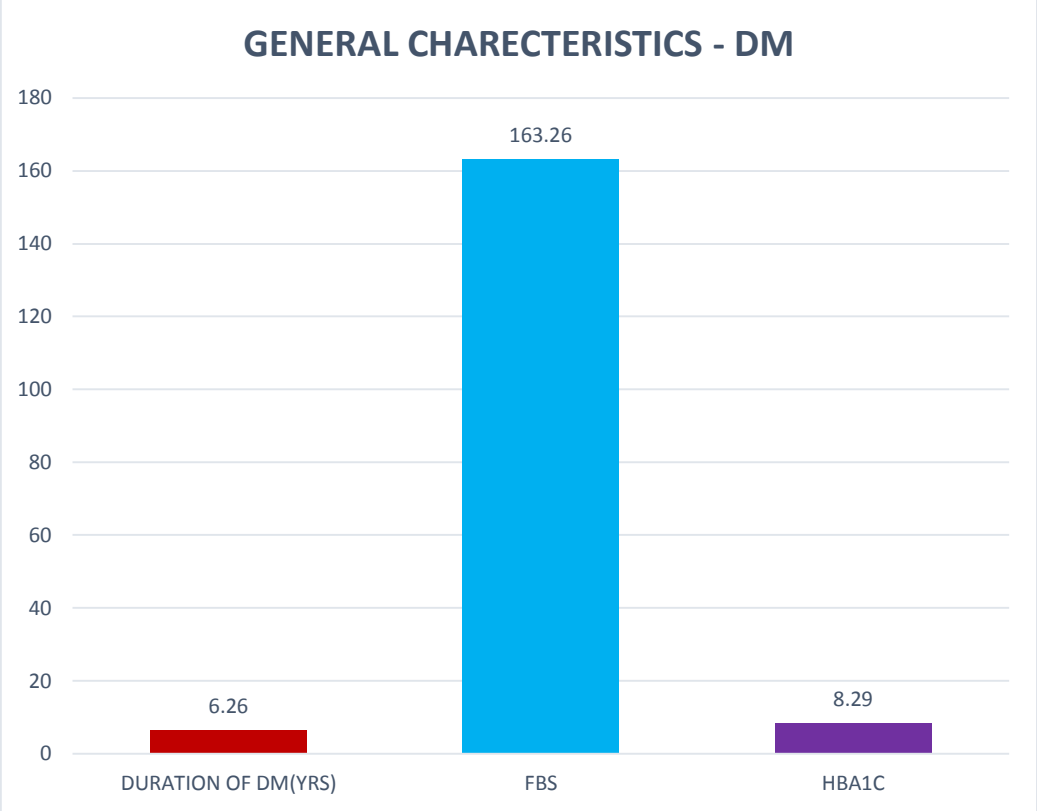


Table 12. General characteristics of Total cholesterol, Triglycerides, HDL

GENERAL CHARECTERISTICS (N = 150) – LIPID		
FACTOR	**MEAN**	**SD**
TOTAL CHOLESTEROL	223.13	24.15
TRIGLYCERIDES	179.35	20.12
HDL	41.37	13.87

Chart 12. General characteristics of Total cholesterol, Triglycerides, HDL

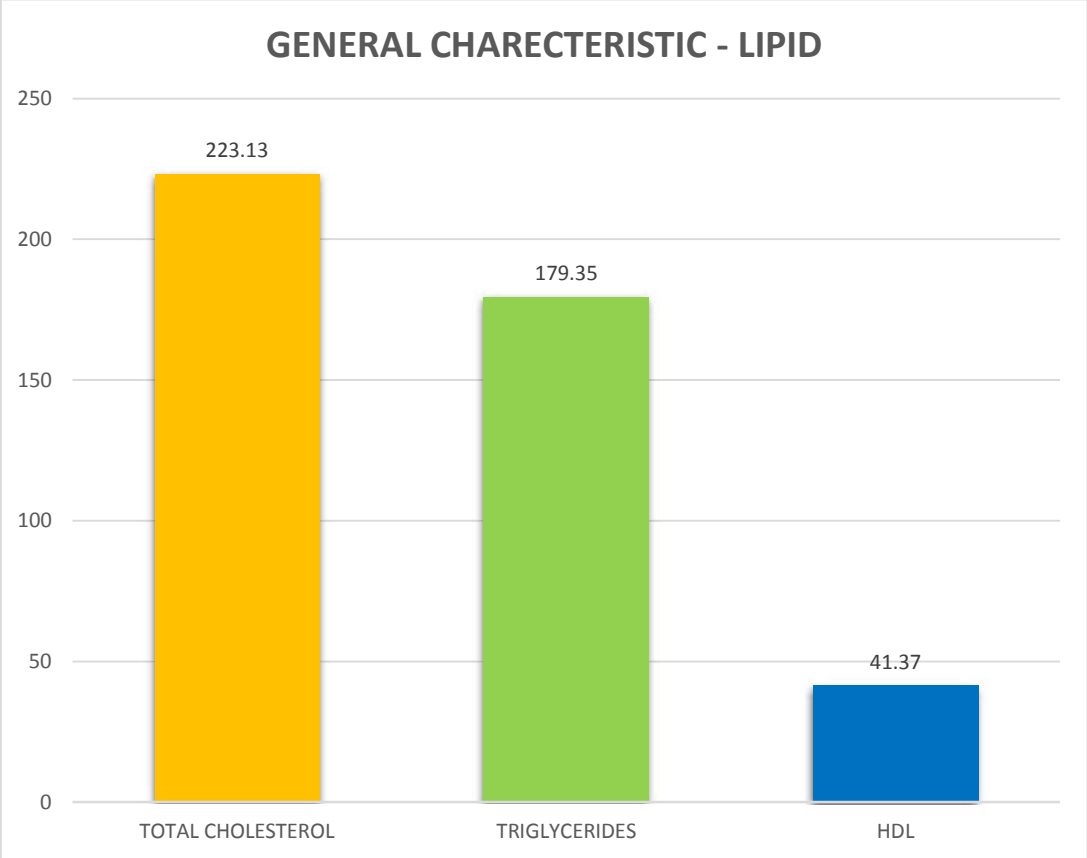


Table 13. General characteristics of complete blood count

GENERAL CHARECTERISTICS (N = 150) – BLOOD		
FACTOR	**MEAN**	**SD**
WBC	6359.13	1350.49
LYMPHOCYTE	2316.96	558.68
NEUTROPHIL	2992.17	811.71
MONOCYTE	409.88	158.3
PLATELET	230633	61546

Table 14. General characteristics of NLR, MLR. PLR

GENERAL CHARECTERISTICS (N = 150) – RATIO		
FACTOR	**MEAN**	**SD**
NEUTROPHIL/LYMPHOCYTE	1.3	0.13
MONOCYTE/LYMPHOCYTE	0.17	0.04
PLATELET/LYMPHOCYTE	99.98	13.79

Table 15. Comparison of means of age in different groups

GROUP	AGE (IN YEARS)	
	MEAN	SD
T2DM	50.28	8.06
T2DM+NPDR	51.76	5.33
T2DM+PDR	56.72	5.68
P VALUE - 0.001		
SIGNIFICANT		
ANOVA		

Chart 13. Comparison of means of Age in different groups

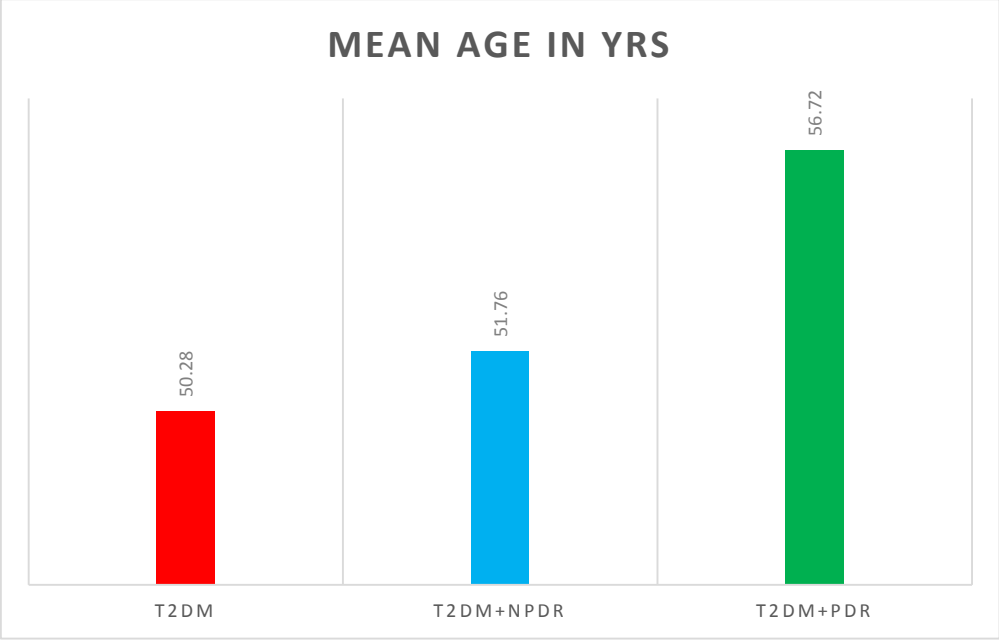


Table 16. Mean duration of DM

GROUP	DURATION OF DM IN YRS	
	MEAN	SD
T2DM	2.48	1.98
T2DM+NPDR	5.68	2.27
T2DM+PDR	10.66	3.34
P VALUE - 0.001		
SIGNIFICANT		
ANOVA		

Chart 14. Mean duration of DM

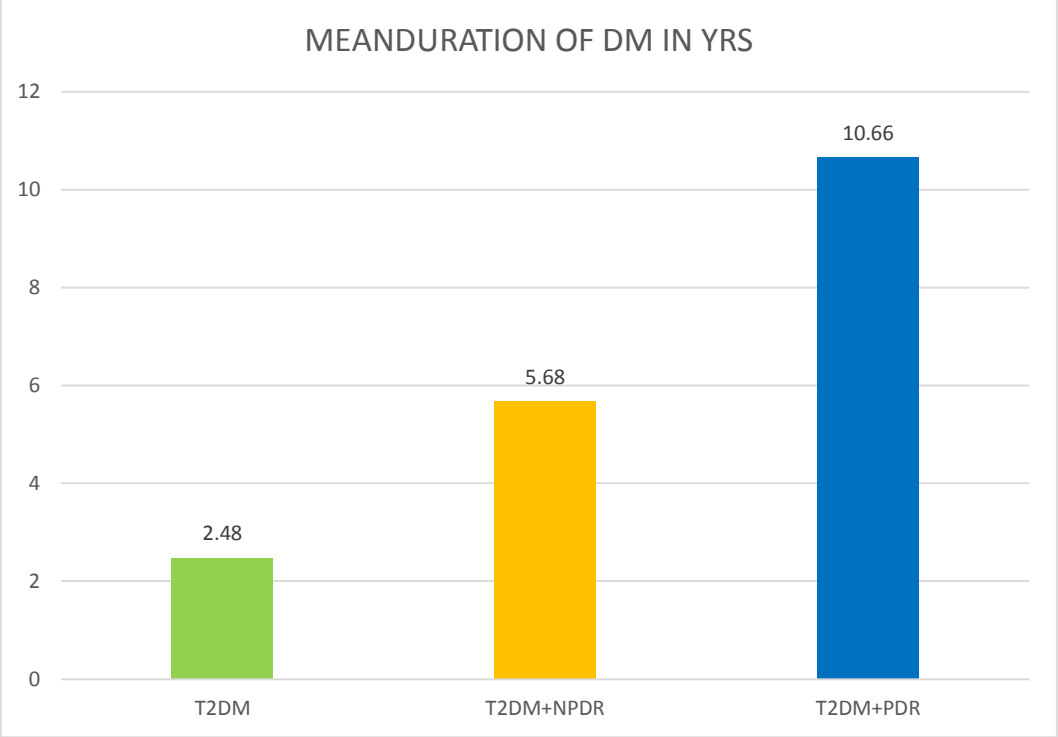


Table 17. Mean systolic BP in three groups

GROUP	SYSTOLIC BP	
	MEAN	SD
T2DM	128	12.4
T2DM+NPDR	137.4	18.6
T2DM+PDR	144.2	19.5
P VALUE - 0.001		
SIGNIFICANT		
ANOVA		

Chart 15 .Mean systolic BP in three groups

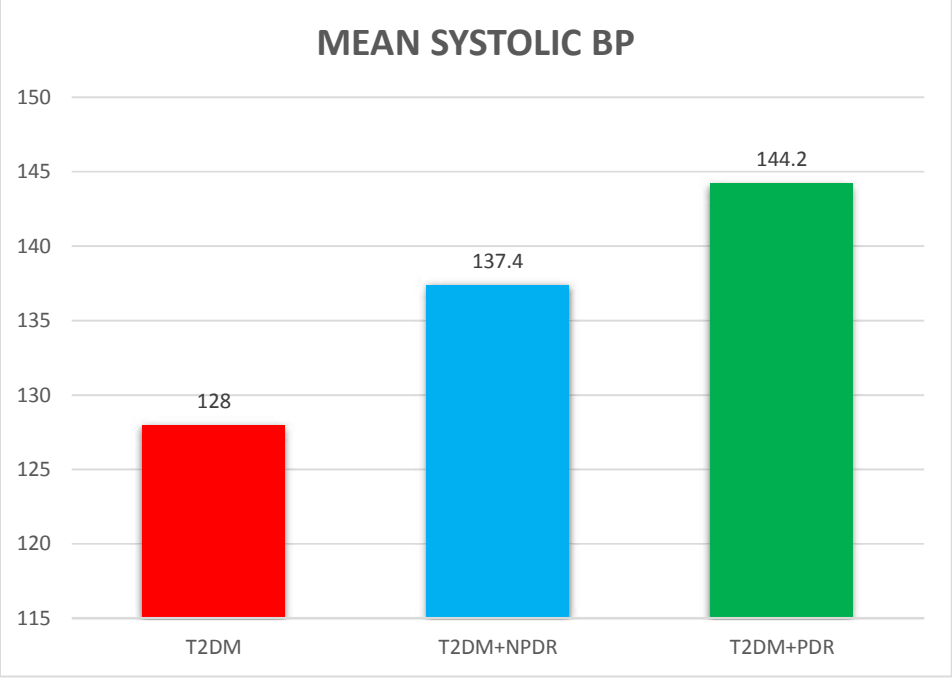


Table 18. Mean diastolic BP in three groups

GROUP	DIASTOLIC BP	
	MEAN	SD
T2DM	84.4	10
T2DM+NPDR	86.4	12.2
T2DM+PDR	90.4	17.49
P VALUE - 0.001		
SIGNIFICANT		
ANOVA		

Chart 16 . Mean diastolic BP in three groups

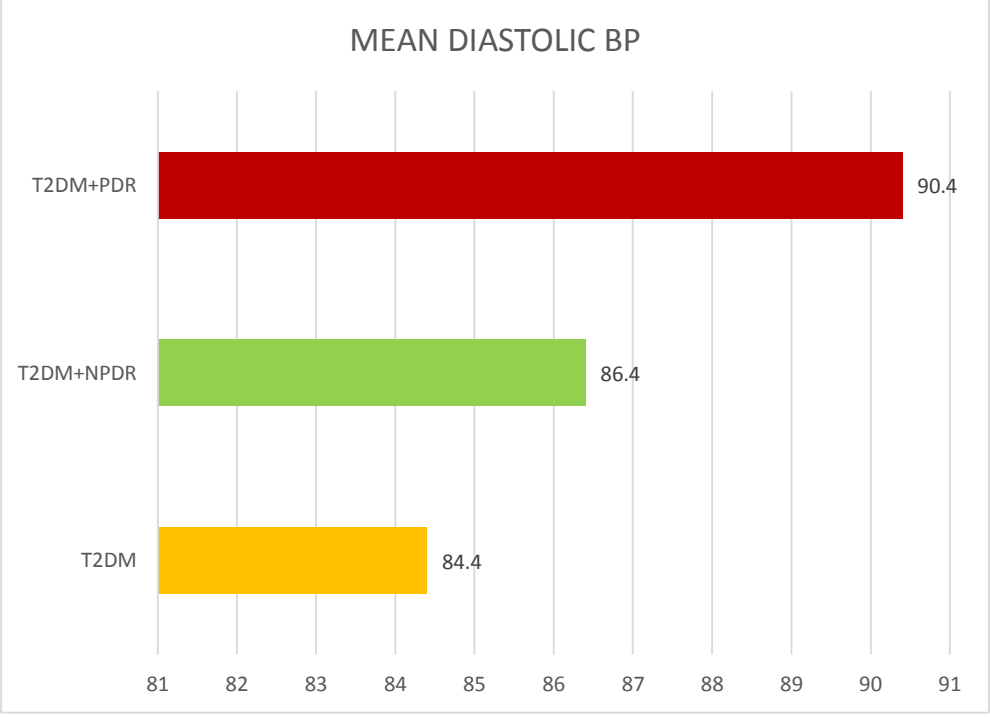


Table 19. Mean fasting blood sugar in three groups

GROUP	FASTING BLOOD SUGAR	
	MEAN	SD
T2DM	137.46	15.6
T2DM+NPDR	166.06	33.7
T2DM+PDR	186.26	34.22
P VALUE - 0.001		
SIGNIFICANT		
ANOVA		

Chart 17.Mean diastolic blood pressure in three groups

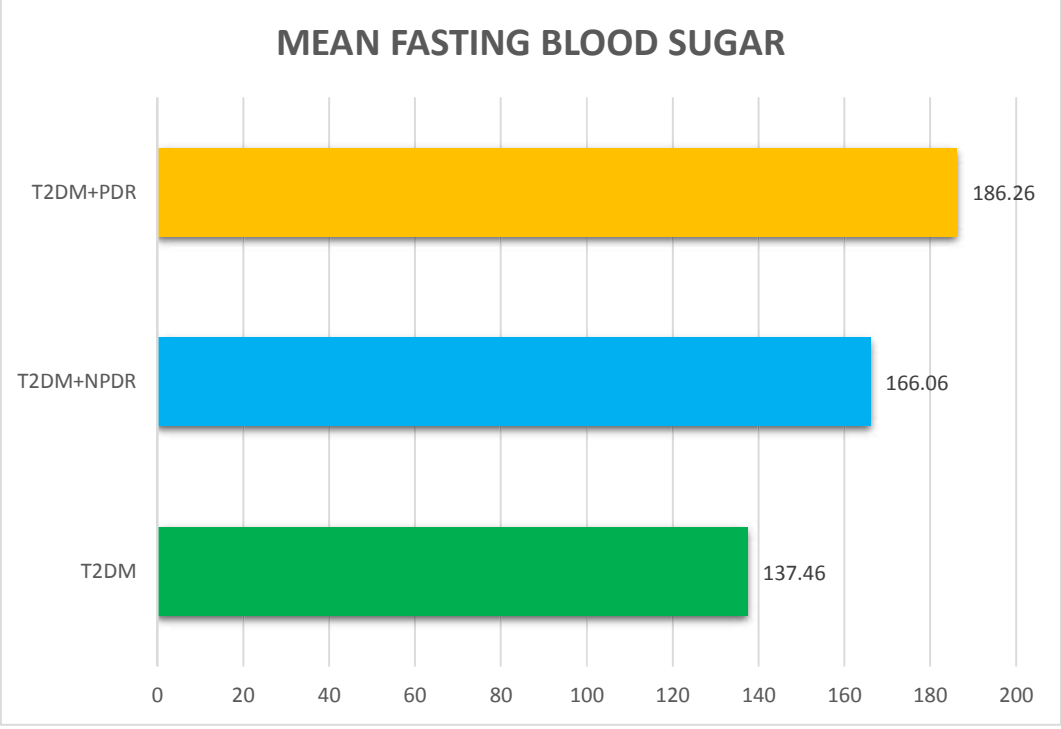


Table 20. Comparison of mean HbA1c in three groups

GROUP	HBA1C	
	MEAN	SD
T2DM	7.46	0.64
T2DM+NPDR	8.09	0.84
T2DM+PDR	9.13	1.25
P VALUE - 0.001		
SIGNIFICANT		
ANOVA		

Chart 18. Comparison of mean HbA1c in all three groups

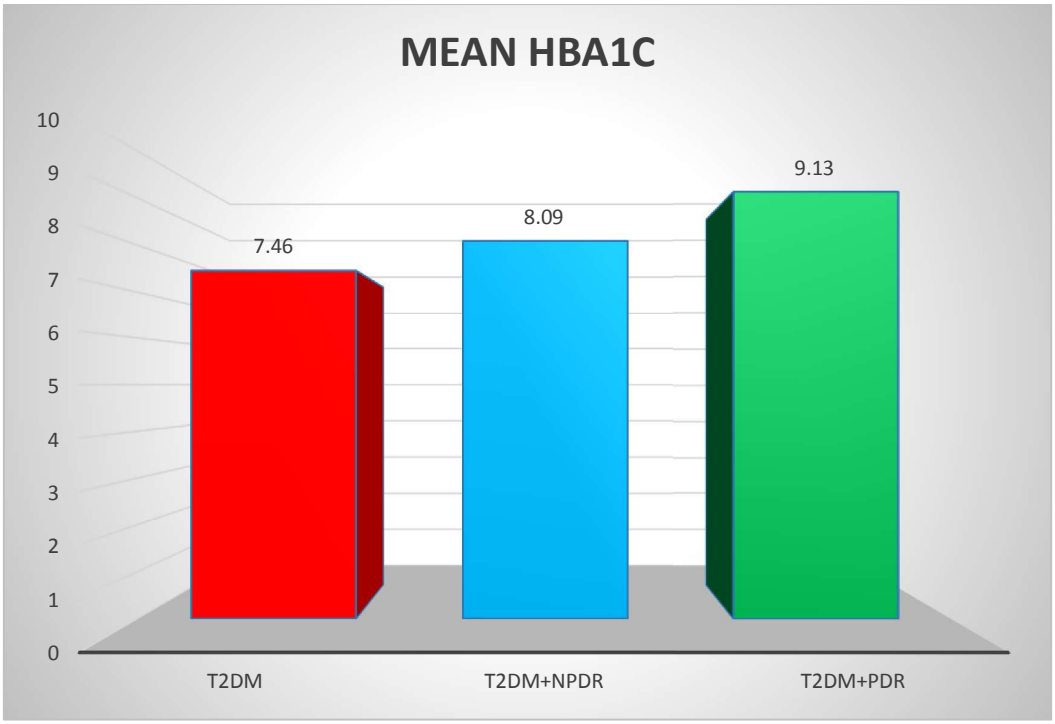


Table 21. Comparison of Total cholesterol in three groups

GROUP	TOTAL CHOLESTEROL	
	MEAN	SD
T2DM	213.5	20.49
T2DM+NPDR	219.08	18.08
T2DM+PDR	236.25	26.99
P VALUE - 0.001		
SIGNIFICANT		
ANOVA		

Chart 19. Comparison of mean chlolesterol in all three groups

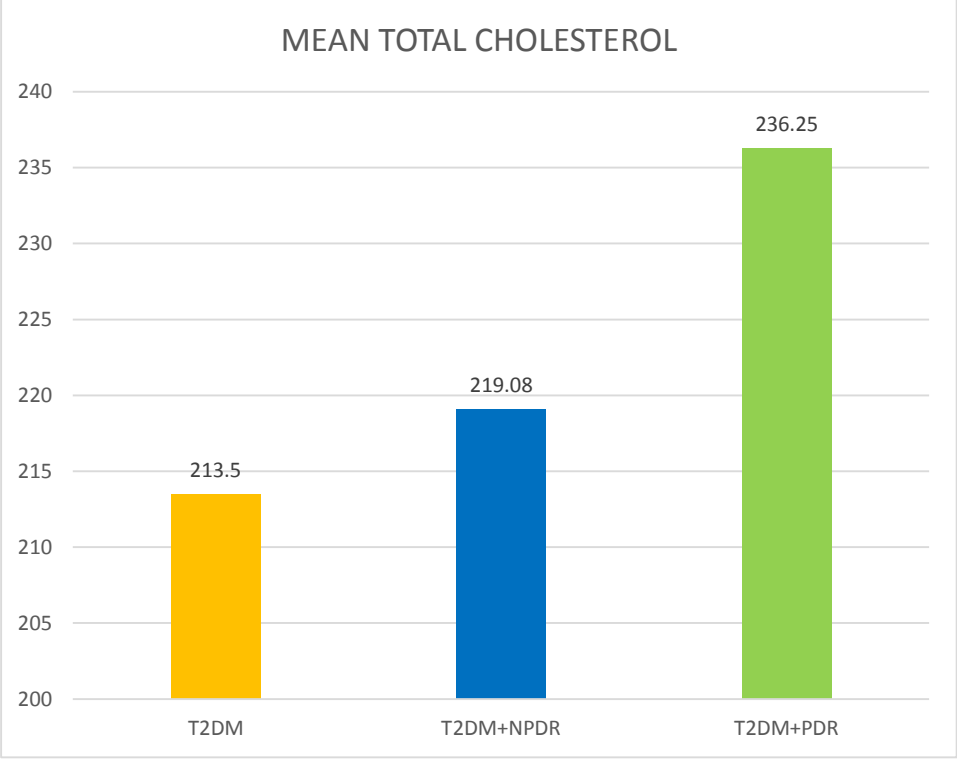


Table 22. Comparison of mean triglycerides in three groups

GROUP	TRIGLYCERIDES	
	MEAN	SD
T2DM	169.32	20.6
T2DM+NPDR	182.06	19.2
T2DM+PDR	186.68	16.8
P VALUE - 0.001		
SIGNIFICANT		
ANOVA		

Chart 20. Comparison of mean triglycerides in three groups

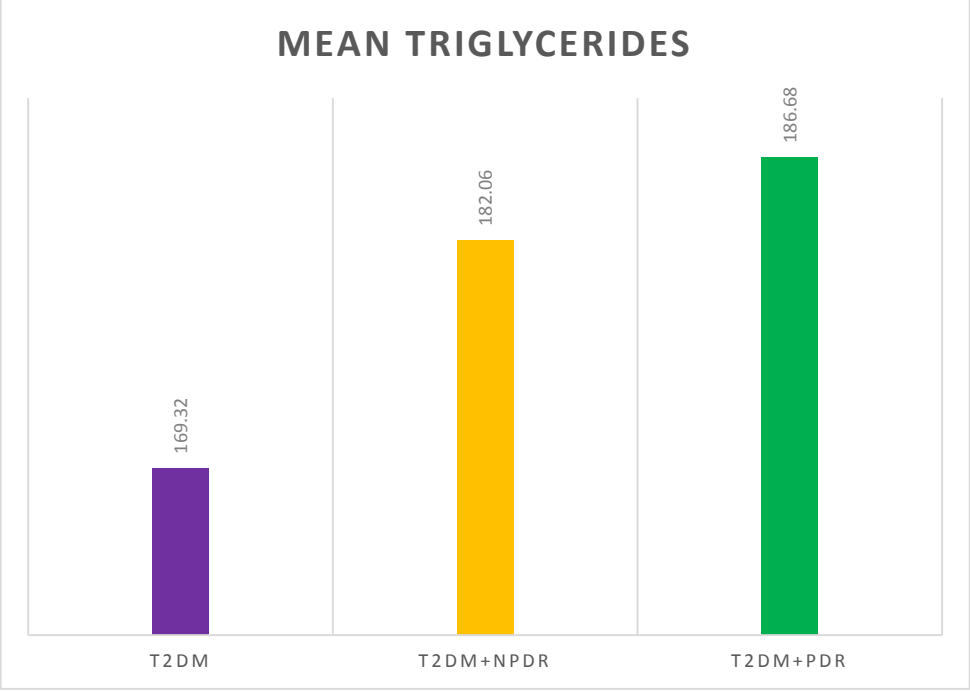


Table 23. Comparison of mean HDL in three groups

GROUP	HIGH DENSITY LIPOPROTEIN	
	MEAN	SD
T2DM	43.4	8.28
T2DM+NPDR	42.48	9.28
T2DM+PDR	37.72	6.18
P VALUE - 0.001		
SIGNIFICANT		
ANOVA		

Chart 21. Comparison of mean HDL in three groups

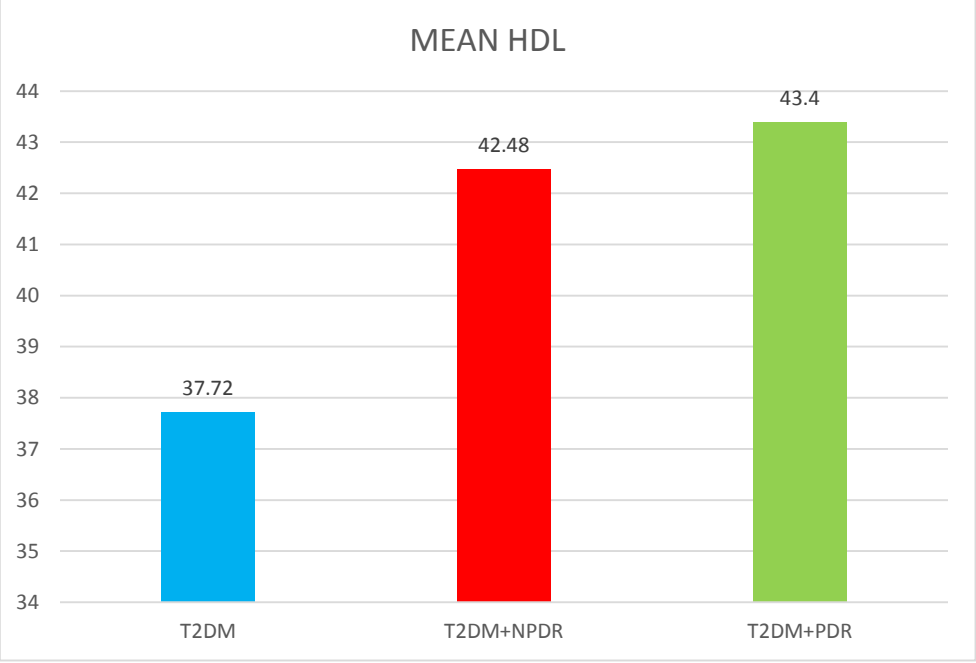


Table 24. Comparison of mean WBC in three groups

GROUP	WHITE BLOOD CELLS	
	MEAN	SD
T2DM	6042	1017
T2DM+NPDR	6546	1425
T2DM+PDR	6490	1496
P VALUE - 0.119		
NON SIGNIFICANT		
ANOVA		

Chart 22. Comparison of mean WBC in three groups

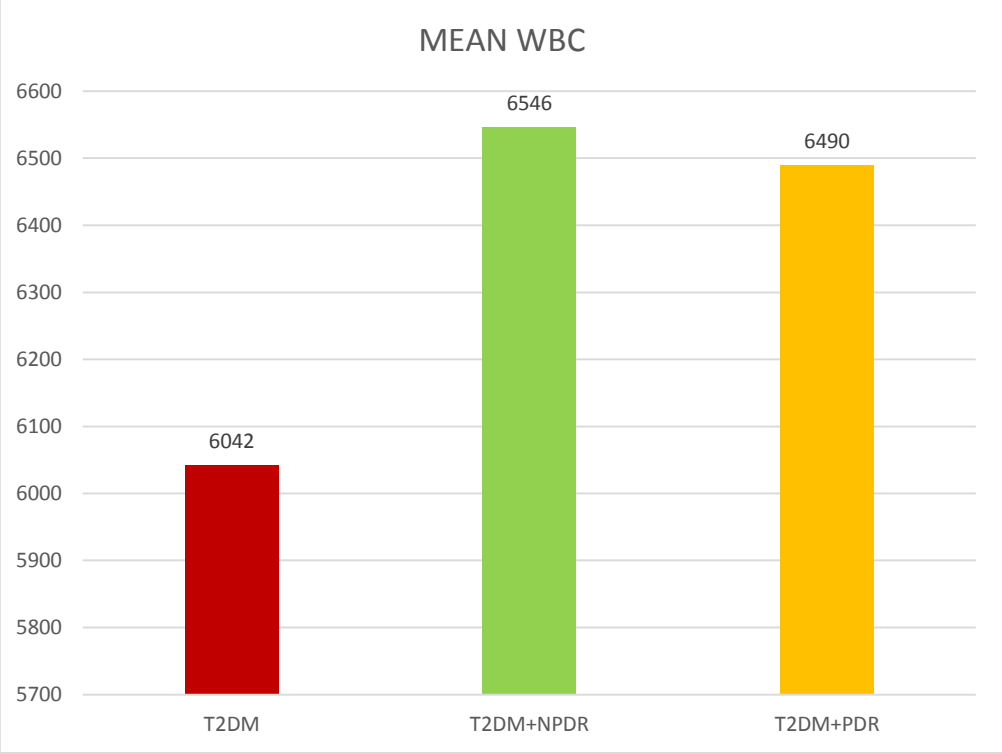


Table 25.Comparison of mean Lymphocyte count in three groups

GROUP	LYMPHOCYTES	
	MEAN	SD
T2DM	2363.2	417
T2DM+NPDR	2342.8	611.52
T2DM+PDR	2250.9	876
P VALUE - 0.567		
NON SIGNIFICANT		
ANOVA		

Chart 23.Comparison of mean lymphocyte count in three groups

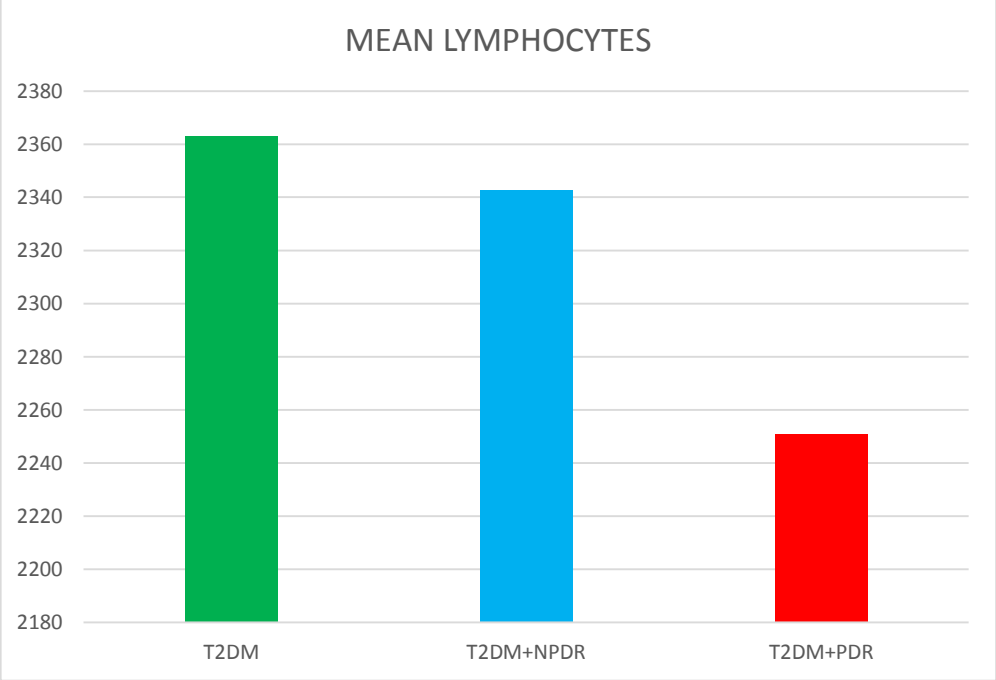


Table 26. Comparison of mean neutrophil count in three groups

GROUP	NEUTROPHIL	
	MEAN	SD
T2DM	2824.1	631
T2DM+NPDR	3011.8	886
T2DM+PDR	3140	876
P VALUE - 0.146		
NON SIGNIFICANT		
ANOVA		

Chart 24. Comparison of mean neutrophil count in three groups

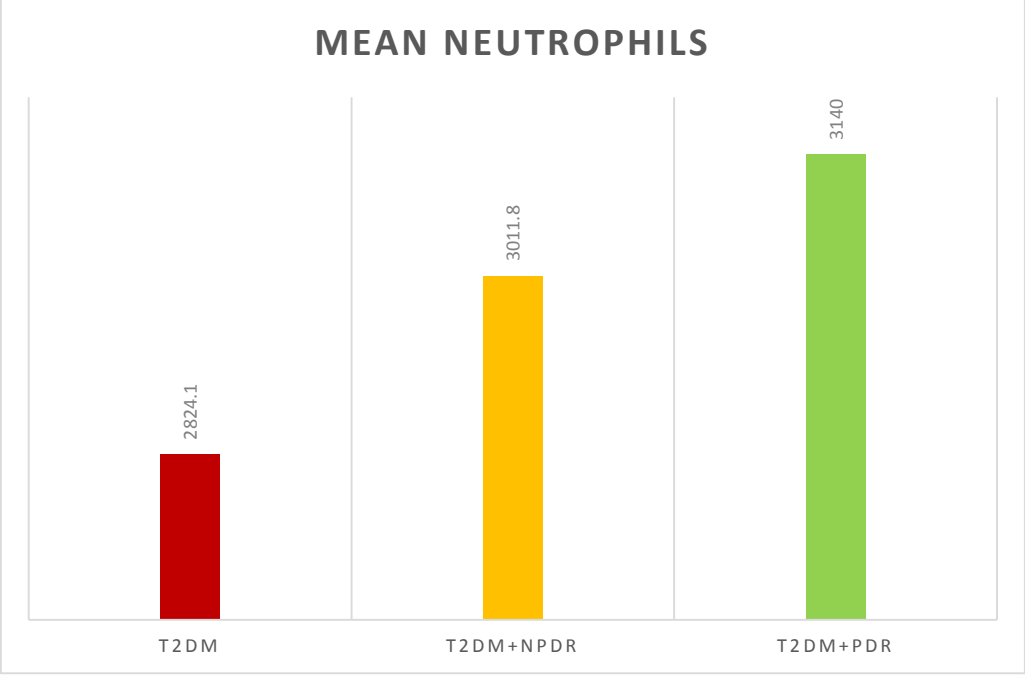


Table 27 . Comparison of mean monocyte count in three groups

GROUP	MONOCYTE	
	MEAN	SD
T2DM	334.1	113.69
T2DM+NPDR	442.1	158.4
T2DM+PDR	453.44	171.2
P VALUE - 0.002		
SIGNIFICANT		
ANOVA		

Chart 25. Comparison of mean monocyte count in three groups

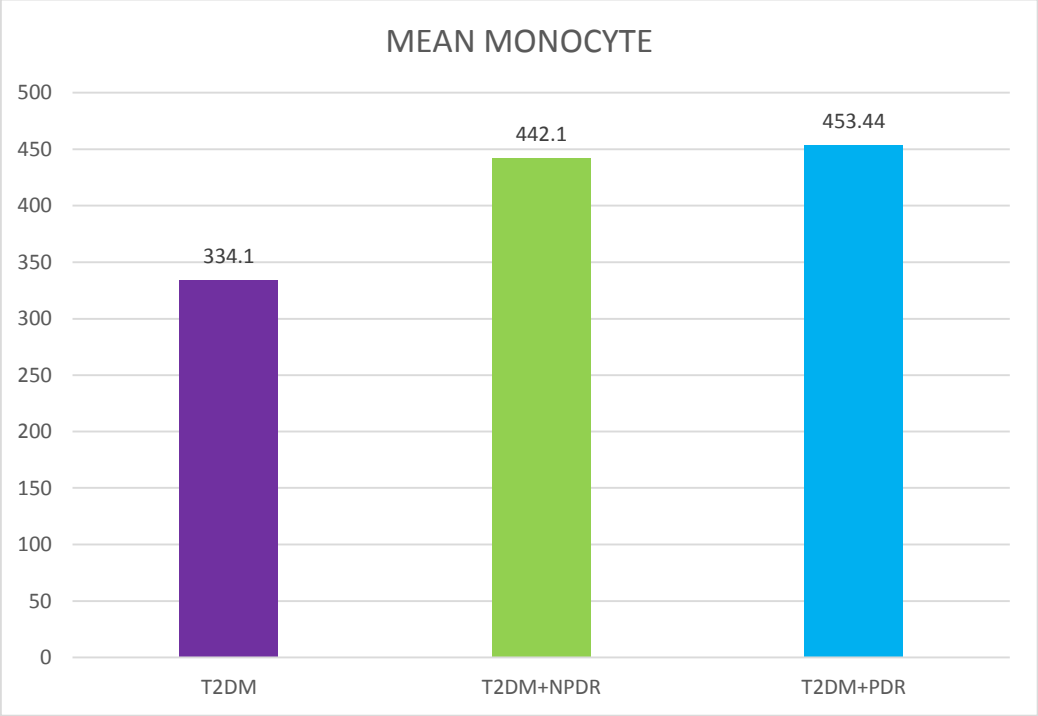


Table 28. Comparison of mean platelet count in three groups

GROUP	PLATELET	
	MEAN	SD
T2DM	211840	29983
T2DM+NPDR	236798	67227
T2DM+PDR	243327	74332
P VALUE - 0.025		
SIGNIFICANT		
ANOVA		

Chart 26. Comparison of mean platelet count in three groups

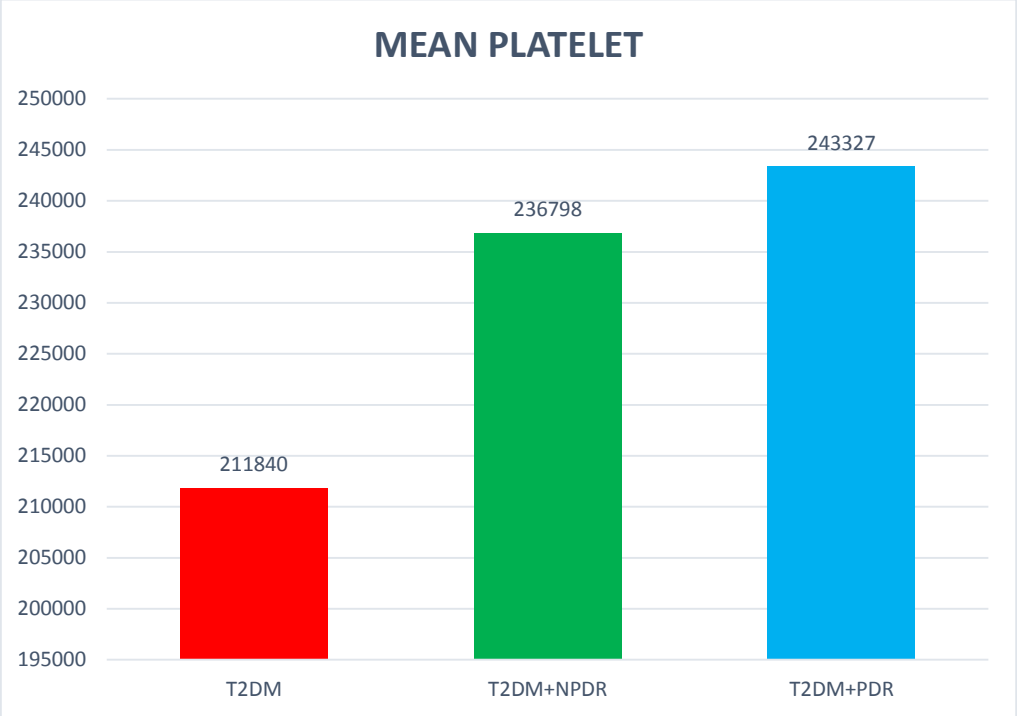


Table 29.Comparison of NLR in three groups

GROUP	NEUTROPHIL/LYMPHOCYTE	
	MEAN	SD
T2DM	1.17	0.1
T2DM+NPDR	1.32	0.08
T2DM+PDR	1.42	0.08
P VALUE - 0.002		
SIGNIFICANT		
ANOVA		

Chart 27. Comparison of NLR in three groups

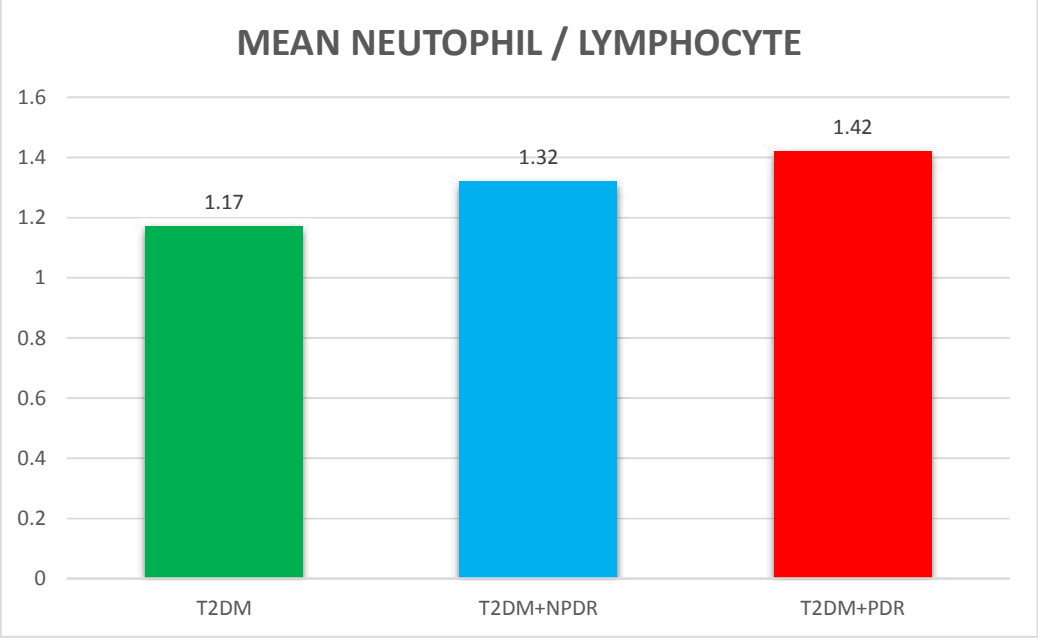


Table 30. Comparison of MLR in three groups

GROUP	MONOCYTE/LYMPHOCYTE	
	MEAN	SD
T2DM	0.13	0.02
T2DM+NPDR	0.19	0.03
T2DM+PDR	0.195	0.04
P VALUE - 0.001		
SIGNIFICANT		
ANOVA		

Chart 28. Comparison of MLR in three groups

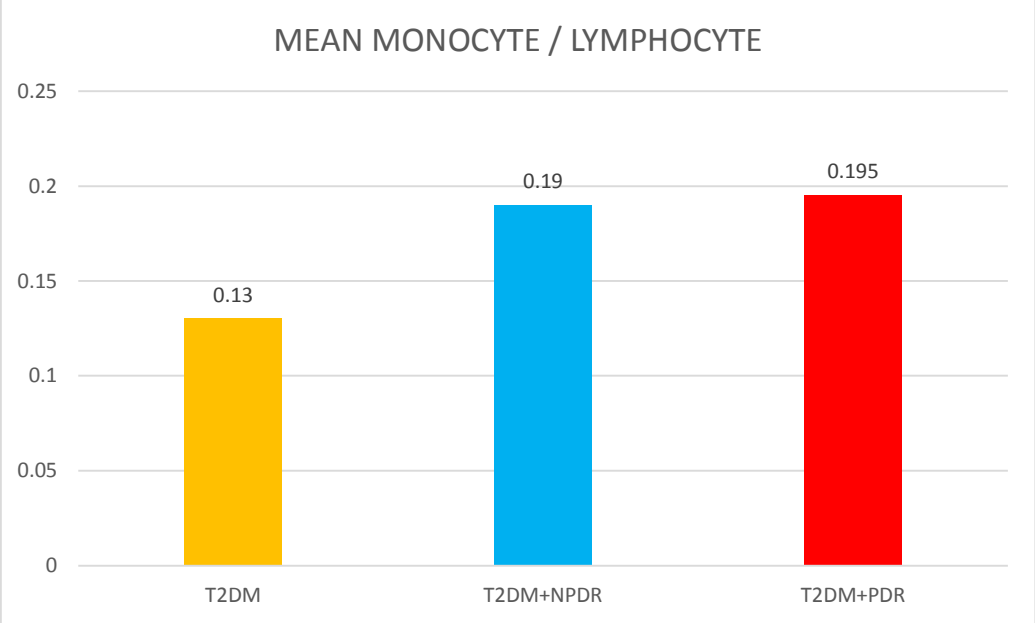
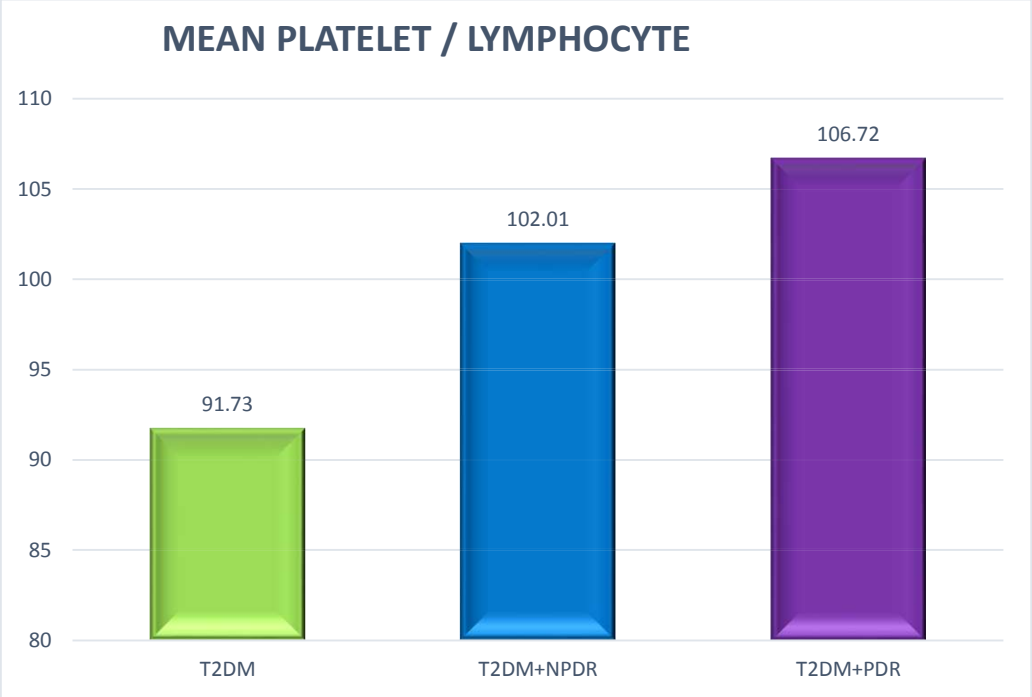


Table 31. Comparison of PLR in three groups

GROUP	PLATELET/LYMPHOCYTE	
	MEAN	SD
T2DM	91.73	17.29
T2DM+NPDR	102.01	9.31
T2DM+PDR	106.72	8.97
P VALUE - 0.001		
SIGNIFICANT		
ANOVA		

Chart 29. Comparison of PLR in three groups



PEARSON CORRELATION WITH RETINOPATHY		
FACTORS	**R VALUE**	**P VALUE**
AGE IN YEARS	0.377	0.001
DURATION OF DM	0.065	0.427
SYSTOLIC BP	0.801	0.001
DIASTOLIC BP	0.339	0.029
FASTING BLOOD SUGAR	0.178	0.001
HBA1C	0.567	0.001
TOTAL CHOLESTEROL	0.586	0.466
TRIGLYCERIDES	0.068	0.001
HDL	0.395	0.001
WBC	0.353	0.001
LYMPHOCYTE	0.278	0.095
NEUTROPHIL	0.137	0.316
MONOCYTE	0.082	0.051
PLATELET	0.16	0.042
NEUTROPHIL/LYMPHOCYTE	0.736	0.001
MONOCYTE/LYMPHOCYTE	0.52	0.001
PLATELET/LYMPHOCYTE	0.43	0.001
P VALUE < 0.05 IS SIGNIFICANT AT 95% CI		

DISCUSSION

Diabetic retinopathy is a microvascular complication of diabetes involving series of multiple events. Powell et al., has reported that some anti inflammatory agents may prevent the disease occurrence, showing that inflammation play a role in diabetic retinopathy pathogenesis.[27]

Lutty et al., verified the association between WBCs and Diabetic retinopathy occurrence[28]. Besides WBC count there are some novel and potential inflammatory markers like Neutrophil Lymphocyte ratio, Monocyte lymphocyte ratio, Platelet Lymphocyte ratio has a positive correlation with occurrence and severity of diabetic retinopathy. There are many number of studies which has found the predictive effects of these ratios in picking up cases with diabetic retinopathy.

In this study, factors like age, duration of diabetes, smoking, fasting blood sugar, HbA1C, lipid profile, NLR, PLR, MLR were assessed and compared between all the three groups to know the predictive effects of the above mentioned factors in finding out the earlier occurrence of Diabetic retinopathy.

In this study majority of them 53.3% lie in the age group of 51 – 60 years. Sex distribution was equal. NPDR is seen in many of male patients, whereas PDR is found equally in both the sexes. Smoking was present in 35% of subjects, showing that majority are non smokers. Among the three groups, NPDR had the maximum smoking population of 21 subjects.

Majority of people around 51.2% had duration of diabetes less than 5 years. Comparison of means by using Anova test showed significant corelation with age and duration of DM. As the duration of DM increases, progression of diabetic retinopathy worsens.

Blood pressure, fasting blood sugar, lipid profile has a significant co relation with a P value of <0.001. HbA1c showed significance by using Anova test. The rate of progression of diabetic retinopathy increases with the increase in mean HbA1c.

The mean WBC, Lymphocyte, Neutrophil did not show any relation with diabetic retinopathy whereas monocyte and platelet showed significant relation. All the three ratio NLR, MLR, PLR showed a significant relation by using Anova.

By using Pearson correlation, age, blood pressure, fasting blood sugar, HbA1c, lipid profile, Total count , NLR, MLR, PLR showed a significant correlation with p value <0.05 at 95%CI. Thus by using both Anova and pearson correlation there is a significant correlation between the NLR, MLR, PLR and diabetic retinopathy.

The advantage in using these ratio is that they show a good stability because they are absolute counts which do not vary much with alteration in physiological, physical and pathological factors. Our results suggest that DM patients with DR had higher ratios compared to diabetics without DR. This is in accordance with findings seen in similar study conducted by Ulu et al.[17] and Wang et al.[18]

CONCLUSION

In conclusion, the NLR, MLR, PLR ratios are significantly increased in the setting of diabetic retinopathy and they also correlate well with the severity of diabetic retinopathy. Thus early detection of these abnormal ratio levels will be helpful to detect diabetic retinopathy and also to assess the progression of the disease in diabetic patients

Hence, these ratios can serve as remarkable markers while evaluating diabetes patients with or without retinopathy and they are of predictive and prognostic value. These are all simple, fast, non invasive and widely available inflammatory biomarkers that can offer an additional information to stratify the risk and to assess the severity of diabetic retinopathy progression.

Further studies should be done to establish the normality value for these ratios for specific population and should be designed to assess the effectiveness of anti inflammatory therapies using the fall of the ratios as a surrogate outcome and assess its role in guiding treatment.

BIBLIOGRAPHY

1. Chan J.C., Malik V., Jia W., Kadowaki T., Yajnik C.S., Yoon K.H., Hu F.B. Diabetes in Asia: Epidemiology, risk factors, and pathophysiology. JAMA. 2009;301:2129–2140.
2. Shaw J.E., Sicree R.A., Zimmet P.Z. Global estimates of the prevalence of diabetes for 2010 and 2030. Diabetes Res. Clin. Pract. 2010;87:4–14. doi: 10.1016/j.diabres.2009.10.007
3. Yamada M., Hiratsuka Y., Roberts C.B., Pezzullo M.L., Yates K., Takano S., Miyake K., Taylor H.R. Prevalence of visual impairment in the adult Japanese population by cause and severity and future projections. Ophthalmic Epidemiol. 2010;17:50–57.
4. Joussen A.M., Poulaki V., Le M.L., Koizumi K., Esser C., Janicki H., Schraermeyer U., Kociok N., Fauser S., Kirchhof B., et al. A central role for inflammation in the pathogenesis of diabetic retinopathy. FASEB J. 2004;18:1450–1452.
5. Tang J., Kern T.S. Inflammation in diabetic retinopathy. Prog. Retin. Eye Res. 2011;30:343–358. doi: 10.1016/j.preteyeres.2011.05.002.
6. El-Asrar A.M. Role of inflammation in the pathogenesis of diabetic retinopathy. Middle East Afr. J. Ophthalmol. 2012;19:70–74. doi: 10.4103/0974-9233.92118
7. Tomić M., Ljubić S., Kaštelan S., Gverović Antunica A., Jazbec A., Poljičanin T. Inflammation, haemostatic disturbance, and obesity:

Possible link to pathogenesis of diabetic retinopathy in type 2 diabetes. Mediat. Inflamm. 2013;2013:818671.

8. Horne B.D., Anderson J.L., John J.M. Which white blood cell subtypes predict increased cardiovascular risk? J. Am. Coll. Cardiol. 2005;45:1638–1643. doi: 10.1016/j.jacc.2005.02.054

9. Gunduz S., Mutlu H., Tural D., Yıldız Ö., Uysal M., Coskun H.S., Bozcuk H. Platelet to lymphocyte ratio as a new prognostic for patients with metastatic renal cell cancer. Asia Pac. J. Clin. Oncol. 2015 doi: 10.1111/ajco.12358

10. Ozaksit G., Tokmak A., Kalkan H., Yesilyurt H. Value of the platelet to lymphocyte ratio in the diagnosis of ovarian neoplasms in adolescents. Asian Pac. J. Cancer Prev. 2015;16:2037–2041.

11. Liu J., Du J., Fan J., Liu K., Zhang B., Wang S., Wang W., Wang Z., Cai Y., Li C., et al. The Neutrophil-to-Lymphocyte Ratio Correlates with Age in Patients with Papillary Thyroid Carcinoma. ORL J. Otorhinolaryngol. Relat. Spec. 2015;77:109–116.

12. Akyel A., Yayla Ç., Erat M., Çimen T., Doğan M., Açıkel S., Aydoğdu S., Yeter E. Neutrophil-to-lymphocyte ratio predicts hemodynamic significance of coronary artery stenosis. Anatol. J. Cardiol. 2015 doi: 10.5152/akd.2015.5909.

13. Oylumlu M., Yıldız A., Oylumlu M., Yuksel M., Polat N., Bilik M.Z., Akyuz A., Aydin M., Acet H., Soydinc S. Platelet-to-lymphocyte ratio is

a predictor of in-hospital mortality patients with acute coronary syndrome. Anatol. J. Cardiol. 2015;15:277–283.

14. Warimwe G.M., Fletcher H.A., Olotu A., Agnandji S.T., Hill A.V., Marsh K., Bejon P. Peripheral blood monocyte-to-lymphocyte ratio at study enrollment predicts efficacy of the RTS, S malaria vaccine: Analysis of pooled phase II clinical trial data. BMC Med. 2013;21:184. doi: 10.1186/1741-7015-11-184

15. Akbas E.M., Demirtas L., Ozcicek A., Timuroglu A., Bakirci E.M., Hamur H., Ozcicek F., Turkmen K. Association of epicardial adipose tissue, neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio with diabetic nephropathy. Int. J. Clin. Exp. Med. 2014;7:1794–1801.

16. Ciray H., Aksoy A.H., Ulu N., Cizmecioglu A., Gaipov A., Solak Y. Nephropathy, but not Angiographically Proven Retinopathy, is Associated with Neutrophil to Lymphocyte Ratio in Patients with Type 2 Diabetes. Exp. Clin. Endocrinol. Diabetes. 2015;123:267–271. doi: 10.1055/s-0035-1547257

17. Ulu S.M., Dogan M., Ahsen A., Altug A., Demir K., Acartürk G., Inan S. Neutrophil-to-lymphocyte ratio as a quick and reliable predictive marker to diagnose the severity of diabetic retinopathy. Diabetes Technol. Ther. 2013;15:942–947. doi: 10.1089/dia.2013.0097

18. Wang R.T., Zhang J.R., Li Y., Liu T., Yu K.J. Neutrophil-Lymphocyte ratio is associated with arterial stiffness in diabetic retinopathy in type 2 diabetes. J. Diabetes Complicat. 2015;29:245–249.

19. Shiny A., Bibin Y.S., Shanthirani C.S., Regin B.S., Anjana R.M., Balasubramanyam M., Jebarani S., Mohan V. Association of neutrophil-lymphocyte ratio with glucose intolerance: An indicator of systemic inflammation in patients with type 2 diabetes. Diabetes Technol. Ther. 2014;16:524–530. doi: 10.1089/dia.2013.0264.

20. Liu L., Geng J., Wu J., Yuan Z., Lian J., Desheng H., Chen L. Prevalence of ocular fundus pathology with type 2 diabetes in a Chinese urban community as assessed by telescreening. BMJ Open. 2013 doi: 10.1136/bmjopen-2013-004146.

21. Romero P., Sagarra R., Ferrer J., Fernández-Ballart J., Baget M. The incorporation of family physicians in the assessment of diabetic retinopathy by non-mydriatic fundus camera. Diabetes Res. Clin. Pract. 2010;88:184–188. doi: 10.1016/j.diabres.2010.02.001

22. Szabó D., Fiedler O., Somogyi A., Somfai G.M., Bíró Z., Ölvedy V., Hargitai Z., Németh J. Telemedical diabetic retinopathy screening in Hungary: A pilot programme. J. Telemed. Telecare. 2015;21:167–173. doi: 10.1177/1357633X1557271

23. Massin P., Erginay A., Ben Mehidi A., Vicaut E., Quentel G., Victor Z., Marre M., Guillausseau P.J., Gaudric A. Evaluation of a new non-mydriatic digital camera for detection of diabetic retinopathy. Diabet. Med. 2003;20:635–641. doi: 10.1046/j.1464-5491.2003.01002.x.

24. Wilkinson C.P., Ferris F.L., Klein R.E., Lee P.P., Agardh C.D., Davis M., Dills D., Kampik A., Pararajasegaram R., Verdaguer J.T. Global

Diabetic Retinopathy Project Group: Proposed international clinical diabetic retinopathy and diabetic macular edema disease severity scales. Ophthalmology. 2003;110:1677–1682. doi: 10.1016/S0161-6420(03)00475-5.

25. Puavilai G., Chanprasertyotin S., Sriphrapradaeng A. Diagnostic criteria for diabetes mellitus and other categories of glucose intolerance: 1997 Criteria by the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus (ADA), 1998 WHO consultation criteria, and 1985 WHO criteria. Diabetes Res. Clin. Pract. 1999;44:21–26. World Health Organization.

27. Varma R., Macias G.L., Torres M., Klein R., Pena F.Y., Azen S.P. Biologic risk factors associated with diabetic retinopathy: The Los Angeles Latino Eye Study. Ophthalmology. 2007;114:1332–1340. doi: 10.1016/j.ophtha.2006.10.023.

28. Powell E.D., Field R.A. Diabetic retinopathy and rheumatoid arthritis. Lancet. 1964;734:17–18. doi: 10.1016/S0140-6736(64)90008-X.

29. Lutty G.A., Cao J.T., McLeod D.S. Relationship of polymorphonuclear leukocytes to capillary dropout in the human diabetic choroid. Am. J. Pathol. 1997;151:707–714.

30. Pitsavos C., Tampourlou M., Panagiotakos D.B., Skoumas Y., Chrysohoou C., Nomikos T., Stefanadis C. Association between low-grade systemic inflammation and type 2 diabetes mellitus among men

and women from the ATTICA Study. Rev. Diabet. Stud. 2007;4:98–104. doi: 10.1900/RDS.2007.4.98

31. Fujita T., Hemmi S., Kajiwara M., Yabuki M., Fuke Y., Satomura A., Soma M. Complement-mediated chronic inflammation is associated with diabetic microvascular complication. Diabetes Metab. Res. Rev. 2013;29:220–226. doi: 10.1002/dmrr.2380.

32. Grossmann V., Schmitt V.H., Zeller T., Panova-Noeva M., Schulz A., Laubert-Reh D., Juenger C., Schnabel R.B., Abt T.G., Laskowski R., et al. Profile of the Immune and Inflammatory Response in Individuals with Prediabetes and Type 2 Diabetes. Diabetes Care. 2015;38:1356–1364. doi: 10.2337/dc14-3008

33. Afzal N., Zaman S., Shahzad F., Javaid K., Zafar A., Nagi A.H. Immune mechanisms in type-2 diabetic retinopathy. J. Pak. Med. Assoc. 2015;65:159–163.

34. Frostegard J. Immune mechanisms in atherosclerosis, especially in diabetes type 2. Front. Endocrinol. (Lausanne) 2013;29:162. doi: 10.3389/fendo.2013.00162.

35. Kaul K., Hodgkinson A., Tarr J.M., Kohner E.M., Chibber R. Is inflammation a common retinal-renal-nerve pathogenic link in diabetes? Curr. Diabetes Rev. 2010;6:294–303. doi: 10.2174/1573399107933608

36. Sasongko M.B., Wong T.Y., Jenkins A.J., Nguyen T.T., Shaw J.E., Wang J.J. Circulating markers of inflammation and endothelial function, and their relationship to diabetic retinopathy. Diabet. Med. 2015;32:686–691. doi: 10.1111/dme.12640.

37. Hudzik B., Szkodzinski J., Gorol J., Niedziela J., Lekston A., Gasior M., Polonski L. Platelet-to-lymphocyte ratio is a marker of poor prognosis in patients with diabetes mellitus and ST-elevation myocardial infarction. Biomark. Med. 2015;9:199–207. doi: 10.2217/bmm.14.100.

38. Xiao W.K., Chen D., Li S.Q., Fu S.J., Peng B.G., Liang L.J. Prognostic significance of neutrophil-lymphocyte ratio in hepatocellular carcinoma: A meta-analysis. BMC Cancer. 2014;14:117. doi: 10.1186/1471-2407-14-117.

39. Bambace N.M., Levis J.E., Holmes C.E. The effect of P2Y-mediated platelet activation on the release of VEGF and endostatin from platelets. Platelets. 2010;21:85–93. doi: 10.3109/09537100903470298

40. Jaipersad A.S., Lip G.Y., Silverman S., Shantsila E. The role of monocytes in angiogenesis and atherosclerosis. J. Am. Coll. Cardiol. 2014;63:1–11. doi: 10.1016/j.jacc.2013.09.019.

ANNEXURE 1

CASE PROFOMA

NAME

AGE / SEX ADDRESS

OCCUPATION OP NO

HISTORY OF PRESENTING ILLNESS

PAST HISTORY

PERSONAL HISTORY

VITALS

GENERAL EXAMINATION

SYSTEMIC EXAMINATION

FUNDUS EXAMINATION

INVESTIGATIONS:

CBC – Hemoglobin, Total count, absolute lymphocyte, neutrophil , monocyte count, platelet count, NLR, MLR, PLR.

FBS

LIPID PROFILE

HbA1C

ANNEXURE – 2

CONSENT FORM

Yourself Mr./Mrs./Ms…….. are being asked to be a participant in the research study titled "***ASSOCIATION BETWEEN DIABETIC RETINOPATHY AND THE NEUTROPHIL LYMPHOCYTE RATIO, PLATELET LYMPHOCYTE RATIO, MONOCYTE LYMPHOCYTE RATIO***" in CMC Hospital, Coimbatore, conducted by DR.KIRUTHIKA J., Post Graduate Student, Department of General Medicine, Coimbatore Medical College. You are eligible after looking into the inclusion criteria. You can ask any question you may have before agreeing to participate.

TOPIC OF RESEARCH

"*ASSOCIATION BETWEEN DIABETIC RETINOPATHY AND THE NEUTROPHIL LYMPHOCYTE RATIO, PLATELET LYMPHOCYTE RATIO, MONOCYTE LYMPHOCYTE RATIO*"

PURPOSE OF RESEARCH

In this study, interventions that are both cost saving and feasible in developing countries like complete hemogram are used to screen for complication of diabetes like Diabetic retinopathy.

PROCEDURES INVOLVED IN THE STUDY:

- Fetching baseline characteristics of the patient like age, gender, height, weight, etc.,
- Properly elicited medical history pertaining to the patient's complaints
- Detailed general and systemic examination as guided by the medical history
- Blood, urine and fundus examination as guided by the clinical examination
- Treatment with standard protocol currently followed in our hospital.
- Continued follow up of patient.
- Recording all the above variants / events into the database and analyzing them by statistical methods to arrive at our objectives.

DECLINE FROM PARTICIPATION

You are hereby made aware that participation in this study is purely voluntary and honorary, and that you have all the rights to decline from participating in it.

PRIVACY AND CONFIDENTIALITY

Privacy of individuals will be respected and any information about you or provided by you during the study will be kept strictly confidential.

AUTHORIZATION TO PUBLISH RESULTS

Results of the study may be published for scientific purposes and/or presented to scientific groups, however you will not be identified.

STATEMENT OF CONSENT

I volunteer and consent to participate in this study. I have read the consent or it has been read to me. The study has been fully explained to me, and I may ask questions at any time.

----------	----------
Signature /Left thumb impression (volunteer)	Date
----------	----------
Signature of witness	Date

ஒப்புதல் படிவம்

பெயர் :

வயது :

பாலினம் :

முகவரி:

கோவை muR மருத்துவக்கல்லூரி மருத்துவமனையில் gapw;rp மருத்துவர் fpUj;jpfh தலைமையில் நடைபெறும் இந்த ஆய்வில் முழு சம்மதத்துடன் கலந்துகொள்ள சம்மதிக்கிறேன் .இந்த ஆய்வில் என்னை பற்றி tptu';fis பாதுகாப்புடன் இந்த ஆய்வில் வெளியிட ஆட்சேபணை இல்லை என்று தெரிவித்துக் கொள்கிறேன் .எந்த neuj;jpy; ஆய்வில் இருந்து எந்த neuj;jpYk;; விலக்கிக்கொள்ளும் உரிமை உண்டு என்று அறிவேன் .

இடம் :

தேதி:

ANNEXURE – III

MASTER CHART

S.No	NAME	AGE	SEX	DURATION	SBP	DBP	FBS	HbA1C	SMOKING	TC	TGL	HDL	WBC	LYMPHOCYTE	NEUTROPHIL	MONOCYTE	PLATELET	N/L	M/L	P/L
1	Sujitha	54	F	3	130	80	142	6.7	No	226	180	36	6200	2480	3100	372	202000	1.25	0.15	81.45
2	Mahali	49	M	1	110	80	132	7	Yes	222	172	32	5500	2200	2640	165	178000	1.2	0.07	80.9
3	Kalimuthu	58	M	5	130	70	145	6.8	Yes	206	160	40	4900	1960	2350	196	224000	1.2	0.1	114.28
4	Krishnan	52	M	4	140	90	128	6.9	Yes	226	190	38	5500	2200	2805	330	184000	1.2	0.15	83.63
5	Shanthi	46	F	1	130	90	116	7.2	No	192	158	36	6200	2480	3100	312	186000	1.25	0.12	75
6	Mohan	56	M	2	120	80	142	6.8	No	196	140	40	4400	1760	2020	264	230000	1.15	0.15	130.68
7	Vijaya	50	F	2	150	90	130	7.6	No	190	152	34	4100	1640	1800	220	200000	1.1	0.03	121.65
8	Karuppusamy	55	M	3	150	100	145	8.2	Yes	200	160	38	7200	2880	3450	234	178000	1.2	0.14	61.8
9	Ramar	52	M	5	120	80	156	8	No	240	200	32	5800	2120	2400	302	192000	1.32	0.13	90.56
10	Subammal	63	F	1	140	90	170	8.6	No	226	196	40	6100	2040	2390	326	206000	1.17	0.15	100.98
11	Ramesh	48	M	2	130	70	125	6.7	No	195	146	42	6800	2560	2900	370	186000	1.15	0.14	72.65
12	Shankar	50	M	2	120	90	137	7.2	No	196	156	34	5000	1920	2400	268	208000	1.25	0.05	108.33
13	Jaya	52	F	4	110	70	148	7.8	No	205	168	38	7300	2920	3700	438	220000	1.27	0.15	75.34
14	Chellammal	53	F	2	130	80	124	6.8	No	246	202	39	5600	2080	1920	362	202000	0.92	0.17	97.11
15	Gnanasundari	51	F	1	140	90	127	7	Yes	218	176	45	6000	2400	2340	340	190000	0.97	0.14	79.16
16	Chithra	48	F	1	120	90	117	6.9	No	176	142	33	6300	2520	2640	378	204000	1.05	0.15	80.95
17	Palanisamy	57	M	1	150	100	163	7.6	No	188	156	30	6800	2720	3400	408	200000	1.25	0.15	73.52
18	Kumar	54	M	1	130	90	144	8.2	Yes	206	170	38	8200	3280	5000	422	198000	1.1	0.12	60.36
19	Mani	48	M	3	130	80	128	7	Yes	176	192	32	6400	2160	3600	384	203000	1.02	0.17	93.98
20	Abdul	56	M	2	160	110	156	7.2	No	186	202	35	8100	3240	4050	486	220000	1.25	0.15	67.9
21	Bharathi	46	F	1	140	90	132	7.5	No	204	168	34	6600	2640	3160	396	192000	1.2	0.15	72.72
22	Stella	4	F	4	140	100	130	7	No	250	174	36	5700	2280	2850	302	197000	1.25	0.13	86.4
23	Lakshmi	50	F	2	130	80	170	9	No	244	176	40	6200	2480	2850	372	207000	1.2	0.15	82.46
24	Krishnaveni	47	F	5	120	80	118	6.4	No	214	188	42	7600	3040	3400	426	186000	1.11	0.14	61.18
25	Annadurai	52	M	1	100	70	148	7.8	Yes	212	210	36	5800	2200	2660	264	216000	1.21	0.12	98.18
26	Kamalaveni	48	F	2	130	90	127	6.7	No	206	140	46	5600	2120	2790	275	178000	1.32	0.13	83.96
27	Mohan	48	M	3	140	100	130	6.5	Yes	216	150	32	6200	2480	3100	372	194000	1.25	0.15	78.22
28	Thulasi	44	F	1	140	90	130	8.6	No	252	165	48	6400	2160	2600	345	192000	1.2	0.16	88.88
29	Shantha	51	F	1	120	70	142	7.8	No	196	148	44	4800	1920	2200	230	202000	1.2	0.12	105.2

30	Kalavathi	50	F	3	130	80	148	8.1	no	189	178	36	5100	2040	1800	310	212000	0.9	0.15	103.92
31	Nagaraj	54	M	2	120	70	140	8	yes	206	164	42	4300	1720	2100	260	196000	1025	0.15	113.95
32	Bhoopathy	46	M	1	130	80	126	7	yes	220	152	40	7300	2920	2900	380	224000	0.9	0.13	76.71
33	Devaki	44	F	1	110	90	116	6.5	no	240	138	28	6100	2440	2900	290	304000	1.2	0.12	124.59
34	Pavithra	47	F	2	120	80	124	7.5	no	198	155	34	6000	2240	2800	340	260000	1.25	0.15	116.07
35	Dhanapal	52	M	2	130	70	140	7.2	no	212	164	36	6500	2600	3300	335	226000	1.28	0.13	86.92
36	Subramani	53	M	2	140	100	123	8.5	no	236	146	54	6300	2520	3120	278	214000	1.24	0.11	84.9
37	Sivakumar	56	M	6	130	80	140	7.8	yes	234	135	32	6100	2440	2900	244	195000	1.222	0.1	79.91
38	Balaji	49	M	4	110	80	125	7	yes	202	174	40	6400	2360	2950	354	252000	1.32	0.14	106.77
39	Alaghar	61	M	7	100	70	136	8.5	yes	212	143	26	5000	2000	2500	300	198000	1.25	0.15	99
40	Sharadha	49	F	2	120	90	128	7.2	no	254	185	42	8200	3280	4000	9390	330000	1.22	0.12	100.6
41	Kutty	45	F	1	110	70	140	7.9	no	196	188	30	5100	2040	2440	204	200000	1.2	0.1	98.03
42	Sarojini	50	F	3	130	80	138	8.5	no	238	200	46	5600	2240	2730	270	236000	1.22	0.12	105.35
43	Savithri	60	F	4	140	100	124	7.8	no	217	165	35	5000	2000	2300	300	210000	1.15	0.15	105
44	Kanagadurga	58	F	5	130	90	136	8	no	214	174	27	5200	2080	2600	330	197000	1.25	0.16	94.71
45	Chithradevi	54	F	3	120	70	118	7.2	no	204	208	45	5300	2120	2540	300	208000	1.2	0.14	98.11
46	Malliga	49	F	2	110	90	134	7	no	225	164	35	7200	2880	3450	432	268000	1.2	0.15	93.05
47	Kalaiselvi	48	F	2	150	90	129	6.9	no	236	202	40	5000	2000	2360	300	250000	1.18	0.15	125
48	Ramani	56	F	2	110	80	144	7.4	no	242	166	54	5700	2040	1900	244	188000	0.9	0.13	92.15
49	Vinisha	46	F	1	130	80	176	7.5	no	198	175	44	8200	3240	3700	486	232000	1.15	0.15	71.6
50	Mariyammal	45	F	3	130	90	186	8	no	192	153	30	5200	2080	2300	250	217000	1.1	0.12	102.88
51	Krishnan	57	M	7	140	100	156	8.6	yes	198	148	38	5400	1620	2025	324	160000	1.25	0.2	99
52	Sembaruthi	54	F	4	140	90	142	7.8	no	200	159	44	6100	2190	2800	310	214600	1.27	0.14	98.03
53	Selvarangam	47	M	5	130	80	189	8.7	yes	250	173	6	6400	2560	3450	460	242600	1.35	0.18	94.71
54	Rukmani	68	F	10	110	90	17	9	no	216	199	46	5800	2370	2900	350	232500	1.2	0.15	98.11
55	Palani	55	M	8	140	100	200	9.3	yes	198	165	36	6600	2400	3120	600	223300	1.3	0.25	93.05
56	Lakshmi	56	F	6	120	80	150	7.9	no	204	150	28	6800	2500	3620	425	312500	1.45	0.17	125
57	Amaranath	61	M	9	140	90	167	8.8	no	252	140	48	5100	2200	2680	330	350500	1.22	0.15	105.92
58	Radha	50	F	5	160	100	192	8	no	246	167	38	7000	3500	4375	700	361200	1.25	0.2	103.2
59	Sivaraj	46	M	4	120	70	202	8.5	yes	234	198	30	6800	2380	3095	520	276300	1.3	0.22	116.1
60	Maharaja	55	M	4	140	100	155	7.8	no	220	206	40	5500	1800	2100	380	224260	1.19	0.21	124.59
61	Krishna	48	M	2	110	70	148	8.2	yes	216	202	46	6000	2200	2500	400	234890	1.17	0.18	106.77
62	Kalimuthu	51	M	5	150	90	173	8.5	yes	196	170	39	7200	2880	3300	690	289720	1.18	0.24	100.6
63	Pappathi	53	F	5	110	60	216	9	no	201	208	42	7000	2450	3030	630	258100	1.24	0.26	105.35
64	Thirupathi	56	M	8	150	80	144	7.5	no	203	190	45	8100	2900	3900	520	325230	1.35	0.18	112.15
65	Sujitha	49	F	3	130	60	154	8.2	no	215	220	40	6000	2200	2700	480	225080	1.26	0.22	102.6

66	Shanthapriya	48	F	4	150	90	175	8.5	no	230	185	38	5800	2400	3100	430	241080	1.28	0.18	100.45
67	Suresh	56	M	10	150	100	160	9	yes	222	168	50	6200	1700	2200	425	195330	1.3	0.25	114.9
68	Shantha	64	F	10	140	90	138	7.5	no	244	200	44	6600	1980	2370	320	238800	1.2	0.16	120.63
69	Mohana	53	F	6	160	90	143	8.2	no	186	168	52	9000	3200	4480	540	352000	1.4	0.17	110
70	Vijaya	43	F	4	150	80	169	8.7	no	246	180	56	7700	2900	3900	580	315750	1.35	0.2	108.88
71	Kaleshwari	49	F	5	110	70	182	8.5	no	228	160	48	6800	2400	3360	360	237500	1.4	0.15	98.96
72	Aruchamy	45	M	6	120	90	153	7.2	yes	215	189	36	5600	1500	2180	190	233060	1.45	0.18	97.11
73	Saraswathy	55	F	5	130	80	196	6.8	no	246	190	32	6600	2160	3200	640	216700	1.5	0.3	100.33
74	Palanisamy	48	M	2	180	100	176	7.3	yes	235	207	38	7200	2600	3600	570	280000	1.38	0.2	108.98
75	Lakshmi	52	F	8	140	70	205	8	no	230	175	40	9500	3300	5100	790	401670	1.54	0.24	121.72
76	Manikandan	54	M	5	130	90	212	7.6	yes	224	180	42	9800	3800	490	760	390400	1.3	0.2	102.76
77	Saravanan	56	M	2	140	100	119	7.5	yes	218	172	42	7800	2900	4350	430	284830	1.5	0.15	98.22
78	Subramani	42	M	3	110	80	126	8	yes	224	191	55	7200	2800	3700	440	268000	1.32	0.16	98.02
79	Malarakodi	46	F	4	140	80	135	7.2	no	217	155	54	5000	1700	2380	230	190800	1.4	0.14	112.28
80	Periyasamy	58	M	7	150	100	183	9.5	no	234	197	56	6900	2600	3500	410	296400	1.36	0.16	114.02
81	Murugesan	52	M	5	130	70	130	9.8	no	212	165	48	6200	1900	2500	340	188290	1.35	0.18	9910
82	Sandhanam	57	M	8	120	70	151	6.8	yes	229	201	38	4100	1300	1900	195	127500	1.46	0.15	98.1
83	Kalaiselvi	48	F	6	120	80	199	6.8	no	242	169	32	5000	1800	2500	306	180900	1.42	0.17	100.05
84	Nagarajan	45	M	4	110	70	183	7	yes	189	180	58	6500	2300	3500	345	232500	1.52	0.15	101.1
85	Suguna	48	F	3	130	90	165	6.9	no	197	140	60	5700	2000	2700	400	196000	1.35	0.2	98
86	Thangam	52	F	5	140	100	190	7.2	no	188	192	44	6200	2100	2730	358	198800	1.3	0.17	94.6
87	Vijayan	59	M	8	110	90	136	6.5	yes	232	208	52	5400	1800	2700	396	151200	1.27	0.22	84
88	Vishwanathan	57	M	6	120	70	213	8.5	no	214	188	40	5900	2100	2800	525	210000	1.33	0.25	100
89	Malliga	50	F	4	160	110	222	7.8	no	202	170	54	4400	1400	1840	252	133000	1.31	0.18	95
90	Karuppusamy	46	M	5	140	90	184	8	yes	200	165	38	8900	2500	3250	375	247675	1.3	0.15	99.07
91	Manjula	50	F	8	150	90	175	7.2	no	236	172	38	5500	2100	2560	420	205800	1.22	0.2	98
92	Shanmugam	45	M	3	170	100	137	9.5	yes	240	190	36	8600	3300	4350	690	282150	1.32	0.21	85.5
93	EswaranSubbu	50	M	2	140	90	144	9.7	yes	228	202	44	8600	3310	4200	628	287970	1.26	0.19	87
94	Ravi	53	M	10	130	80	176	9	no	196	200	48	4000	1400	1890	252	135380	1.35	0.18	96.7
95	Arumugam	55	M	9	180	90	201	8.8	no	198	205	52	4200	1500	1875	330	140550	1.25	0.22	93.7
96	Karthiga	51	F	6	110	70	156	7.6	no	205	180	50	4400	1500	1950	300	142550	1.3	0.2	95
97	Ganeshan	52	M	8	160	100	174	7.2	yes	238	175	40	6700	2400	3240	408	235440	1.35	0.17	98.1
98	Sudha	48	F	7	160	90	158	7.5	no	226	200	36	6800	2000	2600	600	188300	1.3	0.3	94015
99	Karuvendhar	45	M	4	150	100	147	8.5	yes	210	187	42	7100	2840	3300	426	270080	1.37	0.15	95.1
100	Kuppusamy	50	M	6	150	100	185	9	yes	224	202	50	9600	3500	4700	875	336350	1.34	0.25	96.1
101	Mahendaran	62	M	12	160	120	174	8.2	yes	224	209	38	8400	3200	4300	480	384640	1.34	0.15	120.2

102	Subbamal	55	F	7	150	80	165	8.5	no	232	152	36	7000	2500	3500	450	276100	1.4	0.18	110.45
103	Prakash	58	M	9	130	70	252	9.8	no	230	186	44	6000	2160	3100	435	221600	1.43	0.2	102.6
104	Rangasamy	59	M	11	180	110	184	8.8	yes	236	146	52	8200	2900	4350	725	325290	1.5	0.2	112.17
105	Ramesh	48	M	6	110	70	172	8.5	yes	248	165	48	5800	1800	2700	540	180990	1.52	0.3	100.55
106	Sumathy	56	F	9	150	90	216	9.9	no	252	204	40	5300	1900	2500	322	197030	1.32	0.17	103.7
107	Shankaran	55	M	8	140	100	190	9	no	270	175	36	6900	2400	3360	480	300000	1.4	0.2	125
108	Jayalakshmi	56	F	10	190	120	246	9.2	no	226	173	38	4700	1600	2300	350	172970	1.44	0.22	108.11
109	Gunasekar	60	M	10	140	90	218	9.8	yes	242	207	50	7000	2360	3300	590	247110	1.4	0.25	104.71
110	Sakthivel	42	F	4	130	90	182	8.7	yes	380	184	42	5800	2100	2900	630	216720	1.38	0.3	103.2
111	Chellakannu	61	M	12	140	100	204	10.2	yes	228	176	44	8100	2800	4060	560	141720	1.45	0.2	108
112	Robert	54	M	7	120	80	232	11.5	yes	216	188	50	5400	1900	2500	340	191020	1.35	0.18	100.54
113	Shylaja	55	F	9	150	90	168	7.8	no	248	203	54	5600	2000	2800	400	229800	1.4	0.2	114.9
114	Palanisamy	48	M	6	160	100	154	7.5	no	232	193	52	4200	1400	2100	196	173600	1.52	0.14	124
115	Chithra	45	F	5	130	90	169	8.8	no	228	168	40	6700	2300	3450	575	262200	1.5	0.25	114
116	Krishnan	57	M	8	140	100	196	9.2	no	218	196	42	7600	2600	3600	650	281060	1.4	0.25	108.1
117	Ranganathan	54	M	7	150	80	176	9.5	yes	252	202	34	4700	1200	1650	264	116100	1.38	0.22	96.75
118	Jasmine	60	F	9	140	90	225	8.6	no	208	210	32	5500	1900	2660	325	194420	1.4	0.17	102.33
119	Lakshmi	58	F	12	150	100	212	10.5	no	216	185	48	6000	2000	3040	380	241440	1.52	0.19	121.72
120	Sundari	56	F	11	130	90	191	9	no	214	196	58	5800	1800	2800	360	176400	1.54	0.2	98
121	Mary	55	F	11	120	80	126	7.5	no	234	184	60	6200	2000	3100	360	261600	1.55	0.18	130.8
122	Ammu	54	F	12	120	0	135	8	no	247	205	56	5200	1800	2700	396	192780	1.5	0.22	107.1
123	Dhivyaraman	50	F	8	140	90	132	7.8	no	235	177	40	6300	2200	2660	528	220000	1.51	0.24	100
124	Maniyappan	58	M	12	160	100	183	9	yes	220	160	50	7100	2500	3800	375	255000	1.55	0.15	102
125	Sivakumaran	57	M	13	150	100	160	8.5	yes	218	212	48	6400	2600	2600	780	281060	1.5	0.3	108.1
126	Velmani	54	M	11	140	90	194	8.7	yes	206	204	36	8400	3240	4600	355	369420	1.45	0.11	114.02
127	Merlin	50	F	10	120	90	226	11.5	no	202	190	38	7500	2700	3780	486	302610	1.4	0.25	112.08
128	Bhakiyam	62	F	12	130	100	250	11.2	no	232	210	54	4800	1680	2300	302	184800	1.37	0.18	110
129	Abdul	56	M	10	180	110	138	7.5	no	226	194	30	6800	2500	3300	375	256950	1.35	0.15	102.78
130	Annasamy	52	M	8	170	90	240	12	no	196	182	45	5000	1800	2340	378	177660	1.3	0.21	98.7
131	Kalavathi	67	F	15	180	100	119	7.8	no	248	195	36	9800	3500	4900	875	350000	1.42	0.25	100
132	Appusamy	48	M	8	140	90	124	8	yes	252	178	36	6100	2100	2940	420	198660	1.4	0.2	94.6
133	Dhandapani	52	M	12	150	100	193	9	yes	244	185	40	6000	2100	3150	420	202940	1.5	0.2	96.64

134	Kumari	59	F	14	160	100	177	8	no	248	188	42	4800	1800	2250	306	184140	1.25	0.17	102.3
135	Nataraj	58	M	9	160	90	169	8.9	yes	218	192	46	4900	1700	2200	255	167870	1.35	0.15	98.75
136	Usha	56	F	8	140	80	179	9	no	226	206	52	4200	1170	1640	140	118280	1.4	0.12	101.1
137	Manohari	54	F	9	180	100	148	7.8	no	234	194	34	8600	3300	4200	660	322080	1.3	0.2	97.6
138	Udayakumar	57	M	8	130	80	216	10.5	no	248	150	30	7300	2500	3375	375	212500	1.35	0.15	85
139	Malliga	66	F	18	170	90	202	11.2	no	225	164	48	4600	1120	1680	248	118380	1.5	0.22	105.7
140	Riyakath Ali	60	M	10	150	90	184	8.8	yes	216	180	52	7200	2600	3800	286	251680	1.45	0.11	96.8
141	Kamalammal	58	F	13	140	100	155	7.5	no	280	204	28	9700	3800	4820	910	420660	1.27	0.24	110.7
142	Hajira	58	F	12	160	110	205	10.1	no	252	165	32	7000	2520	3150	378	262580	1.25	0.15	104.2
143	Sudha	68	F	15	120	70	198	9.5	no	240	205	46	5500	1820	2400	310	176540	1.3	0.17	97
144	Murugan	58	M	17	110	90	176	8.5	yes	228	192	52	6800	2300	3220	620	219650	1.4	0.27	95.5
145	Murugesan	60	M	14	140	100	150	7	yes	270	185	30	7400	2360	3350	448	273050	1.42	0.19	115.7
146	Duraisamy	70	M	20	110	70	220	12	yes	254	175	37	4700	1410	2040	282	146470	1.45	0.2	103.88
147	Abdul Razak	68	M	16	130	90	246	11	no	236	179	40	7600	2580	3700	670	270900	1.47	0.26	105
148	Poornima	62	F	12	140	100	189	9.5	no	234	200	54	4900	1475	2240	148	155170	1.52	0.1	105.2
149	Nirmala	58	F	15	150	80	187	8.8	no	232	166	52	9600	3260	4890	490	367535	1.5	0.15	112.74
150	Pappathi	52	F	9	130	80	166	9.2	no	240	195	48	9400	3290	4935	494	388285	1.5	0.15	118.02