A Dissertation on

NEUTROPHIL LYMPHOCYTE RATIO AND BLOOD GLUCOSE REGULATION IN TYPE 2 DIABETES CHENNAI – 600 001.

Submitted to

THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY
CHENNAI – 600032

In partial fulfilment of the Regulations
for the Award of the Degree of

M.D. BRANCH - I

GENERAL MEDICINE

DEPARTMENT OF GENERAL MEDICINE
STANLEY MEDICAL COLLEGE
CHENNAI – 600 001

APRIL 2017

CERTIFICATE BY THE INSTITUTION

This is to certify that **Dr. RAMYA DEVI . A,** Post - Graduate Student (May 2014 TO April 2017) in the Department of General Medicine STANLEY MEDICAL COLLEGE, Chennai- 600 001, has done this dissertation on "**NEUTROPHIL LYMPHOCYTE RATIO AND BLOOD GLUCOSE REGULATION IN TYPE 2 DIABETES , CHENNAI – 600001"** under my guidance and supervision in partial fulfillment of the regulations laid down by the Tamilnadu Dr. M. G. R. Medical University, Chennai, for M.D. (General Medicine), Degree Examination to be held in April 2017.

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DECLARATION

I, **Dr. RAMYA DEVI .A,** declare that I carried out this work on "**NEUTROPHIL LYMPHOCYTE RATIO AND BLOOD GLUCOSE REGULATION IN TYPE 2 DIABETES , CHENNAI - 600001**" at the outpatient and Medical wards of Government Stanley Hospital . I also declare that this bonafide work or a part of this work was not submitted by me or any other for any award, degree, or diploma to any other university, board either in India or abroad.

This is submitted to The Tamilnadu DR. M. G. R. Medical University, Chennai in partial fulfilment of the rules and regulation for the M. D. Degree examination in General Medicine.

DR. RAMYA DEVI. A.

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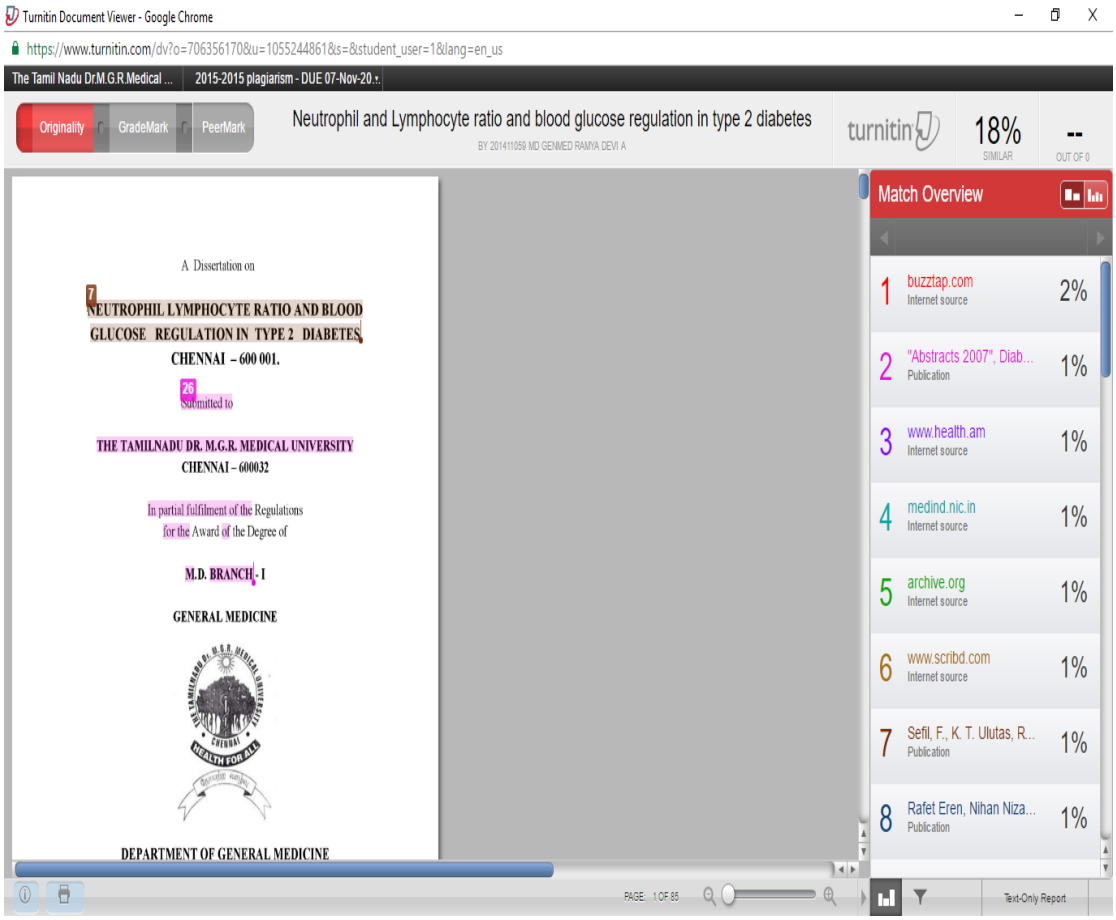
PLAGIARISM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ABBREVIATIONS

NLR - Neutrophil Lymphocyte Ratio

HbA_{1c} - Glycosylated haemoglobin

TGL - Triglyceride

HDL - High Density Lipoprotein

LDL - Light Density Lipoprotein

DCCT - Diabetes Control and Complication Trial

AGE - Advance Glycosylation Endproduct

1. INTRODUCTION

Diabetes mellitus is a chronic disease with hyperglycemia . The metabolic dysfunction affect various organs lead dysfunction and failure . The most common type, Type-II Diabetes Mellitus results from a combination of genetic and acquired factors. Prevalence of Type-II Diabetes is increasing globally and has reached epidemic proportion in many countries especially in India.[4]

The inflammatory process plays a crucial role in the pathogenesis of type 2 diabetes and precedes the onset of the disease[8]. Vascular damage caused by endothelial cells can be influenced by hyperglycaemia, increased free fatty acids, altered lipoproteins, hypertension and diabetes mellitus. Subclinical inflammation may be associated with the increased cardiovascular risk in patients with impaired glucose tolerance. [8]

Neutrophil lymphocyte ratio NLR is novel marker of subclinical inflammation [7]. Many studies heighted increased NLR ratio with chronic complication of diabetes both microvascular and microvascular . There also significant relation between neutrophil lymphocyte ratio and glycosylated haemoglobin . From India very little has been documented about this topic. The objective of the present study is to find the relation between neutrophil lymphocyte ratio and blood glucose regulation in type 2 diabetes patient .

2. REVIEW OF LITERATURE

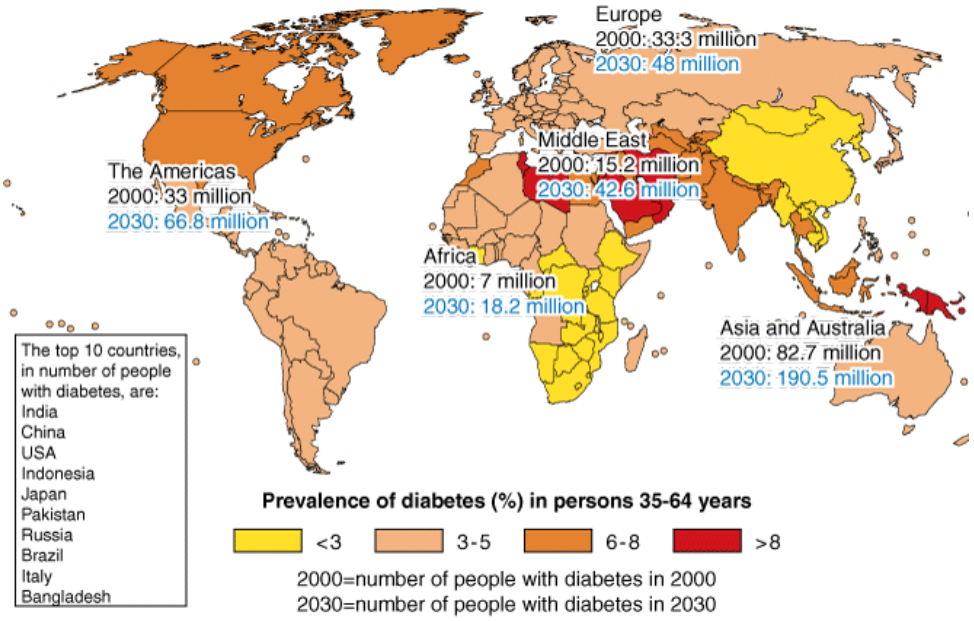
DIABETES MELLITUS

Diabetes Mellitus is a "Group of Metabolic disorders characterized by chronic hyperglycemia associated with alteration in carbohydrate , protein and fat metabolism resulting from defects in Insulin Secretion, Insulin action or both".

The most common morbidity and mortality predictor is blood glucose level. The American Diabetes Association criteria for diagnosis of diabetes include Fasting plasma glucose value of greater than 126 mg/dl or 2 hour plasma glucose level following meals of more than 200mg/l or Random plasma glucose value of greater than 200mg/ml plus symptom of diabetes or Hemoglobin A1c >= 6.5%.

EPIDEMOLOGY

According to the International Diabetes Federation the total number of adult Type-II Diabetes in the world was estimated as 366 million in 2015 which was projected to increase to 592 million by 2035[1]. World diabetic population China ranks first with 98.4 million next India with 65.1 million in 2013 . Five Asian countries occupy first ten world diabetic population . The numbers are estimated to rise to 129.7 million and 101.2 million respectively by 2030.[4]



DIABETES – CLASSIFICATION [23]

I. Type 1 Diabetes mellitus (complete cell destruction, leads to absolute insulin loss)

A. Immune-mediated destruction

B. Idiopathic aetiology

II. Type 2 diabetes mellitus (has combination of insulin resistance with Some insulin deficiency to a dominantly insulin synthesis defect with insulin resistance)

III. Other sub- types of diabetes mellitus

A. Genetic alterations in cell function which manifests by mutations in:

1. Hepatocyte nuclear transcription factor(MODY TYPE 1)
2. Glucokinase (MODY TYPE 2)

3. HNF-1 (MODY 3)
4. Insulin promoter factor-1 (MODY 4)
5. HNF-1 (MODY 5)
6. NeuroD1 (MODY 6)
7. Mitochondrial DNA
8. Subunits for ATP-sensitive potassium channel

B. Genetic abnormalities in insulin action
   1. Type A insulin resistance
   2. Leprechaunism
   3. Rabson-Mendenhall syndrome
   4. Lipodystrophy syndromes

C. Diseases of the exocrine pancreas – eg..pancreatitis, neoplasia, cystic fibrosis, hemochromatosis, fibrocalculous pancreatopathy

D. Endocrinopathies - includes acromegaly, Cushing's syndrome, glucagonoma, pheochromocytoma, hyperthyroidism etc

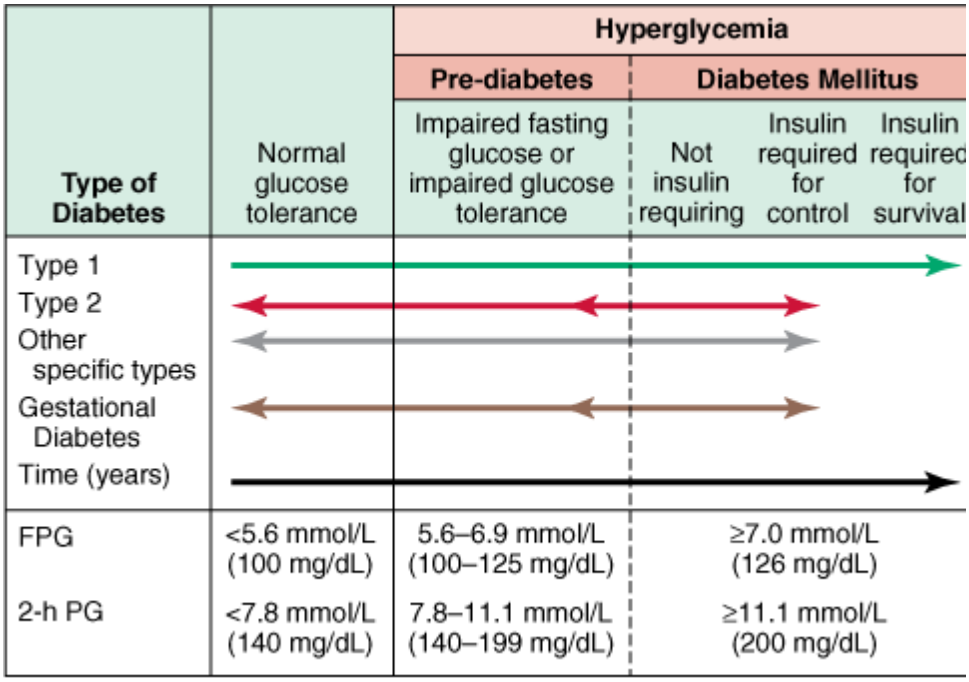
E. Drugs and chemicals — pentamidine, nicotinic acid, glucocorticoids, thyroid hormone, diazoxide, adrenergic agonists, thiazides, phenytoin, interferon, protease inhibitors, clozapine.

F. Infections—congenital rubella, coxsackie virus,

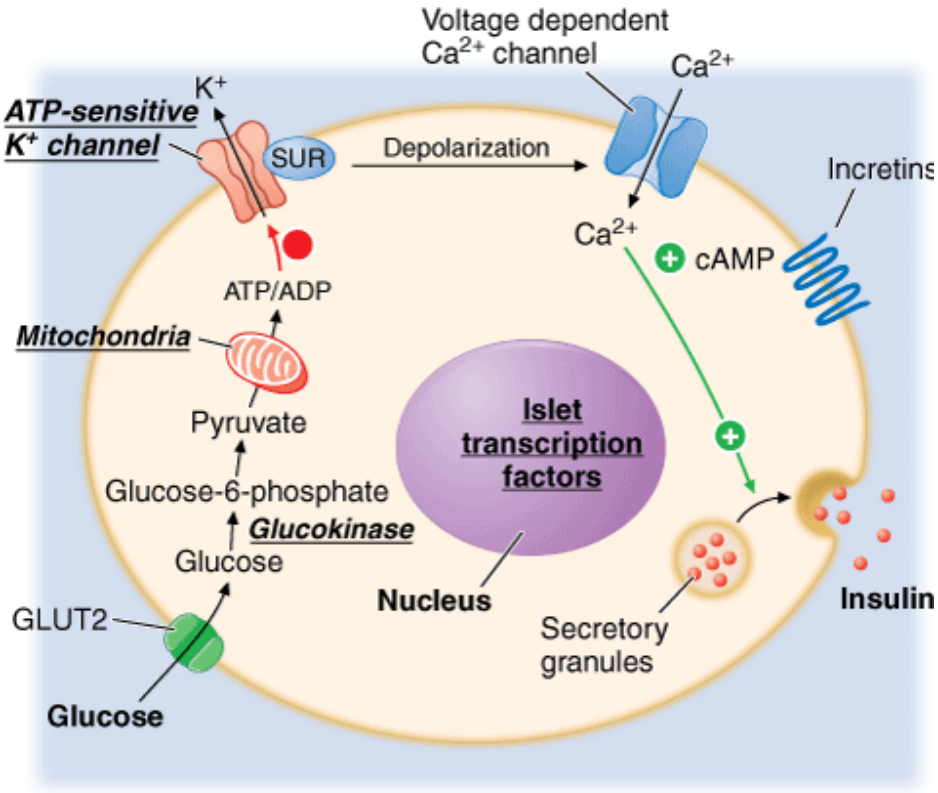
G. Other genetic syndromes associated with diabetes— Turner's syndrome,

Friedreich’s ataxia, Huntington's chorea, Laurence-Moon-Biedl syndrome, myotonic dystrophy, Prader-Willi syndrome,klinefelters and turners syndrome.

1V Gestational diabetes[23]



PHYSIOLOGY OF INSULIN SECRETION



Risk Factors implicated in Diabetes[17]

- Family history of diabetes mellitus
- People with Impaired fasting or post prandial glucose values
- physical inactivity
- overweight
- Race/ethnicity
- Hypertension
- Low HDL cholesterol and high triglyceride level(greater than 250 mg)
- History of Gestational DM or an overweight new born baby
- Polycystic ovarian disease.

MODIFIABLE RISK FOR TYPE 2 DIABETES

OBESITY

One of the strongest modifiable factor for diabetes is obesity and weight gain . BMI body mass index is used as surrogate for obesity calculated by dividing person ‘s weight in kg and height in meters square. There is 2.75 times increase diabetic risk in people with BMI of 25-27 kg /m2 compared to BMI < 22 kg/m2 .

PHYSICAL ACTIVITY

Risk of diabetes is found to be inversely proportional to Physical activity in most population [3] . Numerous studies shown that exercise is related to acute and long term improvement in insulin sensitivity and reduction in insulin concentrations .

SEDENDARY LIFESTYLE

A study revealed that in those people who did sedentary work like watching television or computer for more than 4 hours (2 to 10 hours) had 66% higher risk for diabetes .

DIETARY FACTORS

High fat diet associated with obesity and increased body fat. Studies investigated the effect of different subtypes of fat like saturated , polysaturated , monosaturated fat and omega 3 fatty acids on diabetic risk concluded that beneficial effect of higher intake of PUFA and long

chain n -3 fatty acids [3] and there is deleterious effect due to higher intake of saturated fat . Risk of diabetes in relation to carbohydrate intake was postulated because of hypothesis that carbohydrate ingestion had immediate challenge on beta cells in comparison to protein and fat but study result inconclusive . The postprandial elevation dependent on glucose absorption rate . The glucose absorption rate related to many factors like carbohydrate type and amount of fibre.

RISK FACTORS FOR TYPE 2 DIABETES -NONTRADITIONAL MODIFIABLE

INFLAMMATION

Though the main characterstic of diabetes is insulin resistance and relative insulin deficiency, the underlying mechanism remains unknown. Recently evidence point out that inflammation play a significant role in the development of type 2 diabetes and atherosclerosis. Many number of cross section studies showed raising Neutrophil lymphocyte ratio with diabetes, a marker of subclinical inflammation. Study Data made subclinical inflammation an important determinant of type 2 diabetes mellitus . It is noteworthy ,insulin resistance is reduced by high dose aspirin and improves glucose tolerance in type 2 diabetes[3] .

SMOKING

In Facchini et al study they compared chronic smoker with non smokers found significant higher triglycerides level and lower HDL

cholesterol level and increased insulin concentration after a 75 g oral glucose tolerance test .The mechanism behind insulin resistance in smoking is oxidative stress which cause endothelial dysfunction .

AETIOPATHOGENESIS OF TYPE 2 DIABETES MELLITUS

Genetic factors play siginicant role in type 2 diabetes .Studies of identical twins highlighted genetic factors as a dominant factors in type 2 diabetes etiology revealing 100% concordance .

The current understanding of type 2 DM include triple abnormalities in the genesis of hyperglycemia include

1. Impaired pancreatic insulin secretion

Normal Fasting insulin is 5 -15 mU/ml . Normally insulin secreted in pulsatile fashion called ultradian oscillations ,which secret every 90 to 120 minutes and exaggerated after food intake .The insulin secretion following glucose load show biphasic response . First phase due to stored insulin in granules which released and suppresses hepatic glucose output . This occur within 4 to 5 minutes and return to normal within 10 minutes. The second phase occur due to rise in glucose level which increase peripheral glucose uptake in muscle and adipose tissue [2]. This pulsatile ultradian oscillations of insulin delivery and first phase insulin release lost in type 2 Diabetes Mellitus.

2. Impaired peripheral action of insulin:

Numerous studies provide evidences that hyperinsulinemia antedates type 2 diabetes development . Various tissues like, muscle, splanchnic etc.. involved in insulin resistance [3.]

In muscle there is defect in action of

1. Impaired insulin receptor tyrokinase activity
2. Decreased glucose transporters
3. Diminished glycogen synthase and pyruvate dehydrogenase

3. Increased hepatic glucose output and lipid production

Normally insulin is released into portal vein and transport into liver to suppress hepatic gluconeogenesis after glucose ingestion . Due to insulin resistance ,failure of the liver to perceive signal result in increased hepatic glucose output .

In adipose tissues due to insulin resistance, lipolysis and free fatty acid flux from adipose tissue increased lead to increased lipid (VLDL , triglycerides) production in liver . The accumulation of lipids might led to hepatic steatosis and non alcoholic fatty liver disease with dearranged liver function .

INSULIN RESISTANCE AS A PRIMARY DEFECT

Prospective studies have shown result that hyperinsulinemia and insulin resistance preceed the development of Impaired glucose tolerance.

The stage between normal glucose tolerance and development of type 2 diabetes is IGT. Cross sectional studies have shown that insulin resistance is inherited defect that intiates the diabetic event. .

The hyperglycemia to insulin resistance occurs in three phases

First phase - plasma glucose remains normal despite insulin resistance because of increased insulin secretion .

Second phase - As the insulin resistance progesses there is impaired glucose uptake in the muscle but sufficient insulin produced to maintain hepatic glucose production in normal level . So there is Postprandial hyperglycemia and still normal fasting blood glucose.

Third phase - Hyperglycemia become severe so there is no longer adequate hyperinsulinemia to maintain fasting blood glucose normal.

The resultant fasting and postprandial hyperglycemia stimulate further beta cell and produce hyperinsulinemia which down regulate receptor excerbate insulin resistance.

NATURAL HISTORY OF TYPE 2 DIABETES MELLITUS

To maintain normal glucose hemostasis there should be balance interaction between insulin sensitivity and insulin secretion .

Fasting glucose

The main factor determine fasting blood glucose is Hepatic glucose production . It depend on

- Fasting plasma insulin
- Hepatic sensitivity to insulin
- Fasting substrate availability

In Type 2 Diabetes there is impaired basal insulin secretion and decreased hepatic insulin sensitivity .

Postprandial glucose

It is regulated by ingested glucose clearance , hepatic glucose suppression and peripheral glucose clearance .

In Type 2 Diabetes , there is lack glucagon suppression, delayed & reduced insulin secretion and hepatic and peripheral resistance .

LIPOTOXICITY

Adipose tissue considered as an endocrine organ and it is principle site for energy storage and secretion of adipokines [13] . Adipose tissue influences insulin action by release of free fatty acid and adipose derived proteins .Adipose derived proteins are pro inflammatory peptides and have adverse effect on glucose metabolism and insulin action .

Proinflammatory Cytokines

There is overproduction of pro inflammatory cytokines by the expanded mass of Adipose tissue. The proinflammatory cytokines include interleukin IL-1, IL-18, IL-6, CRP- c reactive protein, restin and tumour necrosis factor (TNF)[1]. The primary source of these proinflammatory cytokines both in the systemic circulation as well as locally is the macrophages derived from adipose tissue. However it is unclear as to how much the paracrine and endocrine effects of these cytokines lead to insulin resistance.[1]

Adiponectin

Adipocytes produce an anti inflammatory cytokine exclusively called Adiponectin. This adiponectin increases the sensitivity of insulin and it inhibits the Inflammatory process in several steps. Adiponectin inhibits the gluconeogenic enzymes and thus reduces the rate of production of glucose in the liver . Adiponectin enhances the transport of glucose in the muscles and increases the oxidation of fatty acids partly because of activation of adenosine monophosphate kinase .Decreased plasma level of the adiponectin contributes to pathogenesis to insulin resistance and type 2 DM .

Diagnosis

American Diabetes Association says that any of the following can be used for diagnosis of diabetes: [5]

- HbA1c or glycosylated haemoglobin test
- FPG -a fasting plasma glucose test
- OGTT - an oral glucose tolerance test

The HbA1c levels give an idea about the glucose value during the past 3 months. It gives a fair idea how treatment is working.[18]

The haemoglobin is present inside the red blood cells. The function of haemoglobin is to transport oxygen to the tissues. When the red blood cells are constantly exposed to high level of blood glucose, the glucose enters inside the cells to form a bond with the haemoglobin to form glycosylated haemoglobin. This hba1c gives the average blood glucose control over the past 3 months. Hence it is necessary to check hba1c values at least twice a year.

The A1C test results could be reported as eAG or as "average glucose," which directly correlates with A1C. eAG is a unit similar to self-monitor on the CBG machine. A1C is reported as a percent and eAG as mg/dl .[16]

eAG is not the same average glucose level as the average of values on the meter. This is because people with diabetes more likely check blood glucose when they are low (usually, in the morning and before meals), the average of these readings is mostly lower than eAG.

Fasting Blood Glucose

It is the blood glucose values which are taken in early morning with fasting for at least 8 hours from previous night.

Oral Glucose Tolerance Test (OGTT)

It's a test to determine how well the body metabolises glucose. Here blood glucose values are taken in fasting. The patient is made to drink a special glucose solution and blood glucose values are taken after 2 hours.

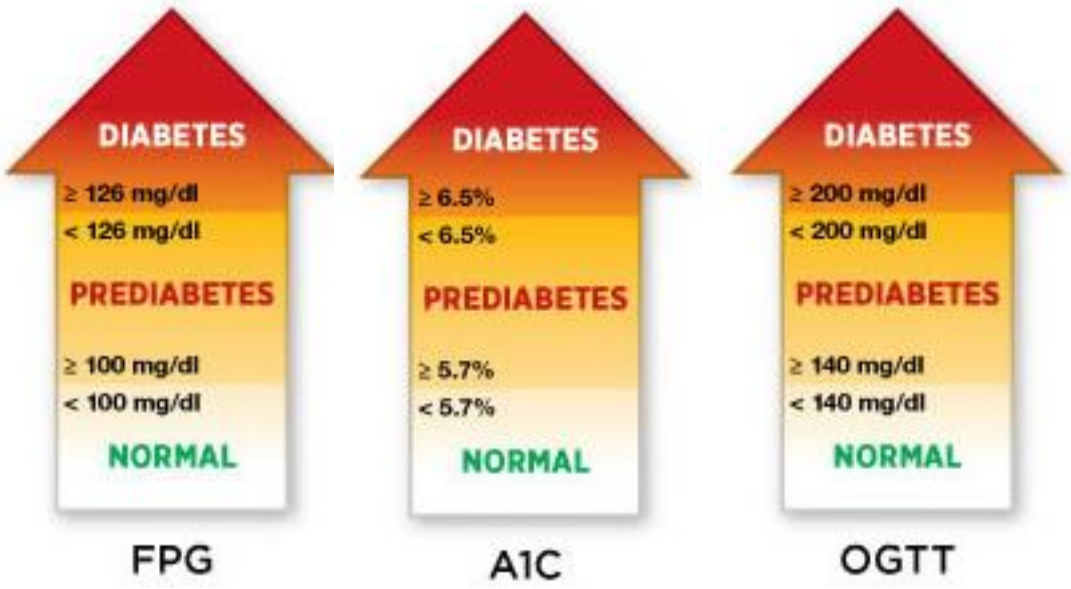
Result	Oral Glucose Tolerance Test (OGTT)
Normal	less than 140 mg/dl
Prediabetes	140 mg/dl to 199 mg/dl
Diabetes	200 mg/dl or higher[16]

Random Plasma Glucose Test

This can be done at any time of the day. When the random plasma glucose values are more than 200mg/dl then it is diagnostic of diabetes

Prediabetes:

Prediabetes is defined as blood glucose levels which are more than normal but not yet high to be diagnosed as diabetes. Both impaired fasting glucose and impaired glucose tolerance come under prediabetes. These people must be regularly followed up for they have a high chance of developing overt diabetes and cardiovascular complications.



COMPLICATION :

The complications of diabetes can be acute or chronic complication

ACUTE COMPLICATION

Diabetic keto acidosis

Hyperglycemic hyperosmolar state

Hypoglycemia

Chronic Complication

Chronic complication are due to the increased blood glucose for a long period of time.[20] It's the duration of diabetes which determines the incidence of complications.

The complications due to diabetes can be divided as macrovascular and microvascular. They affect multiple organ system primarily the kidneys, heart, eyes, brain vessels and peripheral vessels of the limbs. It causes diabetic nephropathy, myocardial infarction, cerebrovascular accidents and gangrene of the limbs. Moreover diabetes predisposes to hyperlipidemia and hypertension which increases the risk of complications.

Many studies like Diabetes Control and Complications Trial (DCCT) proved that insulin dependent diabetes whose managed with intensive insulin therapy resulted in HbA1c 2% lower than conventional insulin and lower incidence of complication [12]. The UKPDS proved 35% reduction in microvascular complication in each reduction in HbA1C % [1]

The vascular complications in diabetes mellitus are mainly due to microangiopathy and atherosclerosis. Damage to the endothelial basement membrane, proliferation of endothelial cells and dysfunction of the endothelial cells are mainly responsible for the microangiopathy. Increased blood glucose causes hardening of the vessel wall and this along with increased lipids in the blood results in lipid deposition in atherosclerotic plaques predisposing to end organ damage.

The pathophysiology involved in development of microvascular and macrovascular complications in diabetes is very complex. There is no clear cut mechanism. Increased blood glucose values for a long duration of time have been found to be the most important single factor causing complications. However not all those who have increased blood glucose develop

complications and sometimes even those who have very good control of blood glucose end up developing the complications of diabetes mellitus.

Increased sugar affects many cell types and their extracellular matrix. These changes result in structural and functional alterations in the tissues.

The cell membranes are formed mainly by the phospholipid bilayers. Hence alterations in lipid metabolism affect the cell membranes resulting in damage to the cells. The oxidation of low-density lipoprotein in hyperglycaemic individuals raises oxidant stress in the vessel wall. This attracts the monocytes and macrophages to the vessel wall were oxidized LDL results in alterations in cell adhesion.it also increases the release of cytokines and growth factors.[20] Moreover Growth factor causes multiplication of smooth muscle resulting in increase in thickness of vessel wall. Further there is increased atherosclerotic plaque formation and microthrombi formation in major blood vessel .the changes in vascular permeability and endothelial cell dysfunction causes end organ damage.

Sustained hyperglycaemia causes linking by sugar with proteins, lipids, and nucleic acids. There is increased deposition of advanced glycation end products in the micro blood vessels of the retina, glomerulus, and endoneurons, as well as the larger blood vessel walls. People who have poorly controlled diabetes mellitus have increased formation of advanced glycation end products. These advanced glycation end products cause change in the structural and functional change in the cells of various tissues. AGE formation on collagen impairs healing of damaged tissues and thus the normal homeostatic process is

deranged. AGE-modified collagen forms in the walls of the large blood vessels and causes vessel wall thickening and narrowness of the lumen. These immobilize the circulating LDL, contributing to formation of atherosclerotic plaque. The formation of AGEs causes increase in basement membrane thickening in the retinal microvasculature and around the nerves and increase in thickness of the mesangium in the glomerulus. The end point of all these changes is causing narrowing of the blood vessels resulting in decreased perfusion to the organs.

Formation of AGE has its effect at the cellular level also resulting in changes in extracellular matrix and causing alterations in cell-to-matrix and matrix-to-matrix interrelations. The binding of AGEs to specific cell receptors which have been identified on the surface of smooth-muscle cells, endothelium, neural cells, monocytes, and macrophages causes increased vascular permeability and thrombotic complications, multiplication of smooth muscle in vasculature, and phenotypic changes in monocytes and macrophages. This causes increased responsiveness of monocytes and macrophages on stimulation, which results in increase in the production of proinflammatory cytokines and associated growth factors. These cytokines and growth factors contribute to the chronic inflammation in the production of atherosclerotic lesions. They also change the wound-healing events. More production of inflammatory mediators causes raised tissue destruction in response to antigens such as the bacteria.

These alterations in protein and lipid metabolism, causes elevated plasma glucose levels which is an important feature of diabetes, which provides a common relation between the different diabetic complications. However, these metabolic changes vary among people. For example, AGEs form in both diabetic and non-diabetic persons, but its accumulation is more in those with diabetes. There are significant differences in AGE formation even within the diabetic population, and it is thought that this may explain the changes in the incidence and progression of diabetic complications[48].

TREATMENT

ORAL AGENTS

INSULIN SECRETOGOGUES

Sulfonylureas

The first generation sulfonylureas are no longer in use nowadays because of the increased side effects associated with these drugs.[2] Chlorpropamide is an example of first generation sulfonylureas.

Second-generation agents which are more potent, have less drug interactions, and produce fewer side effects and hence have replaced the first generation. The mechanism by which sulfonylureas act is by acting on the pancreatic beta cells and causing increase in insulin secretion. This increased insulin secretion overcomes the resistance associated with type 2 diabetes mellitus and hence more amount of glucose is transported inside the cells thereby decreasing the blood glucose value. The sulfonylureas depending upon their varying action duration they are given as single or double dosage

daily[6]. The major adverse effect associated with sulfonylureas is hypoglycaemia. Hence the patients who take these drugs must be educated properly to take adequate amount of food after taking these tablets.

Non sulfonylurea secretogogues

Repaglinide stimulates pancreatic insulin secretion. But the pharmacodynamic properties and mechanism of action are different from sulfonylureas. Repaglinide undergoes rapid absorption, reaches peak plasma levels in 30 to 60 minutes, and undergoes rapid metabolism. The drug is consumed along with meals and reduces the peaks of PPBS which is common in type 2 diabetes but to a greater degree than the sulfonylureas medications. These drugs are used for the treatment of post prandial hyperglycaemia due to their rapid onset and short duration of action. These drugs can also result in hypoglycaemic episodes. Neteglinide is faster acting than repaglinide and can be given in mild to moderate liver dysfunction [2].

INSULIN SENSITIZERS

Biganides

Metformin are biguanides and are preferred agents for obese patients. These drugs decrease blood glucose by decreasing the production and increasing the utilization . It activate AMP dependent protein kinase . These drugs also inhibit the intestinal absorption of glucose. Lactic acidosis and megaloblastic anaemia due to vitamin b12 deficiency are the major adverse effects of these drugs. Biguanides increase the intestinal production of lactate

by anaerobic glycolysis. Metformin is the only oral agent that has been demonstrated to reduce the macrovascular events in type 2 DM.

Thiazolidinedione

The thiazolidinedione group of drugs, which includes troglitazone, rosiglitazone, and pioglitazone, act as agonists of nuclear receptor PPAR gamma which regulates transcription of genes involved in glucose and lipid metabolism. These drugs are used to reverse insulin resistance in type 2 DM. these drugs also tend to increase HDL. The adverse effect of these drugs includes weight gain, edema and plasma volume expansion. Therefore these should be avoided in CHF patients.

Alpha – glucosidase inhibitors

Acarbose- complex carbohydrates are absorbed after conversion to simple carbohydrates by alpha glucosidase. Inhibitors of this enzyme decrease carbohydrate absorption for git. Major adverse effect is flatulence due to fermentation of unabsorbed carbohydrates. These drugs help in restoring beta cell function and prevent new cases of type 2 diabetes in pre diabetes

Dipeptidyl peptidase inhibitors

DPPT IV prolong endogenous GLP -1 action promotes insulin secretion . HbA1C reduction by 0.5 – 0.8%. They include sitaglipin ,saxagliptin ,vildagliptin.

Sodium glucose co transporter 2 inhibitors

Sodium glucose co transporter 2 inhibitor increase urinary glucose excretion and thereby lower blood glucose . They are insulin independent. Adverse effect include urinary tract infections .Drugs include canagliflozin ,dapagliflozin , empagliflozin .

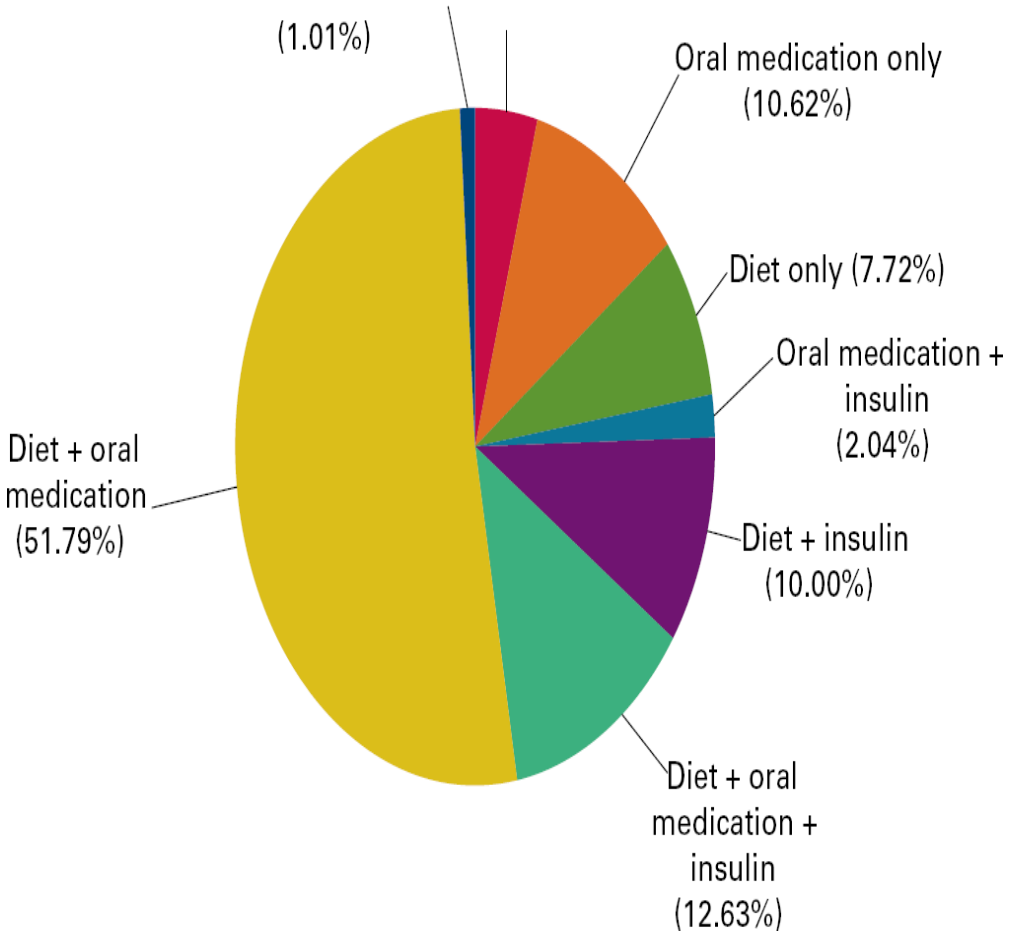


Fig: Chart Showing The Different Treatments for Iabetes and its Efficacy

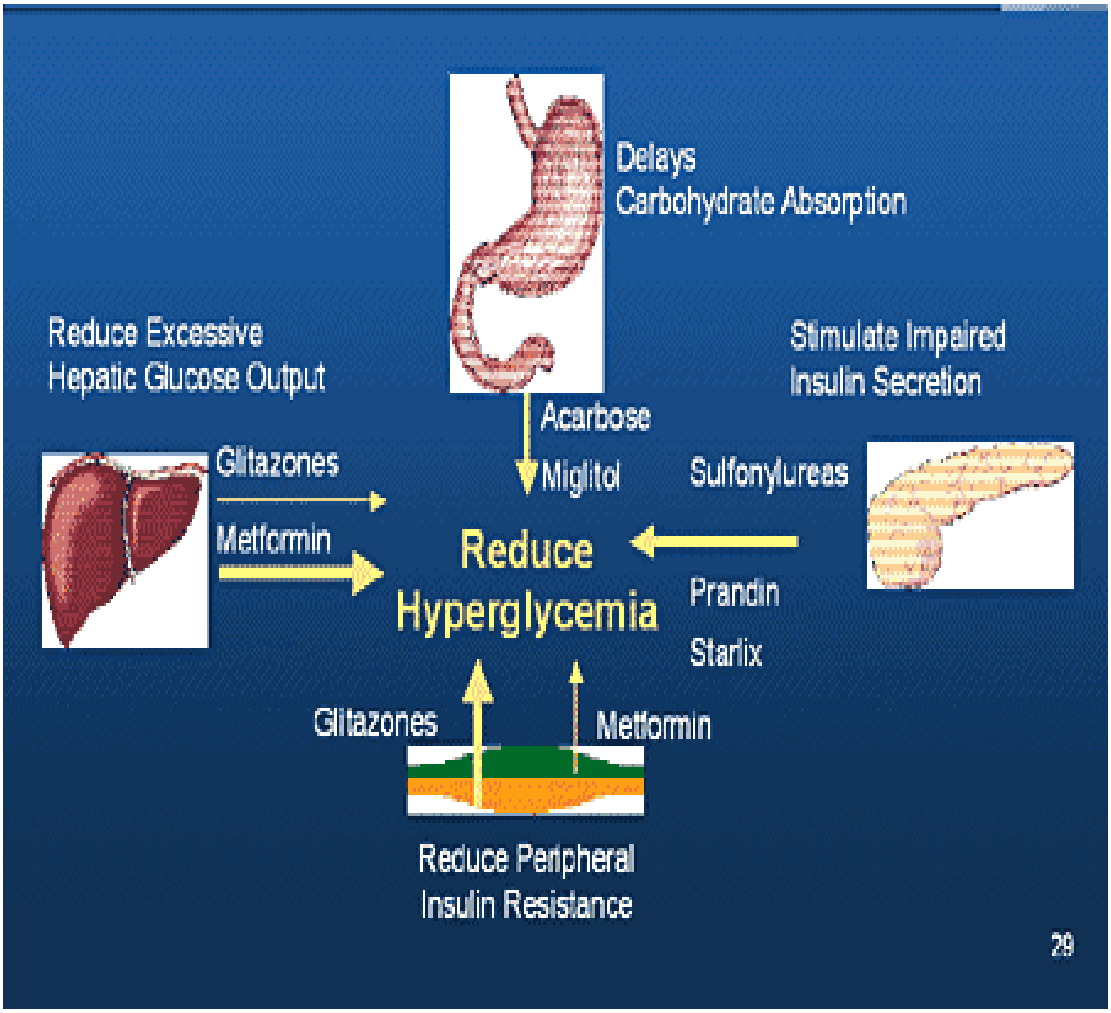


Fig: Diagram showing site of action of anti-diabetic drugs

Table 1 – Non-insulin agents available for treatment of diabetes in the United States

Drug class	Route of administration	Advantages	Disadvantages
Biguanides (metformin)	Oral	Effectively lowers HbA_{1c}, low cost, does not cause weight gain	GI complaints, minimal risk lactic acidosis (contraindica in patients older than 80 y those with elevated creatini
Sulfonylureas (tolbutamide, glyburide, glipizide, glimepiride)	Oral	Available as generics (low cost)	Can cause weight gain
Disaccharidase inhibitors (acarbose, meglitol)	Oral	Do not promote weight gain; safe in patients with renal failure; reinforce carbohydrate restriction through averse response	Flatulence, abdominal disc diarrhea; relatively high co
Thiazolidinediones (rosiglitazone, pioglitazone)	Oral	May preserve beta cells from ongoing destruction	Cause fluid retention (somet leading to heart failure); sti accumulation of adipose tis
Meglitinides (repaglinide, nateglinide)	Oral	Rapid disappearance time results in lower risk of hypoglycemia than with sulfonylureas	Much shorter duration of ac sulfonylureas; thus, these ag be taken before meals; mod high cost
GLP analogs (exenatide)	Parenteral	May result in progressive weight loss in some patients	Nausea (often severe); must injected twice daily; high c
Amylin analogs (pramlintide)	Parenteral	Weight loss can occur	Nausea; unpredictable hyp high cost
DPP-IV inhibitors (sitagliptin)	Oral	No prominent side effects, low risk of hypoglycemia	Does not lead to weight los

HbA_{1c}, glycosylated hemoglobin; GLP, glucagonlike peptide; DPP-IV, dipeptidyl peptidase IV

Insulin

Insulin was discovered by Banting and Best in the year 1921. Glucose is the main stimulus for the release of insulin from the beta cells of the pancreas. Glucose stimulates GLUT-2 and inhibits ATP sensitive k+ channels. The actions of insulin include stimulation of entry of glucose in muscle and fat, inhibition of glycogenolysis and gluconeogenesis and increasing glycolysis and glycogenesis. By all the above mentioned mechanisms insulin decreases the blood glucose levels. It also inhibits lipolysis and favours deposition of triglyceride. It caused increased synthesis of proteins and thus overall has an anabolic action.

The human insulin is prepared by recombinant DNA technology and has rapid absorption and shorter duration of action. Recently ultra-short acting and ultra-long acting preparations have also been developed. All insulin preparations are supplied at neutral pH of 7.2 to 7.4 except glargine which is supplied at pH of 4. Hence it is important that glargine should not be mixed with any other preparation of insulin.

All insulin preparations are given by subcutaneous route only. Only regular insulin can be given by intra venous route. The factors which affect the absorption of insulin include the type and site of injection, the depth of injection and subcutaneous blood flow.

The most common complication of an insulin therapy is hypoglycaemia. This can be treated with intravenous glucose. Some people suffer from hypoglycaemic unawareness. Usually when the blood glucose levels drop less

than 60mg/dl the symptoms of hypoglycaemia becomes apparent. However in patients suffering from hypoglycaemic unawareness there is no symptoms till blood glucose values plummets to 40mg/dl. The patient becomes unconscious and often this condition is life threatening. Then at the site of injection it can cause lipodystrophy. Allergic reactions and sodium and water retention have found to occur.

The indications of insulin therapy include all cases of insulin dependent diabetes mellitus. Among non insulin dependent diabetes mellitus insulin is indicated when glucose levels are not controlled with oral hypoglycaemic agents, in pregnancy and in complications like diabetic ketoacidosis and hyperosmolar coma in in stressful conditions like surgery and infections.

Exogenous insulin usage gives a profile similar to the non-diabetic individual, with a continuous availability of insulin available which is enhanced by increase in availability after each meal[6]. No single insulin preparation is available which are able to achieve this goal with one or two injections daily. Insulin preparation combinations are available which are taken three or more times daily or using a subcutaneous infusion pump more approximate to the ideal conditions, but even in conditional regimes, blood glucose levels can remain unstable.

Ultralente insulin also called as "peakless" insulin is the longest acting insulin.it has a very slow action onset of action and it peaks very minimum and action is for a longer duration. It action resembles the basal metabolic insulin [6]. The intermediate-acting insulin (lente and neutral protamine Hagedorn [NPH])

have their peak action several hours after injection. Peak activity occurs between 4 to 10 hours after injection. Therefore a patient who is using intermediate-acting insulin in the early morning will have peak plasma insulin levels during lunch hours. Regular insulin is shorter acting, with its onset being around about 30 minutes through 1 hour post injection and peaks at 2 -3 hours. Lispro insulin, a rapid acting insulin, due to its rapid absorption, will become active about 15 minutes post injection, and peaks at ½ to 11/2 hours. Rapid- and short-acting insulin are usually taken just before or during meals. Thus, regular insulin when taken before breakfast will peak at midmorning; when taken before lunch, will peak at mid-afternoon.

Insulin preparation	Onset of action	Peak	Duration of action
Lispro (Humalog)	<15 minutes	1-2 hours	3-6 hours
Aspart (Novolog)	<15 minutes	1-2 hours	3-6 hours
Glulisine (Apidra)	<15 minutes	1-2 hours	3-6 hours
Regular (Novolin R, Humulin R)	30-60 minutes	2-4 hours	6-10 hours
Humulin R Regular U-500	30-60 minu tes	2-4 hours	Up to 24 hours
NPH (Novolin N, Humulin N, ReliOn)	2-4 hours	4-8 hours	10-18 hours
Glargine (Lantus)	1-2 hours	Usually no peak	Up to 24 hours
Detemir (Levemir)	1-2 hours	Usually no peak**	Up to 24 hours**

Premixed Insulins***	Onset of action	Peak	Duration of action
Novolin70/30, Humulin 70/30	30-60 minutes	2-10 hours	10-18 hours
Humalog 75/25, Novolog 70/30, Humalog 50/50	10-30 minutes	1-6 hours	10-24 hours

Prevention

Studies have shown that by doing lifestyle modifications we cansubstantially reduce the risk of developing type two diabetes mellitus and the chances of developing cardiovascular diseases. In diabetes prevention program about 3234 obese subjects with impaired glucose tolerance or impaired fasting glucose were put into three groups. One group with intensive lifestyle changes through exercise and low fat diet, second group with metformin with information about exercise and diet and third group on placebo with information on exercise and diet. After three years of follow up it was found out that less number of patients in the intensive lifestyle group developed diabetes .

Daily regular exercise, healthy food habits, having an apt weight plays a major role in preventing diabetes and the complications. These also help in reducing the blood pressure and heart disease among type 2 diabetic patients.

NEUTROPHIL- LYMPHOCYTE RATIO

Normally there are 4000-11000 WBCS/ micro litre in the human blood. Of these granulocytes are the most numerous. Young granulocytes have horse shoe shaped nuclei that become multilobed as the cells grow older. Most of them contain neutrophilic granules.

NEUTROPHILS

Neutrophils have cytoplasmic granules that contain biologically active substances involved in inflammatory reactions. The average half- life of

a neutrophil in the circulation is 6 hours. They are attracted to the endothelial surface by selectins and they roll along it. Neutrophil adhesion molecules of the integrin family helps them to get bound to selectins. They insinuate themselves through the walls of the capillaries by a process known as diapedesis. Many of those that leave the circulation enter the GI tract and are lost from the body.

Neutrophilic granules contain various proteases and in addition they also contain enzymes such as NADPH oxidase, catalase and myeloperoxidases. NADPH oxidase is associated with a sharp increase in oxygen intake and metabolism in the neutrophil, what we call as the "Respiratory burst" and this reaction generates plenty of free O-radicals. The myeloperoxidase catalyses the conversion of Halides and cyanides to their corresponding acid forms. These acids inturn are potent oxidants by themselves.

In addition to myeloperoxidase and NADPH oxidase neutrophil granules also contain an elastase and two metalloproteinases.

The total body neutrophils can be divided into circulating pool (CGP) and marginating granulocyte pool. In these two pools, the cells are equal size and they are in constant equilibrium. MGP represents the neutrophils involved in adhesion and rolling along the endothelial cells in post capillary venules and they are not found in blood obtained by venepuncture. So the neutrophil content actually represents about half of the total no of neutrophils in the vascular compartment.

LYMPHOCYTES

Lymphocytes are motile non phagocytic cells. There are many subpopulations of lymphocytes which interact with each other and with cells of the monocyte macrophage system. They help in maintaining both humoral and cell mediated immunity. Proliferating lymphocytes are enriched with enhanced levels of enzyme n-terminal deoxyribonucleic acid transferase. It is found in immature lymphoid cells in the bone marrow and thymocytes, but not in mature lymphocytes. Adenosine de aminase is present in large amounts in T-lymphocytes and it is necessary for their immune function.

INFLAMMATION

Inflammation is naturally a protective mechanism against invasion of microbes and toxins. The inflammatory response consists of 2 main components- a vascular reaction and a cellular reaction. Both the reactions are mediated by chemical factors that are derived from plasma proteins or cells produced as a result of inflammatory response.

Chronic inflammation is of prolonged duration in which active inflammation, tissue destruction and repair are proceeding simultaneously. Atheroscleorosis and vascular disease are chronic inflammatory processes of the arterial wall induced partly by endogenous toxic plasma lipid components.

Morphological features of chronic inflammation

- ❖ Mononuclear cell infiltration

- ❖ Tissue destruction
- ❖ Healing by connective tissue replacement
- ❖ New blood vessel formation by elaboration of vascular endothelial growth factor and other angiogenic factors.
- ❖ Fibrosis

Most of these elements of chronic inflammation are found in the pathogenesis of complications of diabetes.

NLR IN SUBCLINICAL INFLAMMATION

High Neutrophil lymphocyte ratio is a marker of subclinical inflammation in many disease states of the vascular system. NLR reflects the systemic inflammatory response that accompanies chronic disease but might also be influenced by systemic infections, atherosclerosis, hypertension, chronic renal disease and diabetes.

Subclinical vascular inflammation measured by derived NLR is linked with traditional risk factors of chronic diseases such as smoking, obesity, hypertension and elevated levels of triglycerides.

MECHANISMS

Endothelial dysfunction secondary to cellular response of blood components heralds the onset of inflammation. Endothelial dysfunction leads to impaired production of nitric oxide and prostacylins. This leads to the depletion of anti-atherogenic, antithrombotic and vasodilator properties of the vascular endothelium.

The normal d-NLR is < 2.0 in control population.

DIABETES AND INFLAMMATION

Type 2 diabetes is a prothrombotic, pro atherosclerotic and pro inflammatory condition with high association for cardiovascular morbidity

Diabetes Mellitus has been reported to the associated with acute phase response. In type-2 diabetes sialic acid, alpha-1 acid glycoprotein, c-reactive protein, amyloid and interleukin-6 are increased[3]. Also in parallel leukocyte count is elevated significantly than other markers indicating ongoing subclinical vascular inflammation.

Prospective population based European Prospective Investigation into Cancer and Nutrition (EPIC)- Postsdam study examined type 2 diabetes and the role of central inflammatory cytokines (interleukin IL -6 , IL-1beta and tumor necrosis factor). This study concluded pathogenesis of diabetes involve subclinical immune activation .

DIABETES AND NEUTROPHIL LYMPHOCYTE RATIO

NLR is novel marker in determining inflammation .It includes two markers active nonspecific meditors ,neutrophil and lymphocyte productive component of inflammation .[6]

In type 2 diabetes ,there have been shown defective expression of interleukin -2 receptors led to decresed proliferation of lymphocyte .So the present studies showed increased neutrophil count and decresed lymphocyte count in unregulated diabetes . Based on this studies proved

increased NLR in unregulated diabetes and in relation in complications of type 2 diabetes .

NEUTROPHIL LYMPHOCYTE RATIO AND MALIGNANCY

Many studies proved role of high NLR in prognosis of solid tumors [43] . Mechanisms involved in high NLR in malignancy are

1. Inflammation

2. Cytokine production

3. AIMS AND OBJECTIVE

- To study neutrophil lymphocyte ratio and blood glucose regulation in type 2 diabetes.

4. MATERIALS AND METHOD

PLACE OF STUDY

Stanley Medical College and Hospital, Chennai

Department of General Medicine, OPD, Medical wards

Study population

100

Study design

Prospective and observational Study

ETHICAL COMMITTEE APPROVAL

Ethical committee approval was obtained for the study

OPERATIONAL DEFINITION

CASE DEFINITION

NEUTROPHIL LYMPHOCYTE RATIO

Calculated by dividing the number of neutrophils by number of lymphocytes , usually from peripheral blood sample.

The normal NLR is < 2.0 in control population.

Blood glucose regulation include fasting blood glucose ,postprandial blood glucose, HbA1c.

PATIENT SELECTION

Inclusion criteria

1. Patients with type 2 diabetes mellitus included Newly diagnosed diabetes and know diabetic patient on oral antidiabetic agents and insulin .
2. Age 30 years to 70 years

Exclusion criteria

1) Patients takings statins, asprin, thiazolidinediones,

2) Patients with acute infections

3) Patients with chronic inflammatory conditions like inflammatory bowel disease, osteoarthritis, rheumatoid arthritis, gout, bronchial asthma and chronic hepatits

4) Patients with acute myocardial infarction , cerebral infarction

5) Patients with chronic kidney disease.

METHOLOGY

- Patients aged above 30 years presenting to the Medicine out-patient service and those admitted to the medical wards at Stanley medical college hospital Chennai were included in the present study.

- The data were recorded from each subject with an in-person interview by administering a specific questionnaire.

- Anthropometric measures noted.

- In all the patients, automated blood cell counter is used to determine total WBC, neutrophil and lymphocyte levels and high performance liquid chromatography for HbA1c.

- Peripheral venous blood sample was to be drawn in the morning after 8 - 10 hours of fasting, to measure venous plasma glucose, serum total cholesterol, serum high density lipoprotein (HDL) cholesterol, and serum triglyceride levels.

- PPBS taken 2 hour after food.

- Plasma triglycerides, total cholesterol and HDL-cholesterol were to be measured by enzymatic colorimetric assay using autoanalyser

Measurement of HbA_{1c}

Technique

Cation exchange high performance liquid chromatography.

System

The Biorad D10 haemoglobin Testing System.[38]

HB1AC

Method : Bio Rad HPLC

Normal : 4 to 6%

Good Control: 6 to 7%

Fair Control : 7 to 8%

Poor Control : > 8%

ESTIMATION OF BLOOD GLUCOSE

Method

Glucose oxidase method

HUMAN SUBJECT PROTECTION

The full protocol along with draft questionnaire and Informed consent will be kept in Institutional ethical Committee and approval will be obtained.

INFORMED CONSENT

Consent form will be written in both English and Tamil and consent will be obtained from the participant, confidentiality will be maintained

5. RESULTS AND DISCUSSIONS

Groups

Groups	Definition	Number
NLR < 2	Neutrophil-Lymphocyte Ratio less than 2	41
NLR > 2	Neutrophil-Lymphocyte Ratio greater than 2	59

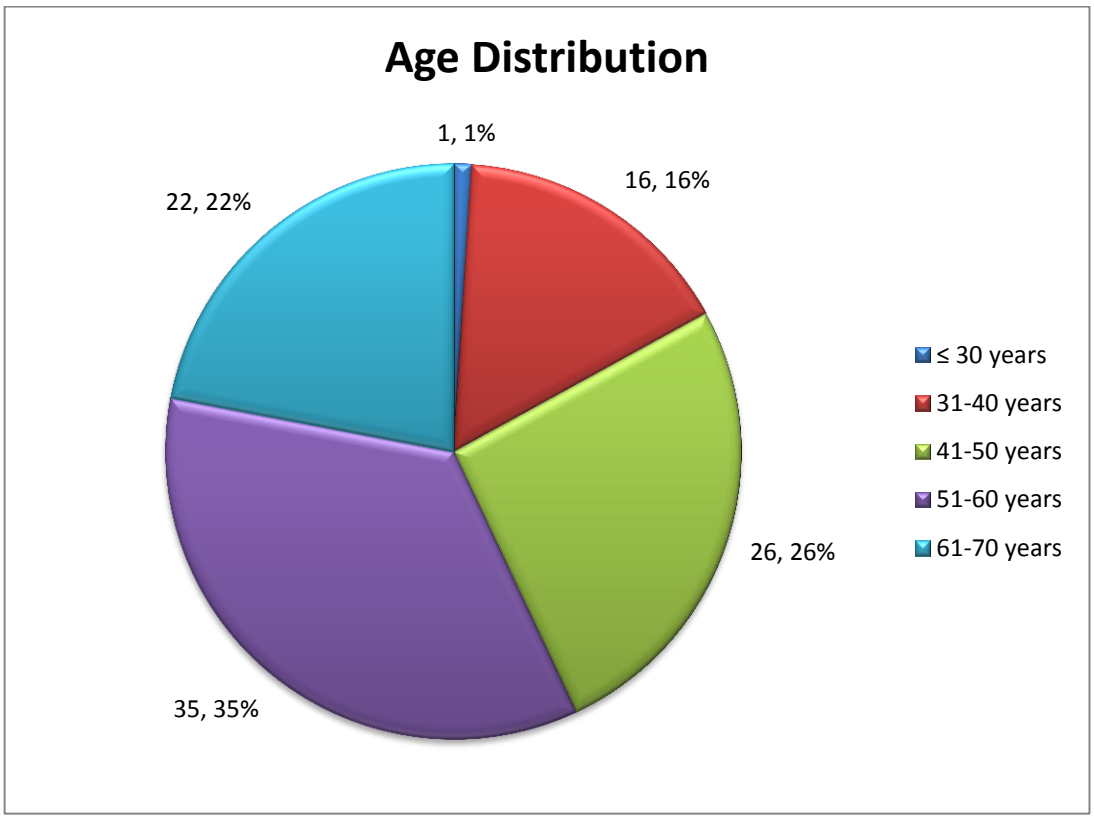
Null Hypothesis

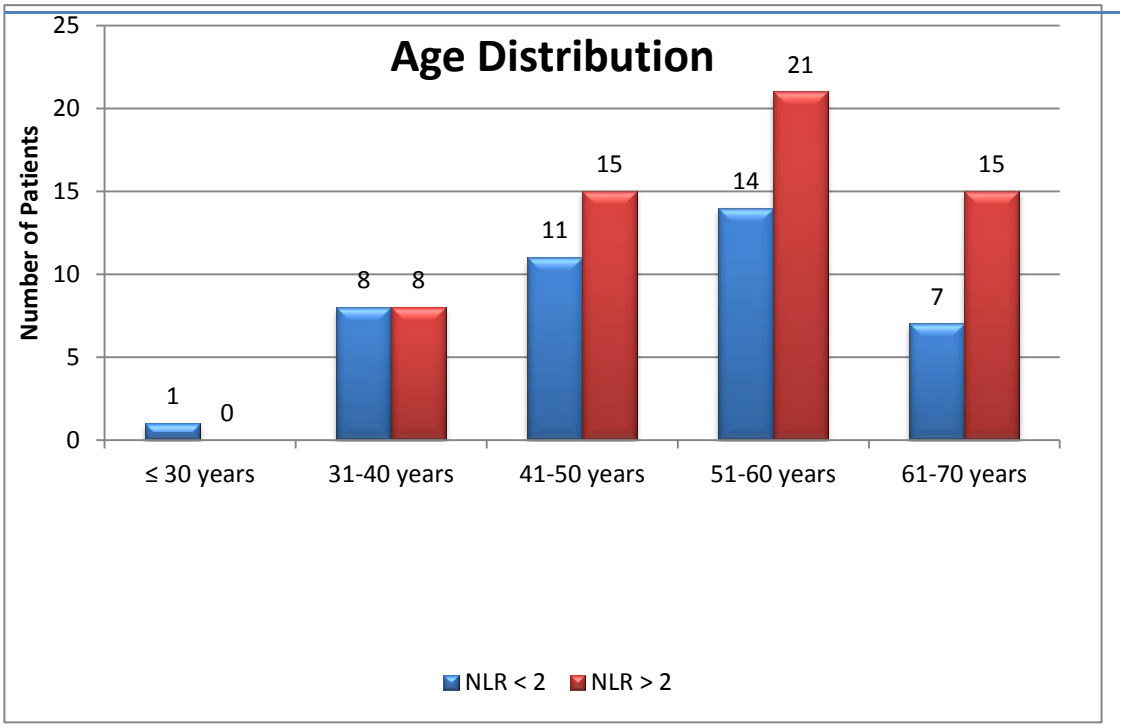
Null Hypothesis : H0	Neutrophil-Lymphocyte Ratio greater than 2 equal in effect Neutrophil-Lymphocyte Ratio less than 2
Alternate Hypothesis : H1	Neutrophil-Lymphocyte Ratio greater than 2 hazardous in effect Neutrophil-Lymphocyte Ratio less than 2

Data Analysis

Descriptive statistics was done for all data and were reported in terms of mean values and percentages. Suitable statistical tests of comparison were done. Continuous variables were analysed with the unpaired t test.. Categorical variables were analysed with the Chi-Square Test and Fisher Exact Test. Statistical significance was taken as $P < 0.05$. The data was analysed using SPSS version 16 and Microsoft Excel 2007.

AGE


Age Distribution
1, 1%
16, 16%
22, 22%
26, 26%
35, 35%
≤ 30 years
31-40 years
41-50 years
51-60 years
61-70 years

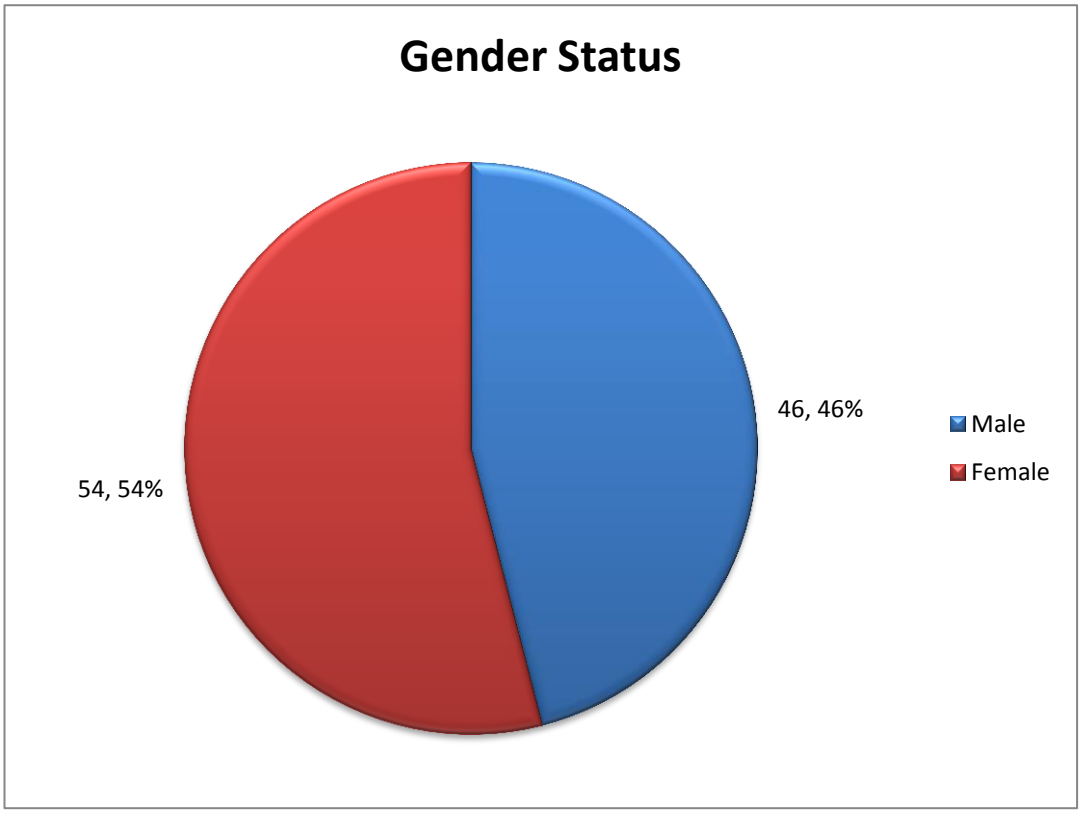

Age Distribution
Number of Patients
25
20
15
10
5
0
1
0
8
8
11
15
14
21
7
15
≤ 30 years
31-40 years
41-50 years
51-60 years
61-70 years
NLR < 2
NLR > 2

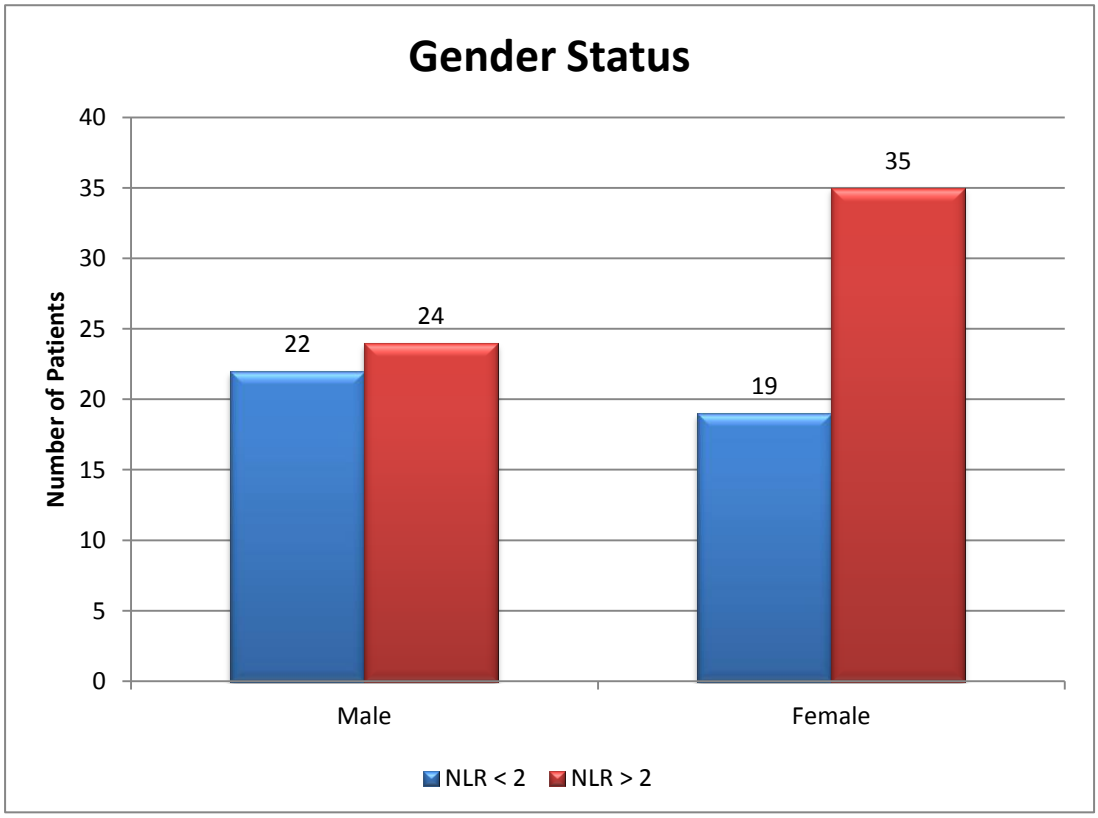
Age Distribution	NLR < 2	%	NLR > 2	%	Combined	%
≤ 30 years	1	2.44	0	0.00	1	1.00
31-40 years	8	19.51	8	13.56	16	16.00
41-50 years	11	26.83	15	25.42	26	26.00
51-60 years	14	34.15	21	35.59	35	35.00
61-70 years	7	17.07	15	25.42	22	22.00
Total	41	100	59	100	100	100

Age Distribution	NLR < 2	NLR > 2	Combined
N	41	59	100
Mean	49.51	53.80	52.04
SD	10.78	10.27	10.64
P value Unpaired t Test		0.0571	

Among the study patients, there was no statistically significant difference in relation to age distribution between NLR < 2 group (mean=49.51, SD=10.78) and NLR > 2 group (mean=53.80, SD=10.27) with a p value of <0.05 as per unpaired t test. Therefore we fail to reject the null hypothesis that there is no difference in age distribution between the study groups.

GENDER

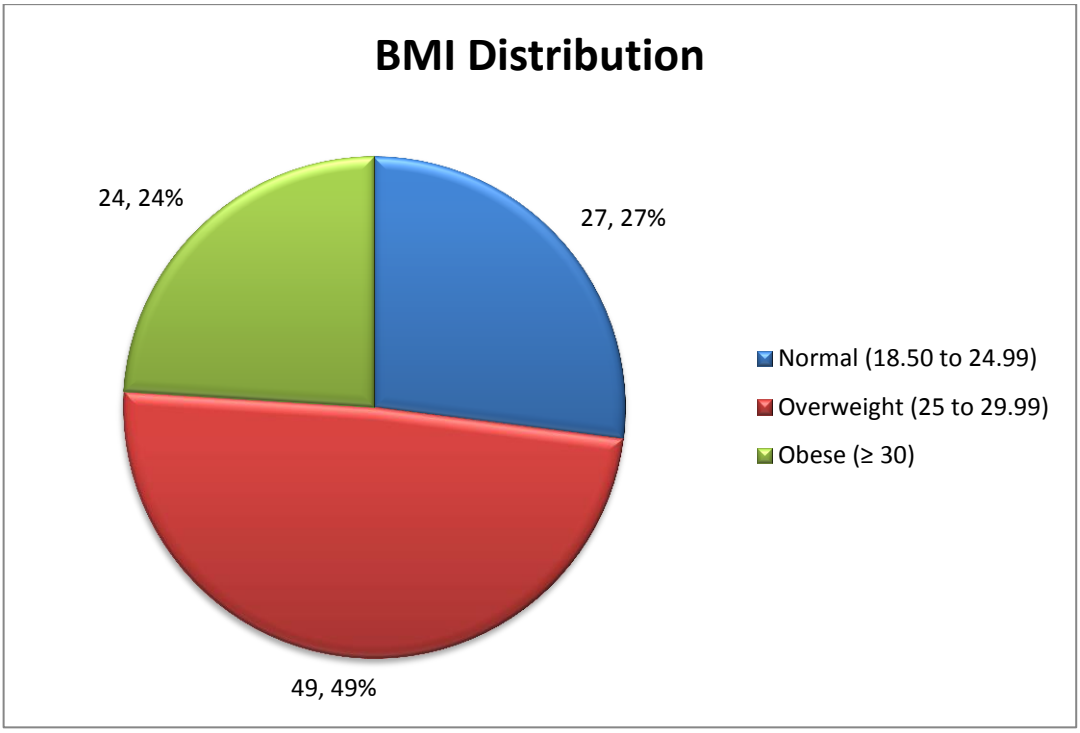

Gender Status
46, 46%
54, 54%
Male
Female

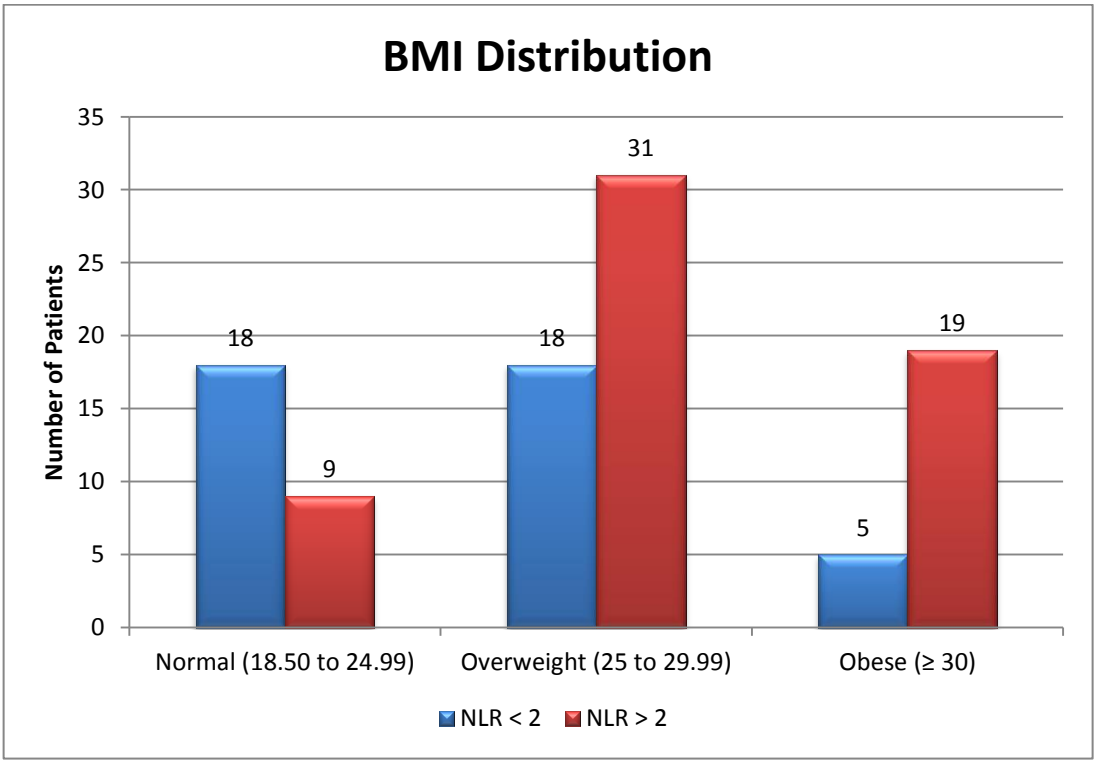

Gender Status
Number of Patients
40
35
30
25
20
15
10
5
0
22
24
19
35
Male
Female
NLR < 2
NLR > 2

Gender Status	NLR < 2	%	NLR > 2	%	Combined	%
Male	22	53.66	24	40.68	46	46.00
Female	19	46.34	35	59.32	54	54.00
Total	41	100	59	100	100	100
P value Chi Squared Test			0.2002			

Among the study patients, there was no statistically significant difference in relation to gender status between NLR < 2 group (majority are males – 53.66%) and NLR > 2 group (majority are females – 59.32%) with a p value of <0.05 as per chi squared test. Therefore we fail to reject the null hypothesis that there is no difference in gender status between the study groups.

BMI


BMI Distribution
24, 24%
27, 27%
49, 49%
Normal (18.50 to 24.99)
Overweight (25 to 29.99)
Obese (≥ 30)


BMI Distribution
Number of Patients
35
30
25
20
15
10
5
0
18
9
18
31
5
19
Normal (18.50 to 24.99)
Overweight (25 to 29.99)
Obese (≥ 30)
NLR < 2
NLR > 2

BMI Distribution	NLR < 2	%	NLR > 2	%	Combined	%
Underweight (≤ 18.49)	0	0.00	0	0.00	0	0.00
Normal (18.50 to 24.99)	18	43.90	9	15.25	27	27.00
Overweight (25 to 29.99)	18	43.90	31	52.54	49	49.00
Obese (≥ 30)	5	12.20	19	32.20	24	24.00
Total	41	100	59	100	100	100

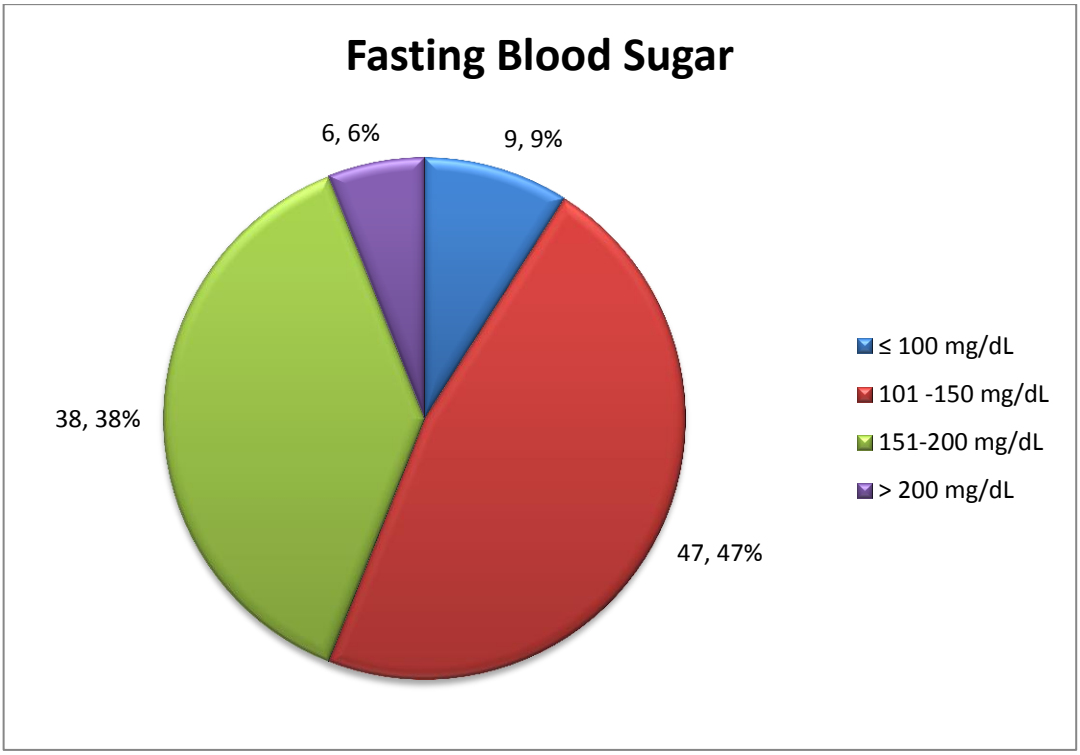
BMI Distribution	NLR < 2	NLR > 2	Combined
N	41	59	100
Mean	26.24	29.08	27.9144
SD	3.68	4.16	4.19
P value Unpaired t Test		0.0007	

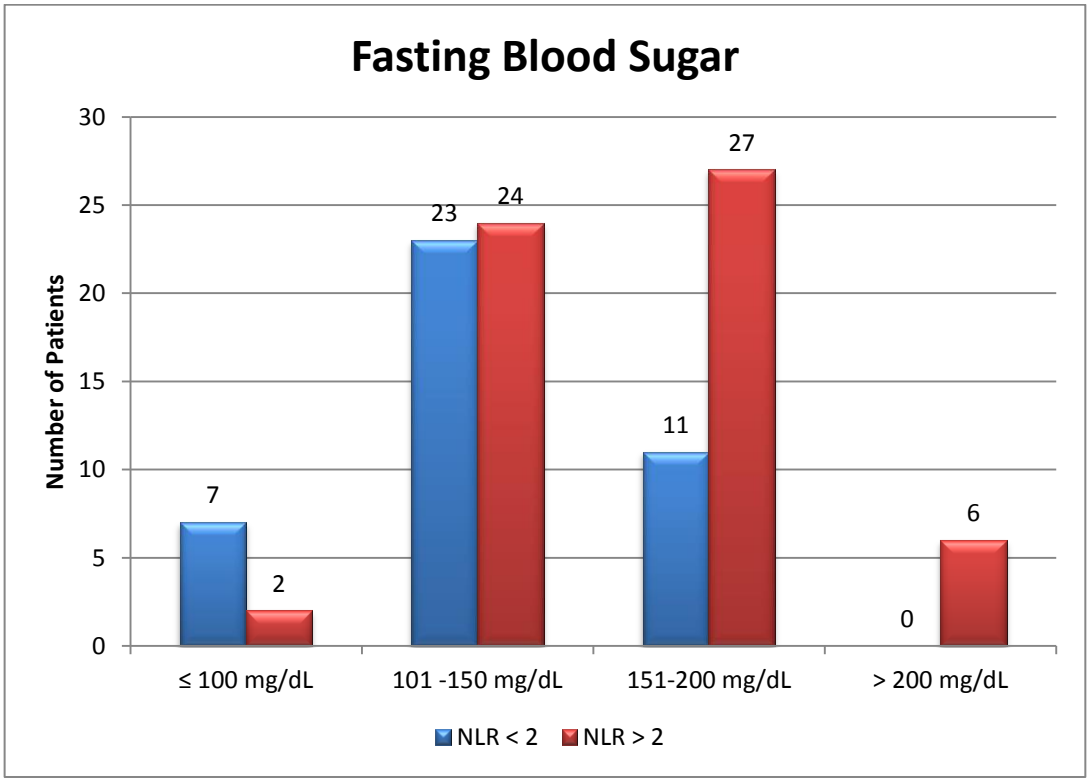
Among the study patients, there was a statistically significant difference in relation to BMI distribution between NLR < 2 group (mean=26.24, SD=3.68) and NLR > 2 group (mean=29.08, SD=4.16) with a p value of <0.05 as per unpaired t test. Therefore we fail to reject the null hypothesis that there is no difference in BMI distribution between the study groups.

Discussion

The mean BMI was significantly less in NLR < 2 group compared to NLR > 2 group by a mean difference of 2.84 (10% lower). This difference is significant with a p-value of 0.0007 as per unpaired t test.

FBS


Fasting Blood Sugar
6, 6%
9, 9%
38, 38%
47, 47%
≤ 100 mg/dL
101 -150 mg/dL
151-200 mg/dL
> 200 mg/dL


Fasting Blood Sugar
Number of Patients
30
25
20
15
10
5
0
7
2
23
24
11
27
0
6
≤ 100 mg/dL
101 -150 mg/dL
151-200 mg/dL
> 200 mg/dL
NLR < 2
NLR > 2

Fasting Blood Sugar	NLR < 2	%	NLR > 2	%	Combined	%
≤ 100 mg/dL	7	17.07	2	3.39	9	9.00
101 -150 mg/dL	23	56.10	24	40.68	47	47.00
151-200 mg/dL	11	26.83	27	45.76	38	38.00
> 200 mg/dL	0	0.00	6	10.17	6	6.00
Total	41	100	59	100	100	100

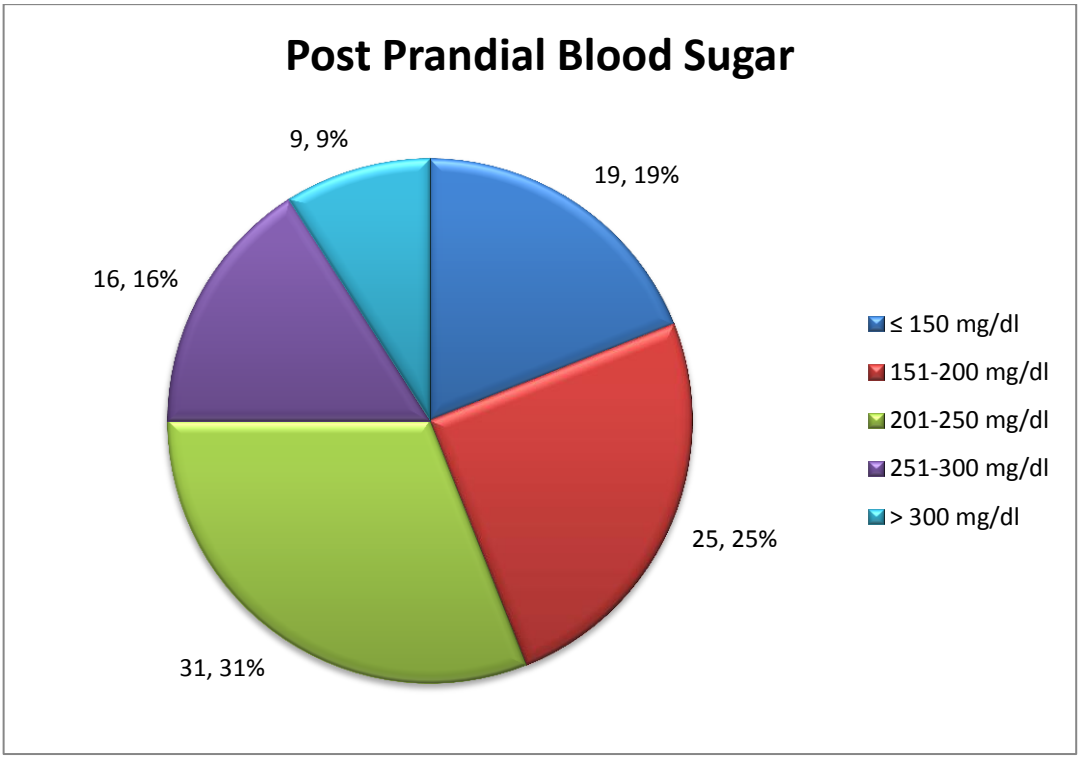
Fasting Blood Sugar	NLR < 2	NLR > 2	Combined
N	41	59	100
Mean	133.83	156.64	147.29
SD	27.14	34.17	33.30
P value Unpaired t Test		0.0006	

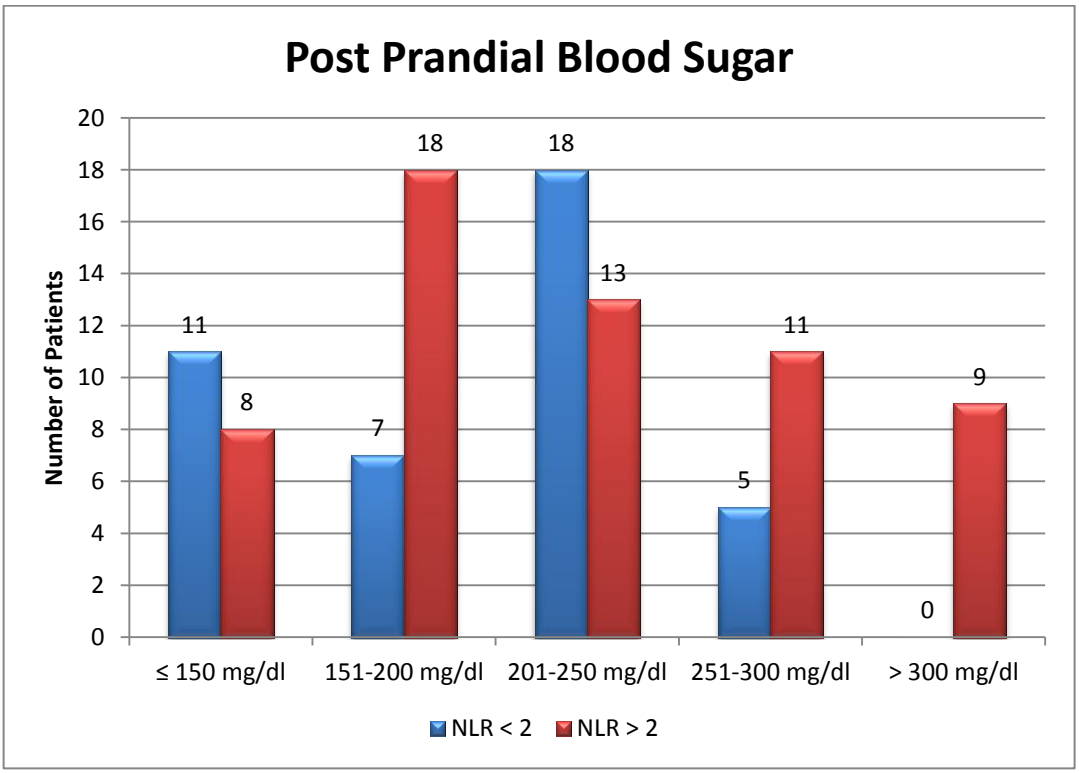
Among the study patients, there was a statistically significant difference in relation to fasting blood sugar distribution between NLR < 2 group (mean=133.83, SD=27.14) and NLR > 2 group (mean=156.64, SD=34.17) with a p value of <0.05 as per unpaired t test. Therefore we fail to reject the null hypothesis that there is no difference in fasting blood sugar distribution between the study groups.

Discussion

The mean FBS was significantly less in NLR < 2 group compared to NLR > 2 group by a mean difference of 22.81 mg/dl (15% lower). This difference is significant with a p-value of 0.0006 as per unpaired t test.

PPBS


Post Prandial Blood Sugar
9, 9%
19, 19%
16, 16%
25, 25%
31, 31%
≤ 150 mg/dl
151-200 mg/dl
201-250 mg/dl
251-300 mg/dl
> 300 mg/dl


Post Prandial Blood Sugar
Number of Patients
20
18
16
14
12
10
8
6
4
2
0
11
8
7
18
18
13
5
11
0
9
≤ 150 mg/dl
151-200 mg/dl
201-250 mg/dl
251-300 mg/dl
> 300 mg/dl
NLR < 2
NLR > 2

Post Prandial Blood Sugar	NLR < 2	%	NLR > 2	%	Combined	%
≤ 150 mg/dl	11	26.83	8	13.56	19	19.00
151-200 mg/dl	7	17.07	18	30.51	25	25.00
201-250 mg/dl	18	43.90	13	22.03	31	31.00
251-300 mg/dl	5	12.20	11	18.64	16	16.00
> 300 mg/dl	0	0.00	9	15.25	9	9.00
Total	41	100	59	100	100	100

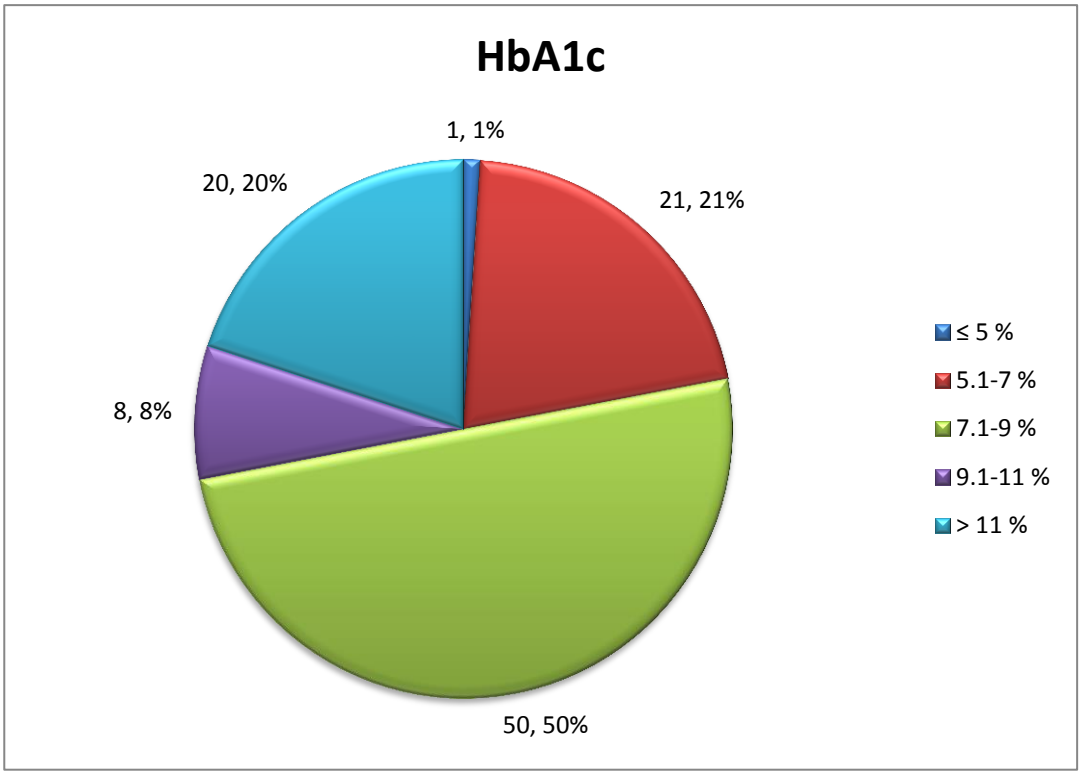
Post Prandial Blood Sugar	NLR < 2	NLR > 2	Combined
N	41	59	100
Mean	195.12	228.61	214.88
SD	45.03	67.43	61.29
P value Unpaired t Test		0.0066	

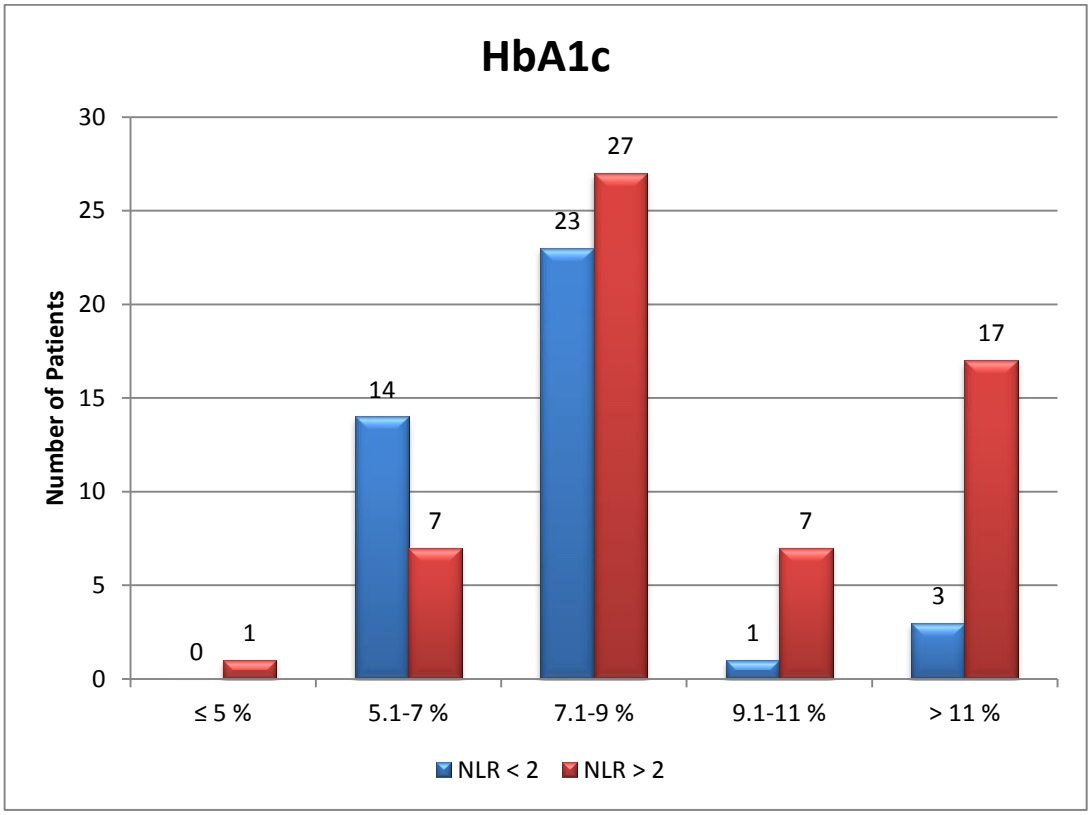
Among the study patients, there was a statistically significant difference in relation to post prandial blood sugar distribution between NLR < 2 group (mean=195.12, SD=45.03) and NLR > 2 group (mean=228.61, SD=67.43) with a p value of <0.05 as per unpaired t test. Therefore we fail to reject the null hypothesis that there is no difference in post prandial blood sugar distribution between the study groups.

Discussion

The mean PPBS was significantly less in NLR < 2 group compared to NLR > 2 group by a mean difference of 33.49 mg/dl (15% lower). This difference is significant with a p-value of 0.0066 as per unpaired t test.

HbA1c


HbA1c
1, 1%
20, 20%
21, 21%
8, 8%
50, 50%
≤ 5 %
5.1-7 %
7.1-9 %
9.1-11 %
> 11 %


HbA1c
Number of Patients
30
25
20
15
10
5
0
0
1
14
7
23
27
1
7
3
17
≤ 5 %
5.1-7 %
7.1-9 %
9.1-11 %
> 11 %
NLR < 2
NLR > 2

HbA1c	NLR < 2	%	NLR > 2	%	Combined	%
≤ 5 %	0	0.00	1	1.69	1	1.00
5.1-7 %	14	34.15	7	11.86	21	21.00
7.1-9 %	23	56.10	27	45.76	50	50.00
9.1-11 %	1	2.44	7	11.86	8	8.00
> 11 %	3	7.32	17	28.81	20	20.00
Total	41	100	59	100	100	100

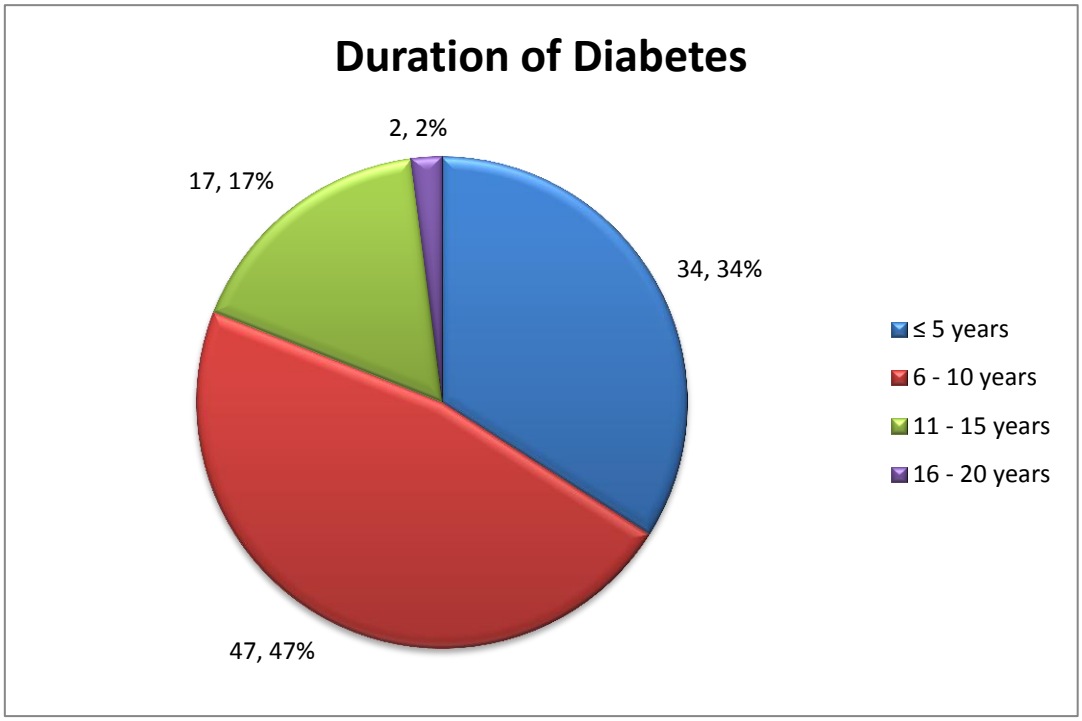
HbA1c	NLR < 2	NLR > 2	Combined
N	41	59	100
Mean	7.71	9.65	8.854
SD	1.75	2.98	2.71
P value Unpaired t Test		0.0003	

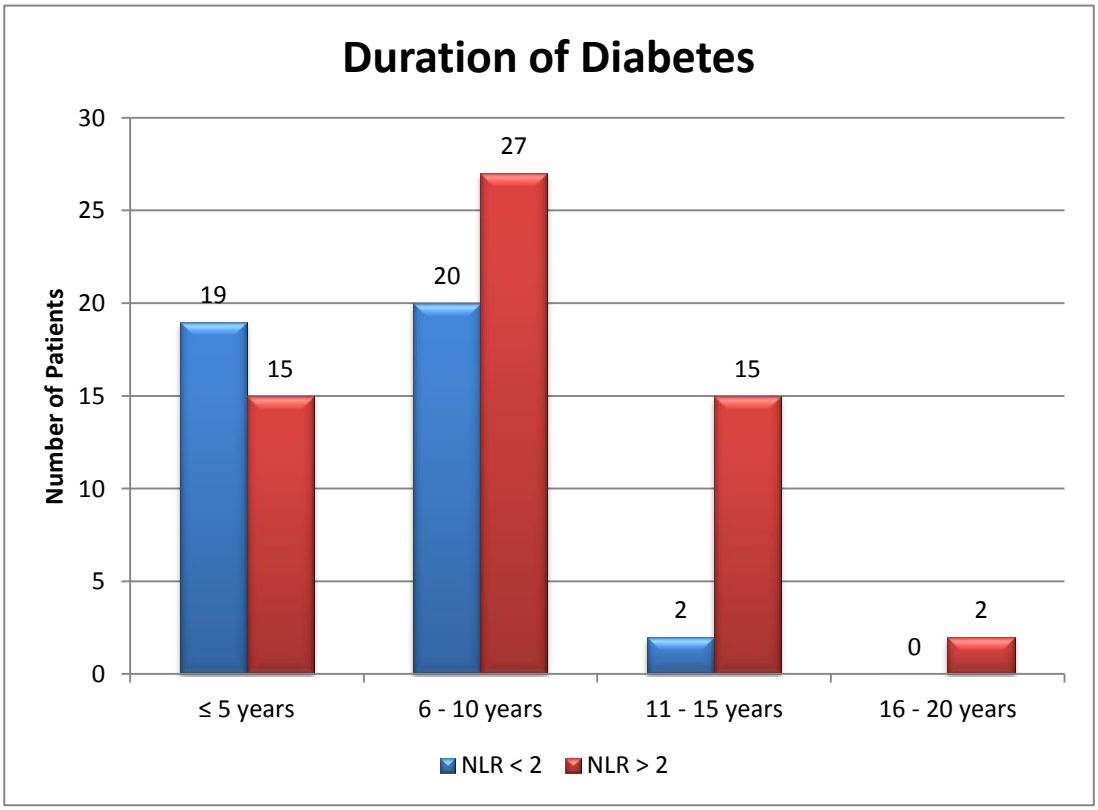
Among the study patients, there was a statistically significant difference in relation to Glycated hemoglobin distribution between NLR < 2 group (mean=7.71, SD=1.75) and NLR > 2 group (mean=9.65, SD=2.98) with a p value of <0.05 as per unpaired t test. Therefore we fail to reject the null hypothesis that there is no difference in Glycated hemoglobin distribution between the study groups.

Discussion

The mean HbA1c was significantly less in NLR < 2 group compared to NLR > 2 group by a mean difference of 1.94% (20% lower). This difference is significant with a p-value of 0.0003 as per unpaired t test.

DURATION OF DIABETES





Duration of Diabetes	**NLR < 2**	**%**	**NLR > 2**	**%**	**Combined**	**%**
≤ 5 years	19	46.34	15	25.42	34	34.00
6 - 10 years	20	48.78	27	45.76	47	47.00
11 - 15 years	2	4.88	15	25.42	17	17.00
16 - 20 years	0	0.00	2	3.39	2	2.00
Total	41	100	59	100	100	100

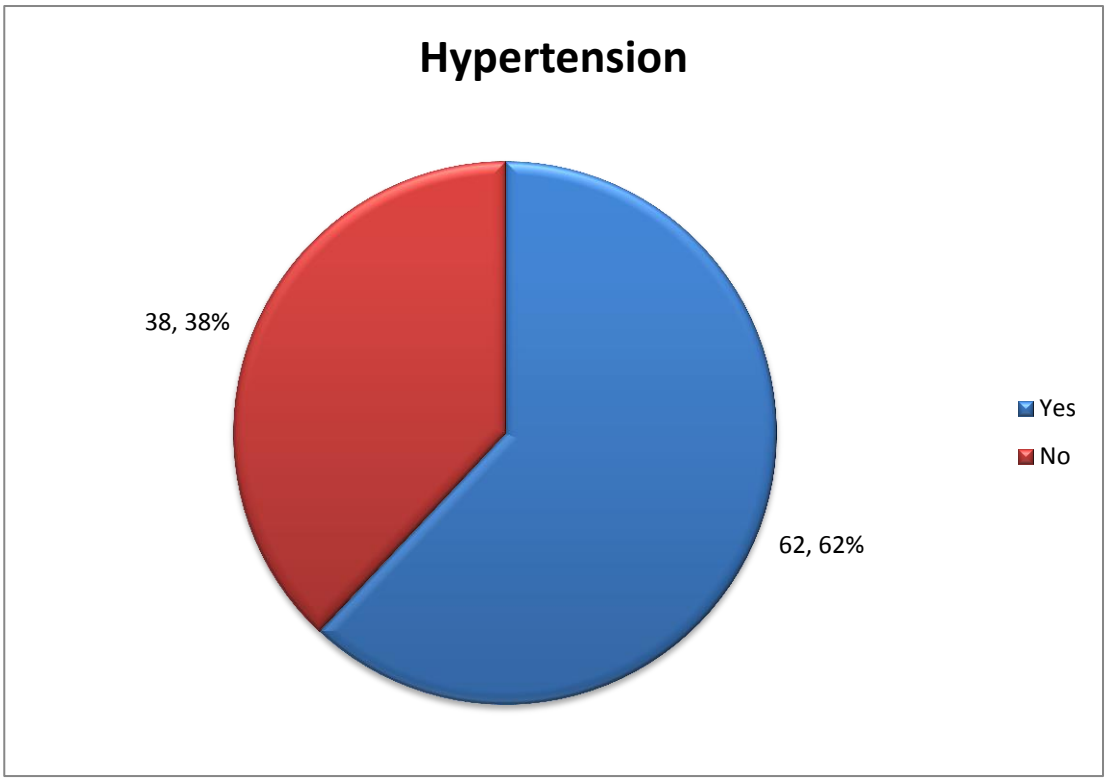
Duration of Diabetes	NLR < 2	NLR > 2	Combined
N	41	59	100
Mean	6.00	7.93	7.14
SD	2.88	3.68	3.49
P value Unpaired t Test		0.0059	

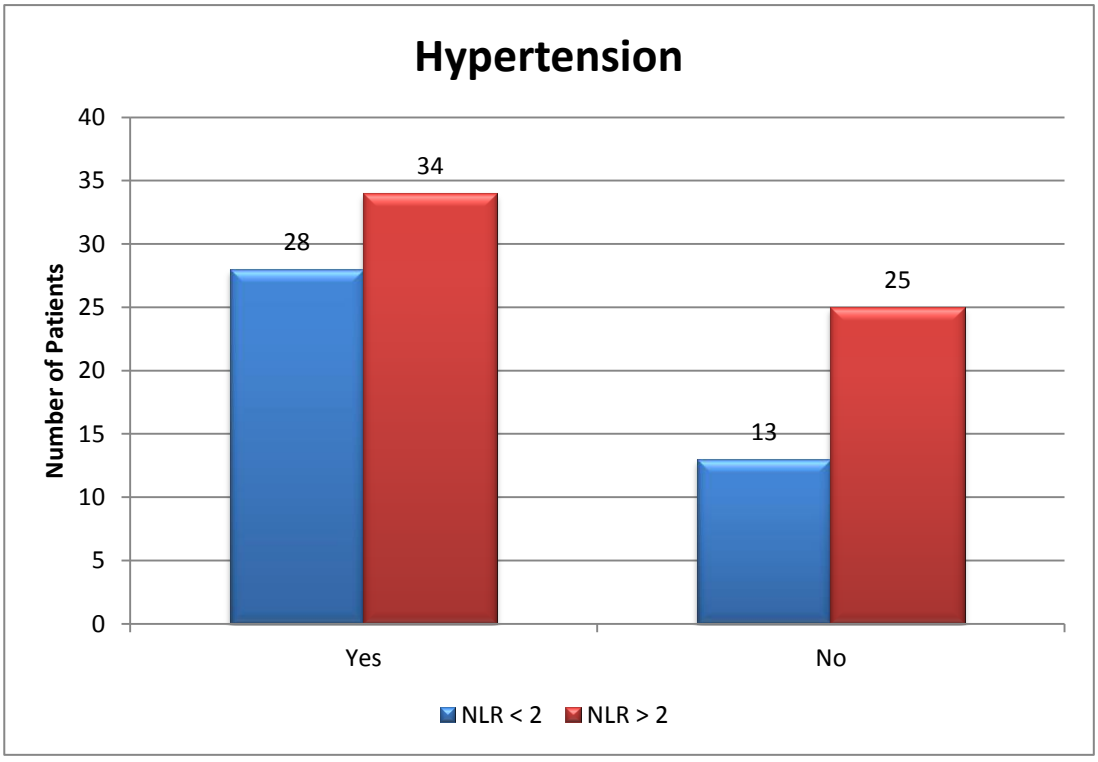
Among the study patients, there was a statistically significant difference in relation to duration of diabetes distribution between NLR < 2 group (mean=6.00, SD=2.88) and NLR > 2 group (mean=7.93, SD=3.68) with a p value of <0.05 as per unpaired t test. Therefore we fail to reject the null hypothesis that there is no difference in duration of diabetes distribution between the study groups.

Discussion

The mean duration of diabetes was significantly shorter in NLR < 2 group compared to NLR > 2 group by a mean difference of 1.93 years (24% shorter). This difference is significant with a p-value of 0.0059 as per unpaired t test.

HYPERTENSION

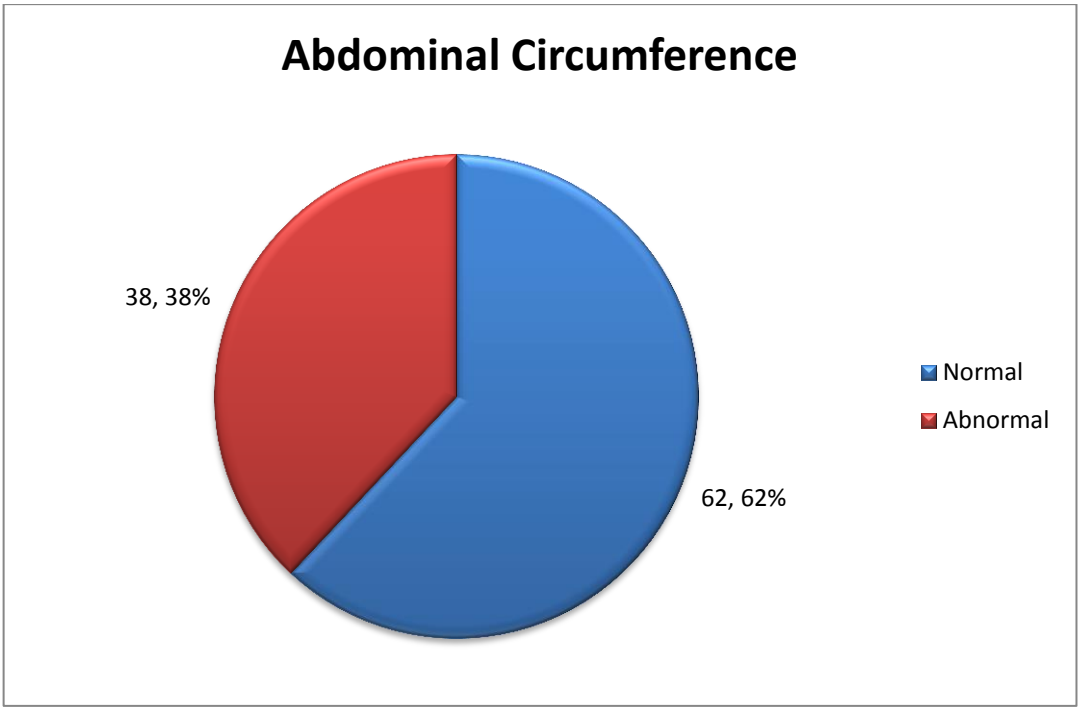


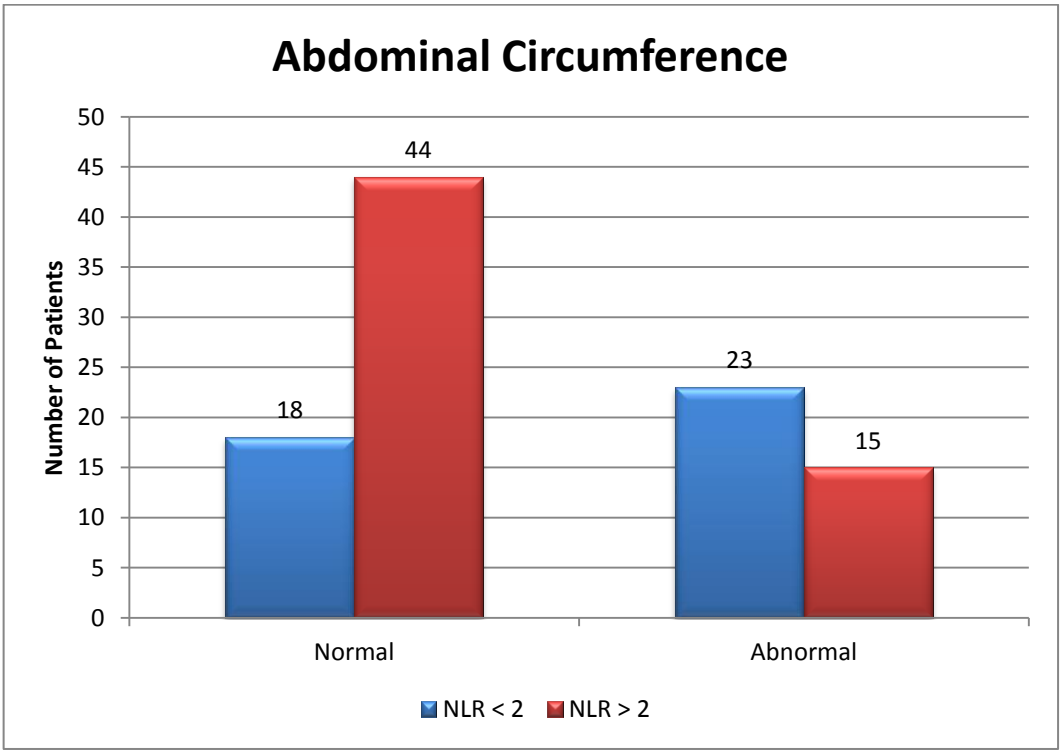


Hypertension	**NLR < 2**	**%**	**NLR > 2**	**%**	**Combined**	**%**
Yes	28	68.29	34	57.63	62	62.00
No	13	31.71	25	42.37	38	38.00
Total	41	100	59	100	100	100
P value Chi Squared Test			0.2798			

Among the study patients, there was no statistically significant difference in relation to hypertension status between NLR < 2 group (majority are hypertensives – 68.29%) and NLR > 2 group (majority are hypertensives– 57.63%) with a p value of <0.05 as per chi squared test. Therefore we fail to reject the null hypothesis that there is no difference in hypertension status between the study groups.

ABDOMINAL CIRCUMFERENCE





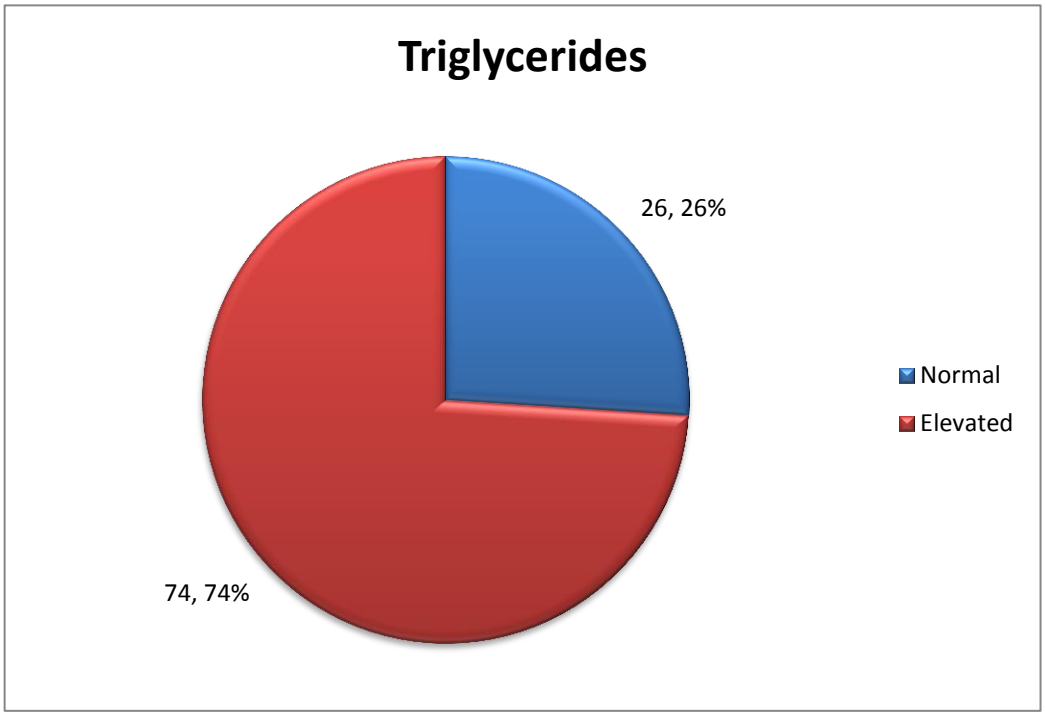
Abdominal Circumference	NLR < 2	%	NLR > 2	%	Combined	%
Normal	23	56.10	15	25.42	38	38.00
Abnormal	18	43.90	44	74.58	62	62.00
Total	41	100	59	100	100	100
P value Chi Squared Test			0.0019			

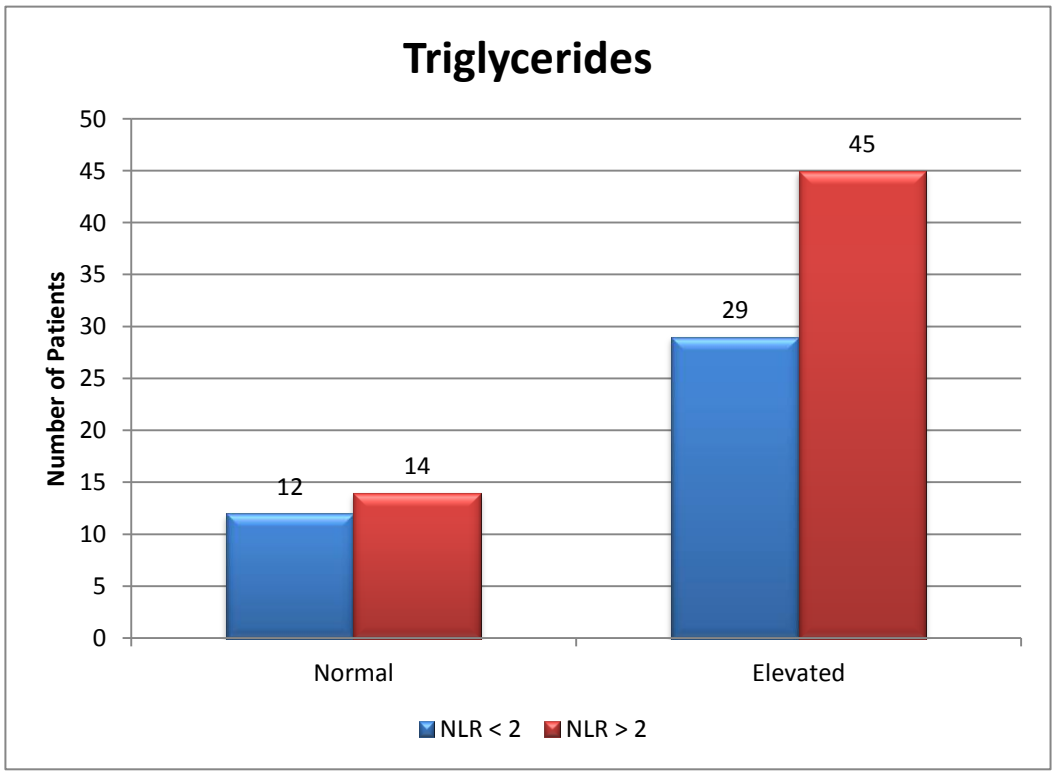
Among the study patients, there was statistically significant difference in relation to abdominal circumference status between NLR < 2 group (majority are normal AC – 56.10%) and NLR > 2 group (majority are abnormal AC – 74.58%) with a p value of <0.05 as per unpaired t test. Therefore we fail to reject the null hypothesis that there is no difference in abdominal circumference status between the study groups.

Discussion

The incidence of abnormal abdominal circumference was significantly less in NLR < 2 group compared to NLR > 2 group by a percentage difference of 30.67% (41% less). This difference is significant with a p-value of 0.0019 as per chi squared test.

TRIGLYCERIDES

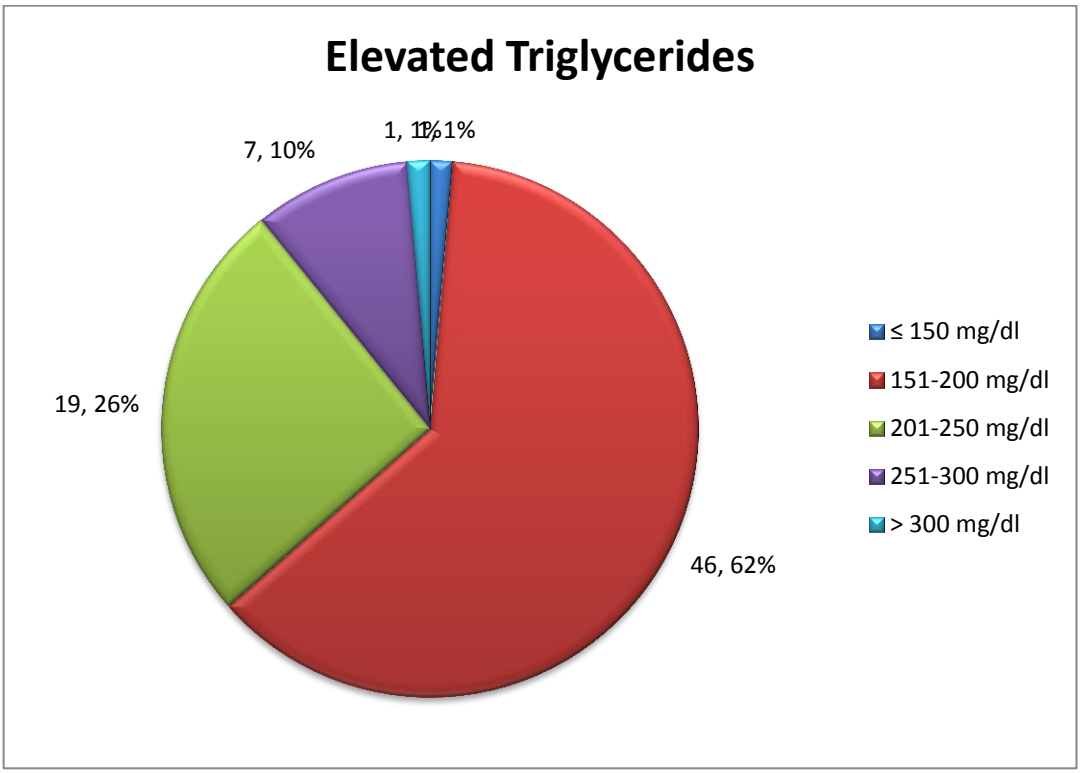


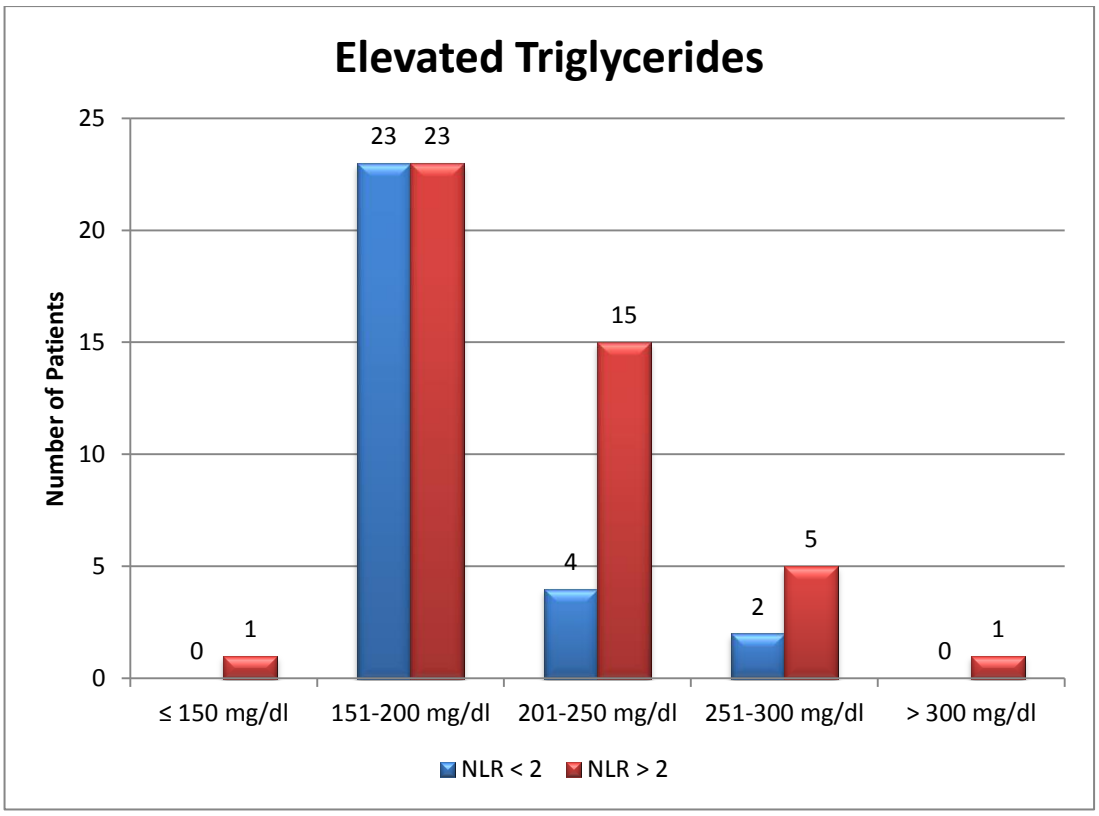


Triglycerides	**NLR < 2**	**%**	**NLR > 2**	**%**	**Combined**	**%**
Normal	12	29.27	14	23.73	26	26.00
Elevated	29	70.73	45	76.27	74	74.00
Total	41	100	59	100	100	100
P value Chi Squared Test			0.5345			

Among the study patients, there was no statistically significant difference in relation to triglycerides status between NLR < 2 group (majority have elevated TGL – 70.73%) and NLR > 2 group (majority have elevated TGL – 76.27%) with a p value of <0.05 as per chi squared test. Therefore we fail to reject the null hypothesis that there is no difference in triglycerides status between the study groups.

ELEVATED TRIGLYCERIDES



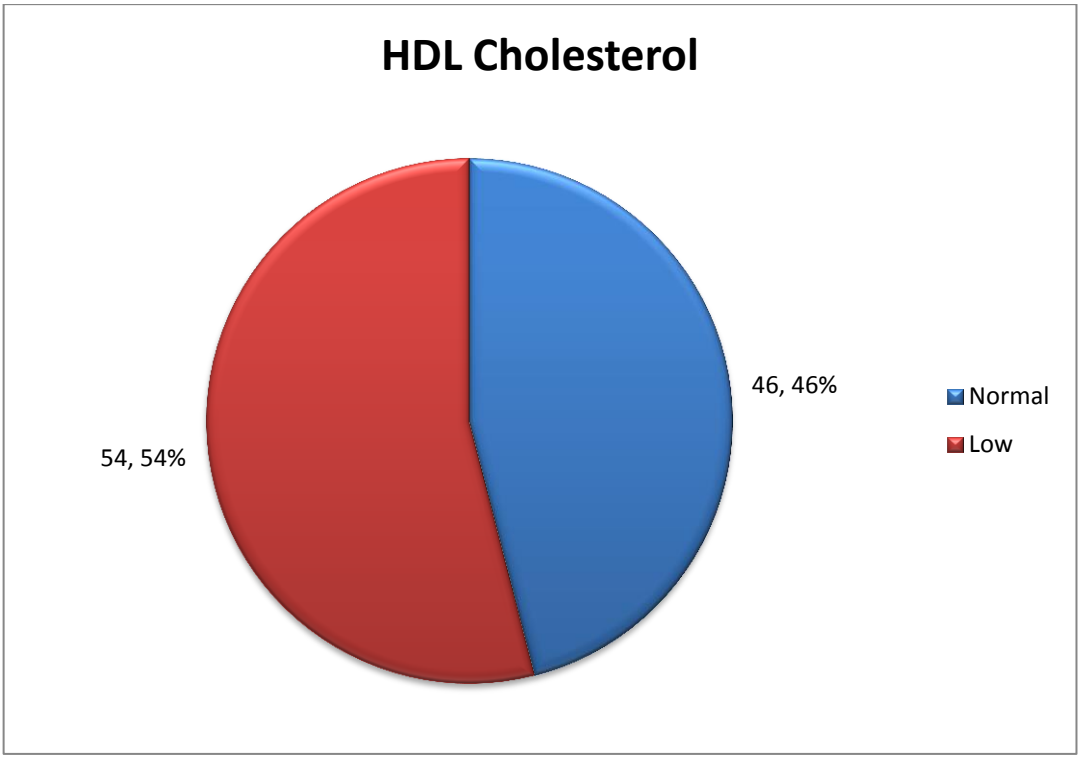


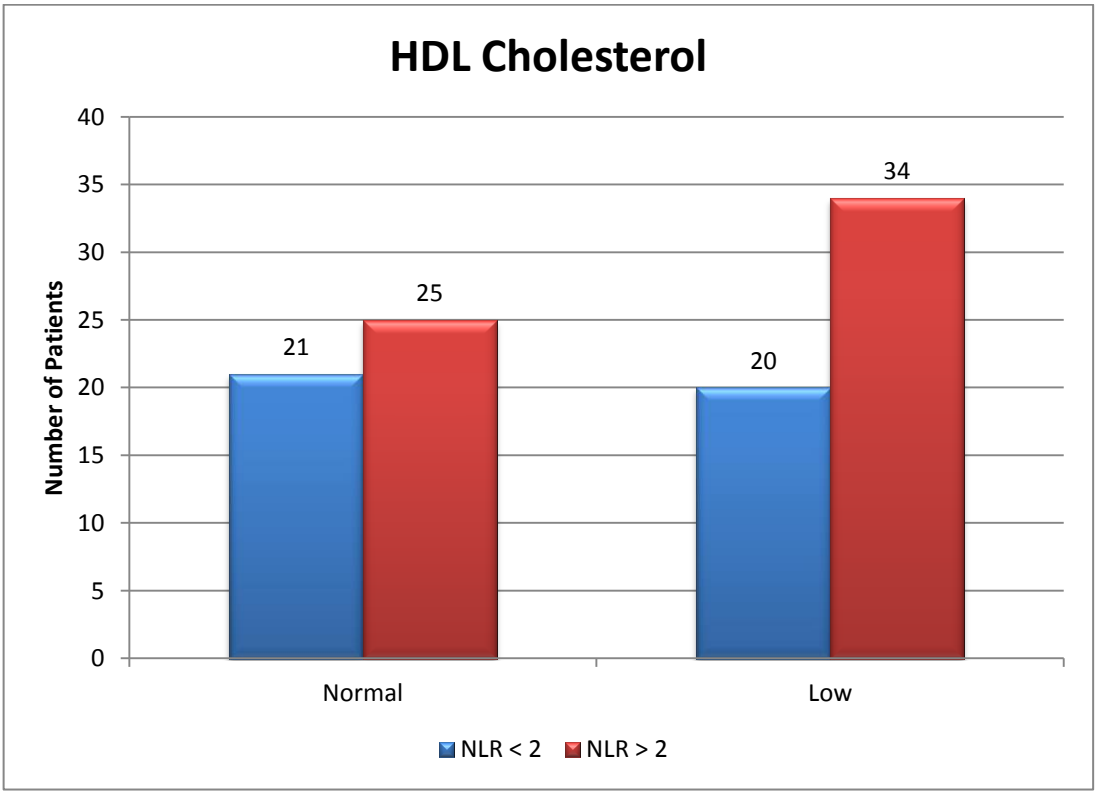
Elevated Triglycerides	NLR < 2	%	NLR > 2	%	Combined	%
≤ 150 mg/dl	0	0.00	1	2.22	1	1.35
151-200 mg/dl	23	79.31	23	51.11	46	62.16
201-250 mg/dl	4	13.79	15	33.33	19	25.68
251-300 mg/dl	2	6.90	5	11.11	7	9.46
> 300 mg/dl	0	0.00	1	2.22	1	1.35
Total	29	100	45	100	74	100

Elevated Triglycerides	NLR < 2	NLR > 2	Combined
N	29	45	74
Mean	196.93	208.16	203.7568
SD	29.96	43.67	39.04
P value Unpaired t Test		0.2298	

Among the study patients elevated triglycerides, there was no statistically significant difference NLR < 2 group (mean=196.93, SD=29.69) and NLR > 2 group (mean=208.16, SD=43.67) with a p value of <0.05 as per unpaired t test. Therefore we fail to reject the null hypothesis that there is no difference in elevated triglycerides distribution in the study patients.

HDL CHOLESTEROL

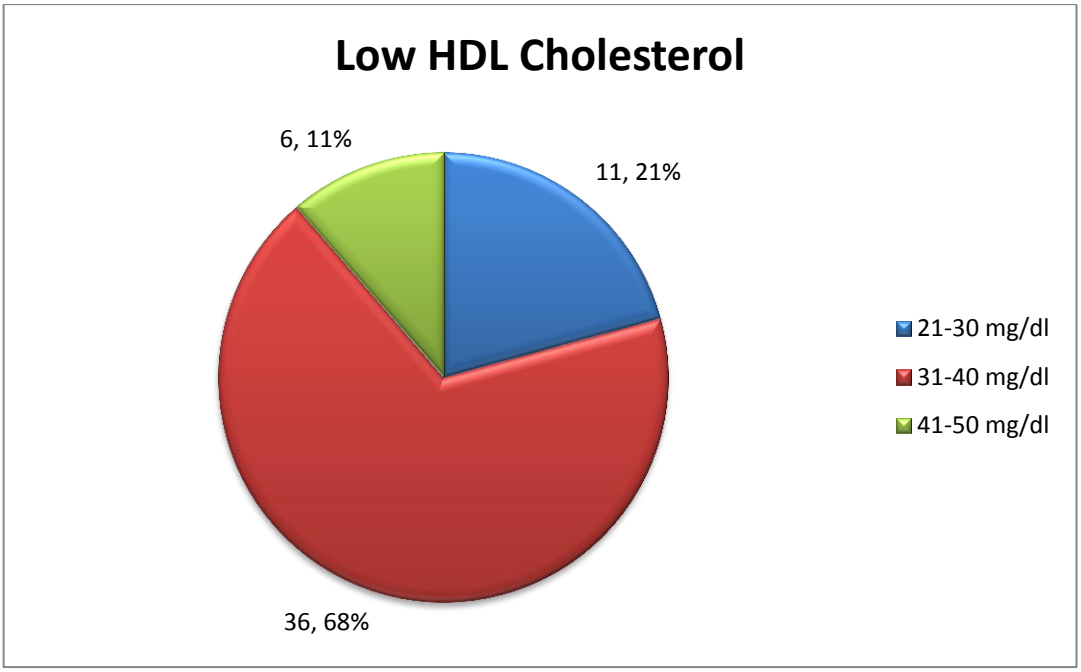


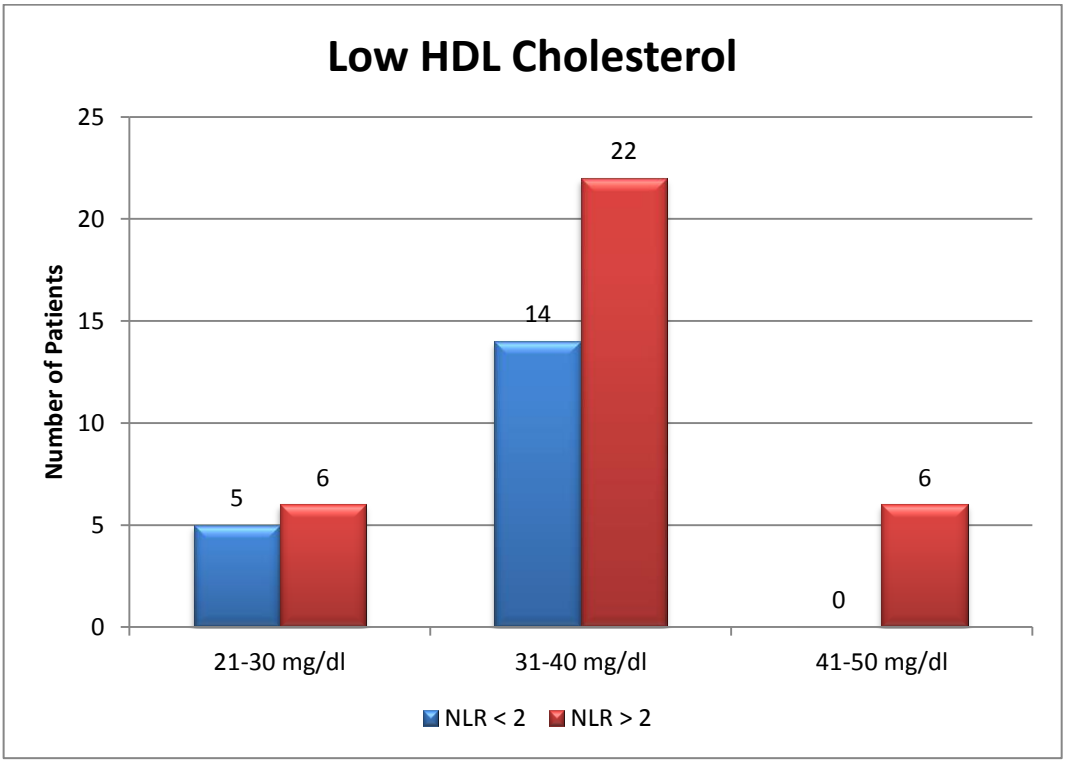


HDL Cholesterol	NLR < 2	%	NLR > 2	%	Combined	%
Normal	21	51.22	25	42.37	46	46.00
Low	20	48.78	34	57.63	54	54.00
Total	41	100	59	100	100	100
P value Chi Squared Test			0.3827			

Among the study patients, there was no statistically significant difference in relation to HDL cholesterol status between NLR < 2 group (majority have normal HDL cholesterol – 51.22%) and NLR > 2 group (majority low HDL cholesterol – 57.63%) with a p value of <0.05 as per chi squared test. Therefore we fail to reject the null hypothesis that there is no difference in HDL cholesterol status between the study groups.

LOW HDL CHOLESTEROL



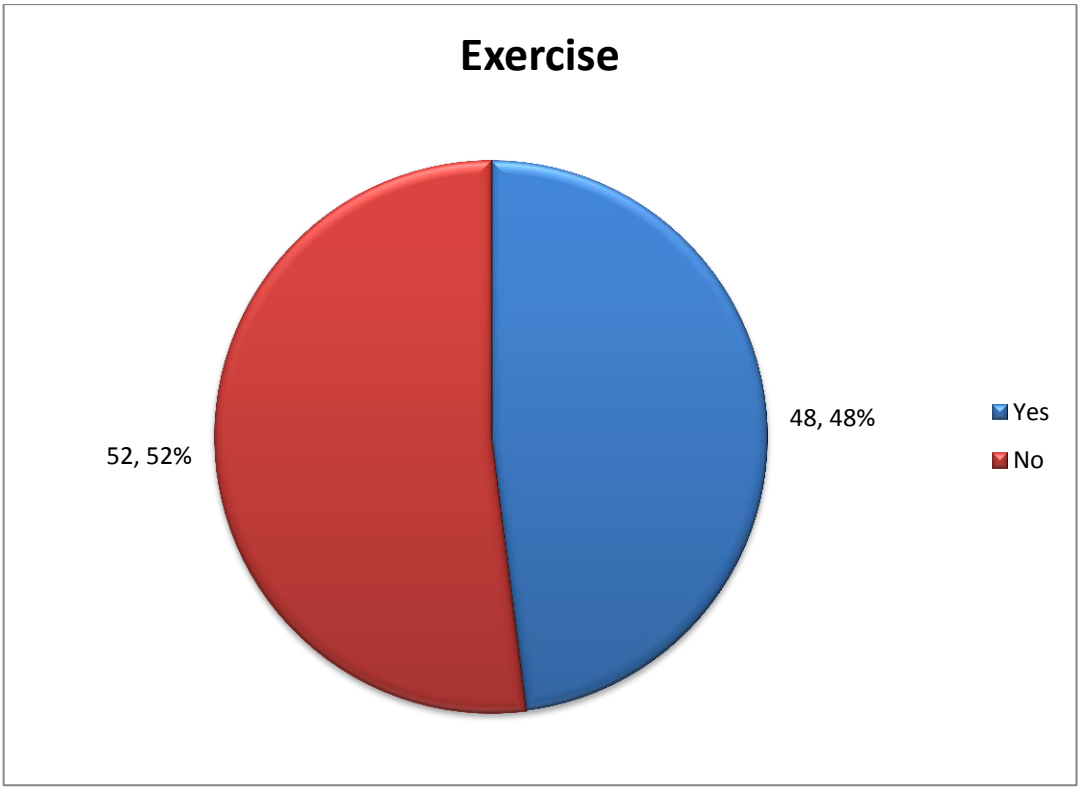


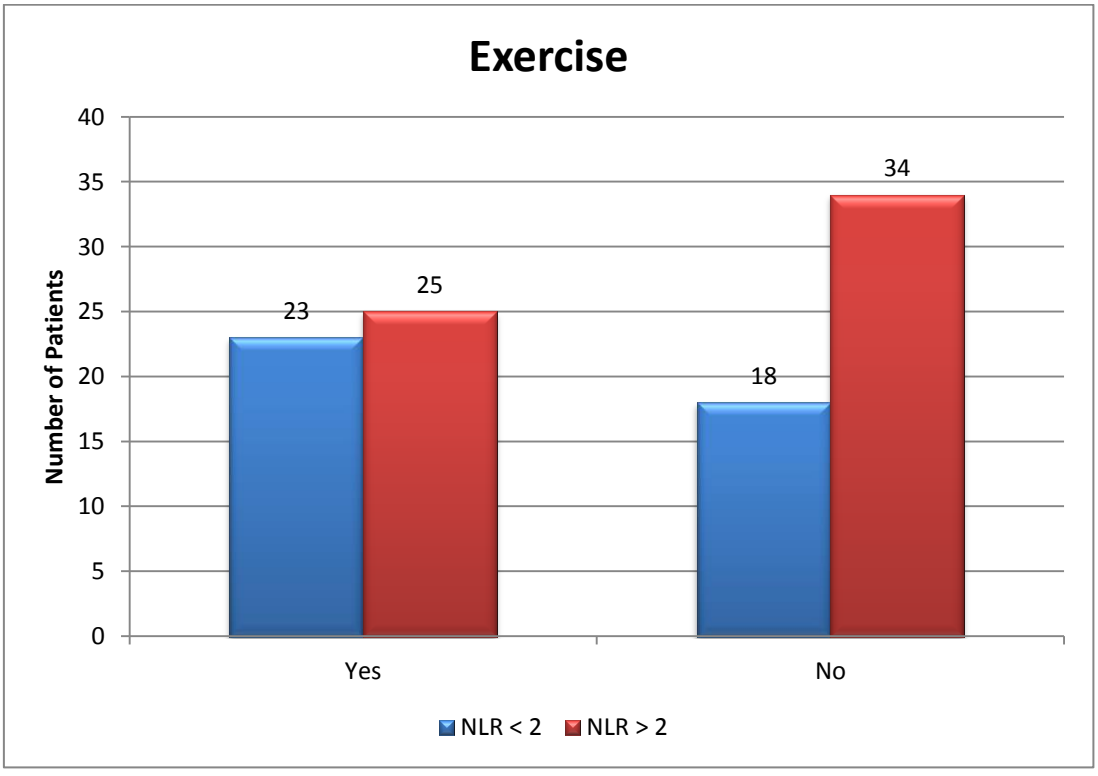
Low HDL Cholesterol	NLR < 2	%	NLR > 2	%	Combined	%
21-30 mg/dl	5	26.32	6	17.65	11	20.75
31-40 mg/dl	14	73.68	22	64.71	36	67.92
41-50 mg/dl	0	0.00	6	17.65	6	11.32
Total	19	100	34	100	53	100

Low HDL Cholesterol	NLR < 2	NLR > 2	Combined
N	19	34	53
Mean	33.47	35.76	34.94
SD	3.29	5.51	4.92
P value Unpaired t Test		0.1049	

Among the study patients low HDL cholesterol, there was no statistically significant difference NLR < 2 group (mean=33.47, SD=3.29) and NLR > 2 group (mean=35.76, SD=5.51) with a p value of <0.05 as per unpaired t test. Therefore we fail to reject the null hypothesis that there is no difference in low HDL cholesterol distribution in the study patients.

EXERCISE

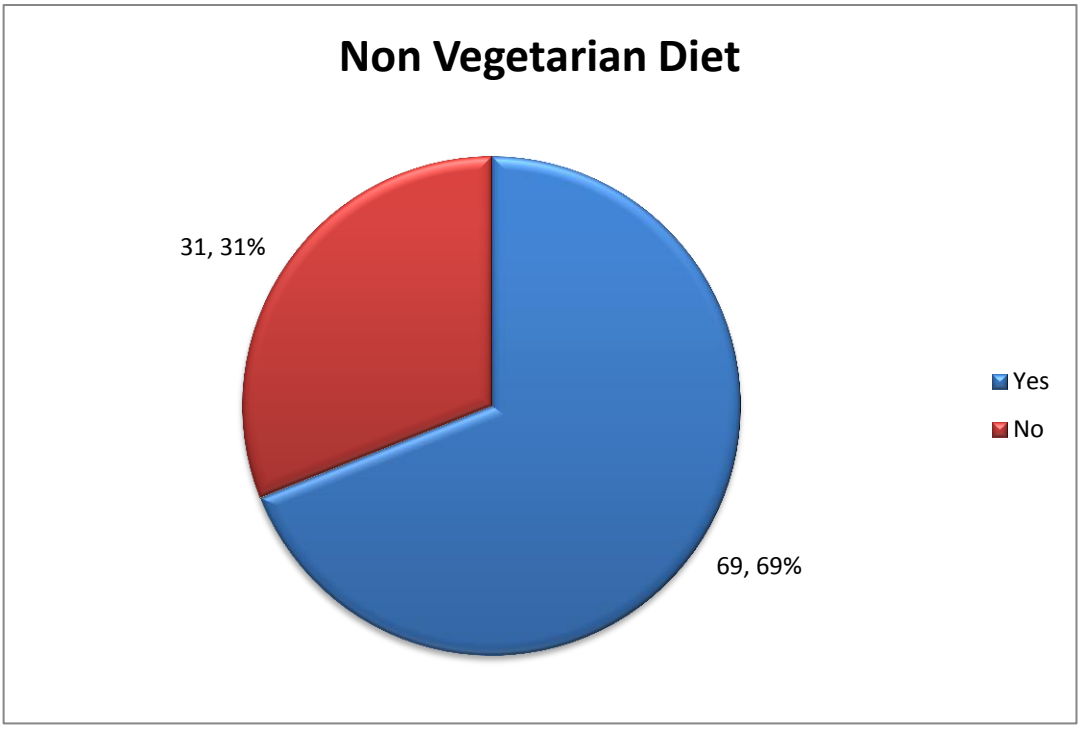

Exercise
52, 52%
48, 48%
Yes
No

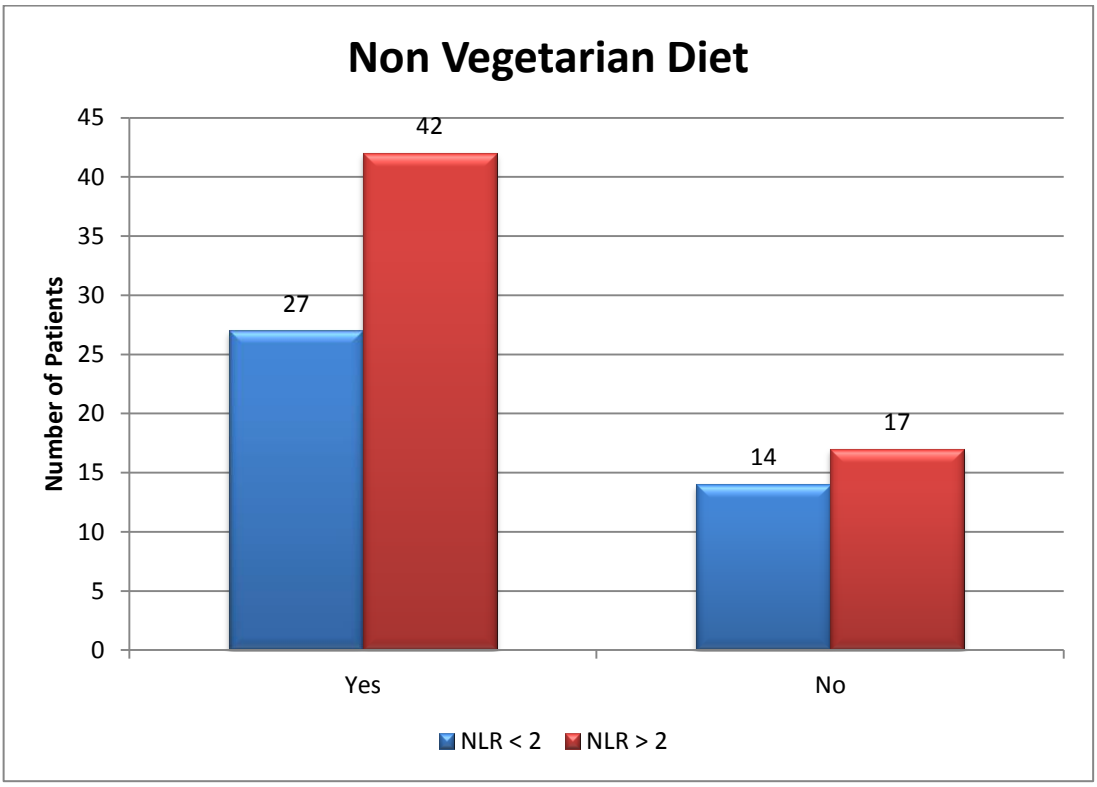

Exercise
Number of Patients
40
35
30
25
20
15
10
5
0
23
25
18
34
Yes
No
NLR < 2
NLR > 2

Exercise	**NLR < 2**	**%**	**NLR > 2**	**%**	**Combined**	**%**
Yes	23	56.10	25	42.37	48	48.00
No	18	43.90	34	57.63	52	52.00
Total	41	100	59	100	100	100
P value Chi Squared Test			0.1767			

Among the study patients, there was no statistically significant difference in relation to exercise status between NLR < 2 group (majority do exercise – 56.10%) and NLR > 2 group (majority don't do exercise – 57.63%) with a p value of <0.05 as per chi squared test. Therefore we fail to reject the null hypothesis that there is no difference in exercise status between the study groups.

NON VEGETARIAN DIET





Non Vegetarian Diet	NLR < 2	%	NLR > 2	%	Combined	%
Yes	27	65.85	42	71.19	69	69.00
No	14	34.15	17	28.81	31	31.00
Total	41	100	59	100	100	100
P value Chi Squared Test			0.5706			

Among the study patients, there was no statistically significant difference in relation to non vegetarian diet status between NLR < 2 group (majority eat NV diet – 65.85%) and NLR > 2 group (majority eat NV diet – 71.19%) with a p value of <0.05 as per chi squared test. Therefore we fail to reject the null hypothesis that there is no difference in non vegetarian diet status between the study groups.

CONCLUSION

The following were the conclusion of this study

- The association between the study groups and age distribution is considered to be not statistically significant.

- The association between the study groups and gender distribution is considered to be not statistically significant

- In this study we can safely conclude that significant increase in BMI is associated with increase in NLR ratio in our study subjects especially in the overweight and obese category. In other words overweight and obesity was 1.10 times more in patients with NLR > 2 compared to those with NLR < 2.

- In this study we can safely conclude that significant increase in Fasting blood sugar is associated with increase in NLR ratio in our study subjects especially in > 150 mg/dl category. In other words high fasting blood sugar was 1.17 times more in patients with NLR > 2 compared to those with NLR < 2.

- In this study we can safely conclude that significant increase in post prandial blood sugar is associated with increase in NLR ratio in our study subjects especially in > 250 mg/dl category. In other words high post prandial blood sugar was 1.17 times more in patients with NLR > 2 compared to those with NLR < 2.

- In this study we can safely conclude that significant increase Glycosylated hemoglobin is associated with increase in NLR ratio in our study subjects especially in > 9% category. In other words high Glycosylated hemoglobin was 1.25 times more in patients with NLR > 2 compared to those with NLR < 2.

- In this study we can safely conclude that significant increase duration of diabetes is associated with increase in NLR ratio in our study subjects especially in > 10 years category. In other words duration of diabetes was 1.32 times more in patients with NLR > 2 compared to those with NLR < 2.

- The association between the study groups and hypertension is considered to be not statistically significant.

- In this study we can safely conclude that significant increase abdominal circumference is associated with increase in NLR ratio in our study subjects.

- In other words abnormal abdominal circumference was 1.70 times more in patients with NLR > 2 compared to those with NLR < 2.

- There is no statistical significant between study groups and TGL and HDL levels

- Exercising status is found to have a negative correlation with NLR .

- There is no difference in non vegetarian diet status between the study groups.

SUMMARY

This study undertaken to establish Neutrophil Lymphocyte Ratio which can be easily calculated from a simple peripheral blood count and therefore, is much simpler and cheaper than measuring more sophisticated inflammatory cytokines in patients with diabetes.

Thus there is positive correlation of NLR with blood glucose , HBA_{1c} duration of diabetes , BMI and abnormal abdominal diameter proved. Increase Glycosylated haemoglobin is associated with increase in NLR ratio in our study subjects especially in > 9% category.

So with simple Neutrophil Lymphocyte Ratio test, if steps to reduce inflammation are taken early in people with diabetes the morbidity and mortality can be reduced.

BIBLIOGRAPHY

1. Harrisons principles of internal medicine 19th edition, chapter 422, The metabolic syndrome, Pages (2450 – 2454).

2. Seshiah ‘s - Handbook on Diabetes Mellitus - reprint 6 th edition

3. International textbook of diabetes mellitus Wiley Blackwell 4th edition .

4. http://www.apiindia.org/medicine_update_2013/chap40.pdf

5. American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care 2013; 36(suppl 1): S67–S74

6. Relationship Between Neutrophil-Lymphocyte Ratio and Microvascular Complications in Egyptian Patients with Type 2 Diabetes Eman Youssef Moursy1, Magdy Helmy Megallaa1, Reham Fadl Mouftah2, Soha Magdy Ahmed3

7. Investigation of neutrophil lymphocyte ratio and blood glucose regulation in patients with type 2 diabetes mellitusFatih Sefil1, Kemal Turker Ulutas2, Recep Dokuyucu1, Ahmet Taner Sumbul3, Erhan Yengil,

8. Centers for Disease Control and Prevention (CDC). (2003) Prevalence of diabetes and impaired fasting glucose in adults – United States, 1999–2000. *MMWR Morbidity and Mortality Weekly Report*, 52, 833–837.

9. Neutrophil-to-lymphocyte ratio in diabetes mellitus patients with and without diabetic foot ulcer Cüneyt Kahraman1, Gündüz Yümün2, Nilüfer Kuzeyli Kahraman1, Nazli Dizen Namdar3, Süleyman Cosgun1

10. Evaluation of neutrophil to lymphocyte ratio as an indicator of presence of coronary artery disease in diabetic patients safak sahin1, savas sarikaya2, lutfi akyol3, fatih altunkas4, Kayihan Karaman4

11. Wild, S., Roglic, G., Green, A. *et al.* (2004) Global prevalence of diabetes. *Diabetes Care*, 27, 1047–1053.

12. The Diabetes Control and Complications Trial Research Group: The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. N Engl J Me 1993:329:977-986.

13. Lewis MR and Tracy RP. The role of the immune system in the insulin resistance syndrome. Curr Diab Rep 2002; 2: 96–99. 2. Gu¨ ndogan K, Bayram F, Capak M, et al.

14. Association of peripheral total and differential leukocyte counts with metabolic syndrome and risk of ischemic cardiovascular diseases in patients with type 2 diabetes mellitus. Diabetes Metab Res Rev 2007; 23: 111–118. 5. de Rooij SR, Nijpels G, Nilsson PM, et al.

15. Low-grade chronic inflammation in the relationship between insulin sensitivity and cardiovascular disease (RISC) population: associations with insulin resistance and cardiometabolic risk profile. Diabetes Care 2009; 32: 1295–1301. 6. Ferna´ ndez-Real JM and Ricart W.

16. Insulin resistance and chronic cardiovascular inflammatory syndrome. Endocr Rev 2003; 24: 278–301. 7. Coller BS.

17. White blood cell count is associated with macroand microvascular complications in Chinese patients with type 2 diabetes. Diabetes Care 2004; 27: 216–222. 10. Imtiaz F, Shafique K, Mirza SS, et al.

18. Lymphocyte ratio as a measure of systemic inflammation in prevalent chronic diseases in Asian population. Int Arch Med 2012; 5: 2.11. Buyukkaya E, Karakas MF, Karakas E, et al

19. Correlation of neutrophil to lymphocyte ratio with the presence and severity of metabolic syndrome. Clin Appl Thromb Hemost 2014; 20: 159–163. 12. Alberti KG and Zimmet PZ.

20. Elevated white blood cell count in subjects with impaired glucose tolerance. Diabetes Care 2004; 27: 491–496. 4. Tsai JC, Sheu SH, Chiu HC, et al.

21. Prevalence of metabolic syndrome in the Mediterranean region of Turkey: evaluation of hypertension, diabetes mellitus, obesity, and dyslipidemia. Metab Syndr Relat Disord 2009; 7: 427–434. 3. Ohshita K, Yamane K, Hanafusa M, et al.

22. Vozarova B, Weyer C, Lindsay RS, et al. High white blood cell count is associated with a worsening of insulin sensitivity and predicts the development of type 2 diabetes. Diabetes 2002; 51: 455–461.

23. Andersson C, van Gaal L, Caterson ID, et al. Relationship between HbA1c levels and risk of cardiovascular adverse outcomes and allcause mortality in overweight and obese cardiovascular high-risk women and men with type 2 diabetes. Diabetologia 2012; 55: 2348–2355.

24. Yousefzadeh P and Wang X. The effects of dipeptidyl peptidase-4 inhibitors on cardiovascular disease risks in type 2 diabetes mellitus. J Diabetes Res 2013; 2013: 459–821.

25. Stulc T, Ceska R, Marinov I, et al. The effect of simvastatin and fenofibrate on the expression of leukocyte adhesion molecules and lipopolysaccharide receptor CD14 in type 2 diabetes mellitus. Neuro Endocrinol Lett 2012; 33(suppl 2): 73–77. .

26. Eckel RH, Wassef M, Chait A, et al. Prevention Conference VI: Diabetes and Cardiovascular Disease: Writing Group II: pathogenesis of atherosclerosis in diabetes. Circulation 2002; 105: e138–e143.

27. Saito Y, Takahashi I, Iwane K, et al. The influence of blood glucose on neutrophil function in individuals without diabetes. Luminescence 2013; 28: 569–573.

28. Danaei G, Lawes CM, Vander Hoorn S, et al. Global and regional mortality from ischaemic heart disease and stroke attributable to higher-than-optimum blood glucose concentration: comparative risk assessment. Lancet 2006; 368: 1651–1659.

29. Duffy BK, Gurm HS, Rajagopal V, et al. Usefulness of an elevated neutrophil to lymphocyte ratio in predicting long-term mortality after percutaneous coronary intervention. Am J Cardiol 2006; 97: 993–996.

30. Sen N, Afsar B, Ozcan F, et al. The neutrophil to lymphocyte ratio was associated with impaired myocardial perfusion and long term adverse outcome in patients with STelevated myocardial infarction undergoing primary coronary intervention. Atherosclerosis 2013; 228: 203–210. .

31. Khodabandehlou T, Zhao H, Vimeux M, et al. Haemorheological consequences of hyperglycaemic spike in healthy volunteers and insulin-dependent diabetics. Clin Hemorheol Microcirc 1998; 19: 105–114.

32. Suzuki T, Futami-Suda S, Igari Y, et al. Low-molecular-weight lipoprotein (a) and low relative lymphocyte concentration are significant and independent risk factors for coronary heart disease in patients with type 2 diabetes mellitus: Lp(a) phenotype, lymphocyte, and coronary heart disease. Lipids Health Dis 2013; 12: 31.

33. Chang FY and Shaio MF. Decreased cellmediated immunity in patients with noninsulin-dependent diabetes mellitus. Diabetes Res Clin Pract 1995; 28: 137–146.

34. Azab B, Zaher M, Weiserbs KF, et al. Usefulness of neutrophil to lymphocyte ratio in predicting short- and long-term mortality after non-ST-elevation myocardial infarction. Am J Cardiol 2010; 106: 470–476.

35. Papa A, Emdin M, Passino C, et al. Predictive value of elevated neutrophil- lymphocyte ratio on cardiac mortality in patients with stable coronary artery disease. Clin Chim Acta 2008; 395: 27–31.

36. Xu Y, Zhao Z, Li X, et al. Relationships between C-reactive protein, white blood cell count, and insulin resistance in a Chinese population. Endocrine 2011; 39: 175–181. 29. Rodrı´guez-Mora´ n M and Guerrero-Romero F. Increased levels of C-reactive protein in noncontrolled type II diabetic subjects. J Diabetes Complicat 1999; 13: 211–215.

37. Veronelli A, Laneri M, Ranieri R, et al. White blood cells in obesity and diabetes: effects of weight loss and normalization of glucose metabolism. Diabetes Care 2004; 27: 2501–2502.

38. http://www.thebiomedicapk.com/articles/274.pdf

39. National Health and Nutrition Examination Survey (NHANES III). *Journal of Clinical Endocrinology andMetabolism*, 87, 489–499.

40. Barker, J.M., Yu, J., Yu, L. *et al.* (2003) Autoantibody "subspecificity" in type 1 diabetes. *Diabetes Care*, 28, 850–855.

41. Kordonouri, O., Maguire, A.M., Knip, M. *et al.* (2009) Other complications and associated conditions with diabetes in children and adolescents. *Pediatric Diabetes*, 10, 204–210.

42. Asfar B. The relationship between neutrophil lymphocyte ratio with urinary protein and albumin excretion in newly diagnosed patients with Type 2 Diabetes. Am J Med Sci 2013; 347(3): 217-20.

43. Prognostic role of neutrophil-to-lymphocyte ratio in solid tumors: a systematic review and meta-analysis Templeton AJ[1], McNamara MG[1], Šeruga B[1], Vera-Badillo FE[1], Aneja P[1], Ocaña A[1], Leibowitz-Amit R[1], Sonpavde G[1], Knox JJ[1],

44. Neutrophil to lymphocyte ratio (NLR) for prediction of distant metastasis-free survival (DMFS) in early breast cancer: a propensity score-matched analysis

45. Shimada H, Takiguchi N, Kainuma O, et alHigh preoperative neutrophil–lymphocyte ratio predicts poor survival in patients with gastric cancer. *Gastric Cancer* 2010*;*13*:*170–6. doi:10.1007/s10120-010-0554-3

46. Ross R. Atherosclerosis an inflammatory disease. N Engl J Med 1999; 340: 115-26.

47. Narayan KM, Gregg EW, Fagot-Campagna A, Engelau MM, Vinicor F. Diabetes: a common, growing, serious, costly and potentially preventable public health problem. Diabetes Res Clin Pract 2000; 50: S77-84.

48. Fujita T, Hemmi S, Kajiwara M, Yabuki M, Fuke Y, Satomura A, et al. Complement-mediated chronic inflammation is associated with diabetic microvasvular complication. Diabetes Metab Res Rev 2013; 29: 220-6.

49. Nguyen D, Shaw L, Grant M. Inflammation in the pathogenesis of microvascular complications in diabetes. Front Endocrinol 2012; 3: 170.

50. Rajala MW, Scherer PE. Mini review: the adipocyte–at the crossroads of energy homeostasis, inflammation, and atherosclerosis. Endocrinology 2003, 144(9): 3765

51. Bhutta H, Agha R, Wong J, Tang TY, Wilson YG, Walsh SR. Neutrophil lymphocyte ratio predicts medium-term survival following elective major vascular surgery: a cross sectional study. Vasc Endovascular Surg 2011; 45: 227–31.

52. Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. Homeostasis model assessment: Insulin resistance and beta cell function from fasting plasma glucose and insulin concentrations in man. Diabetologia 1985; 28: 412-19.

53. Gibson PH, Croal BL, Cuthbertson BH, Small GR, Ifezulike AI, Gibson G, et al. Preoperative neutrophil-lymphocyte ratio and outcome from coronary artery bypass grafting. Am Heart J 2007; 154: 995-1002.

PROFORMA

NAME:

AGE: 1. 30-40yrs 2. 40-60yrs 3. >60yrs **SEX:** 1.M 2.F

LOCALITY: **CONTACT NO:**

COMPLAINTS :

PAST H/O

DIABETES:	1. Yes	2. No If yes specify_____
HYPERTENSION	1. Yes	2. No If yes specify_____
RENAL FAILURE	1. Yes	2. No If yes specify_____
AUTOIMMUNE DISORDER	1. Yes	2. No If yes specify_____
CARDIAC ILLNESS	1. Yes	2. No If yes specify_____
STROKE	1. Yes	2. No If yes specify_____
CONNECTIVE TISSUES DISORDER	1. Yes	2. No If yes specify_____
INFLAMMATORY BOWEL DISEASE	1. Yes	2. No If yes specify_____
OSTEOARTHRITIES	1. Yes	2. No If yes specify_____
RHEUMATOID ARTHRITIS	1. Yes	2. No If yes specify_____
GOUT	1. Yes	2. No If yes specify_____
BRONCHIAL ASTHMA	1. Yes	2. No If yes specify_____

OTHERS _____

H/O CHRONIC DRUG INTAKE:

H/O OF ANY RECENT FEVER : 1. YES 2 .NO

PERSONAL H/O

FOOD : 1.veg 2.Non veg

SMOKING : 1. Yes 2. No

ALCOHOL INTAKE: 1. Yes 2. No

EXERCISE OF ATLEAST 30 MINS FOR 5 DAYS A WEEK: 1. Yes 2. No

VITALS-

BP: PR: RR:
TEMPERATURE-

BMI: ABD DIAMETER:

SYSTEMIC EXAMINATION-

CVS: RS: PA:

CNS:

INVESTIGATIONS

CBC : **NEUTROPHIL LYMPHOCYTE RATIO**

RFT :

FBS :

PPBS:

HBA1C:

LIPID PROFILE :

HDL-

TRIGLYCERIDES-

ECG FINDINGS-

COMMENT:

GOVT.STANLEY MEDICAL COLLEGE, CHENNAI- 600 001

INFORMED CONSENT

DISSERTATION TOPIC: "NEUTROPHIL LYMPHOCYTE RATIO AND BLOOD GLUCOSE REGULATION IN TYPE 2 DIABETES "

PLACE OF STUDY: GOVT. STANLEY MEDICAL COLLEGE, CHENNAI

NAME AND ADDRESS OF PATIENT:

I, _____ have been informed about the details of the study in my own language.

I have completely understood the details of the study.

I am aware of the possible risks and benefits, while taking part in the study.

I understand that I can withdraw from the study at any point of time and even then, I will continue to receive the medical treatment as usual.

I understand that I will not get any payment for taking part in this study.

I will not object if the results of this study are getting published in any medical journal, provided my personal identity is not revealed.

I know what I am supposed to do by taking part in this study and I assure that I would extend my full co-operation for this study.

Name and Address of the Volunteer:

Signature/Thumb impression of the Volunteer

Date:

Witnesses:
(Signature, Name & Address)

Date:
Name and signature of investigator:

GOVT.STANLEY MEDICAL COLLEGE, CHENNAI- 600 001

INFORMED CONSENT

DISSERTATION TOPIC: "NEUTROPHIL LYMPHOCYTE RATIO AND BLOOD GLUCOSE REGULATION IN TYPE 2 DIABETES "

நான்இந்தஆராய்ச்சியில்விவரங்களைமுற்றிலும்புரிந்துகொண்டேன்.
ஆய்வில்பங்குஎடுத்துபோது,
சாத்தியமானஅபாயங்கள்மற்றும்பயன்களைபற்றிநான்அறிந்துள்ளேன்.

நான்எந்தவொருவேளையிலும்ஆய்வில்இருந்துதிரும்பமுடியும், அதன்பின்னர், நான்வழக்கம்போல்மருத்துவசிகிச்சைபெறமுடியும்என்றுபுரிந்துகொள்கிறேன்.

நான்ஆய்வில்பங்குஎடுத்துபணம்எதையும்பெறமுடியாதுஎன்றுஅறிந்துள்ளேன். இந்தஆய்வின்முடிவுகள்எந்தமெடிக்கல்ஜர்னலில்வெளியிடப்படஇருந்தால்நான்எதிர்க்கவில்லை, என்தனிப்பட்டஅடையாளத்தைவெளிப்படுத்தப்பட்டுஇருக்ககூடாது.

நான்இந்தஆய்வில்பங்கெடுப்பதன்மூலம்நான்என்னசெய்யபோகிறேன்என்று தெரியும்.
நான்இந்தஆய்வில்என்முழுஒத்துழைப்பையும்கொடுப்பேன்என்றுஉறுதியளிக்கிறேன்.

தன்னார்வளர்
பெயர்மற்றும்முகவரி
கையொப்பம் /விரல்ரேகை:

சாட்சி
பெயர்மற்றும்முகவரி
கையொப்பம் / விரல்ரேகை:

ஆராய்ச்சியாளராக
கையொப்பம்மற்றும்தேதி

ETHICAL COMMITTEE APPROVAL

INSTITUTIONAL ETHICAL COMMITTEE,
STANLEY MEDICAL COLLEGE, CHENNAI-1

Title of the Work : Neutrophil lymphocyte ratio and Blood Glucose regulation in type 2 Diabetes.

Principal Investigator : Dr. A Ramya Devi

Designation : PG, MD (General Medicine)

Department : Department of General Medicine
Government Stanley Medical College,
Chennai-01

The request for an approval from the Institutional Ethical Committee (IEC) was considered on the IEC meeting held on 24.03.2016 at the Council Hall, Stanley Medical College, Chennai-1 at 2PM

The members of the Committee, the secretary and the Chairman are pleased to approve the proposed work mentioned above, submitted by the principal investigator.

The Principal investigator and their team are directed to adhere to the guidelines given below:

1. You should inform the IEC in case of changes in study procedure, site investigator investigation or guide or any other changes.
2. You should not deviate from the area of the work for which you applied for ethical clearance.
3. You should inform the IEC immediately, in case of any adverse events or serious adverse reaction.
4. You should abide to the rules and regulation of the institution(s).
5. You should complete the work within the specified period and if any extension of time is required, you should apply for permission again and do the work.
6. You should submit the summary of the work to the ethical committee on completion of the work.

MEMBER SECRETARY,
IEC, SMC, CHENNAI

MASTER CHART

SL NO	AGE	SEX	BMI	DIABETIC				HYPERTENSION	AB DIAME	TGL	HDL	EXERICSE	NV	NLR>2
				FBS	PPBS	HBAIC	DURATION	Y OR N	Y OR N	Y OR N	Y OR N	Y OR N	Y OR N	Y OR N
1	56	F	31.8	152	204	8.4	4	N	Y- 100	Y-274	Y-47	N	Y	**Y**
2	69	M	25.7	164	184	7.2	8	Y	N	Y-170	N	N	Y	**Y**
3	35	M	29.2	114	124	6.1	2	N	Y-98	Y-160	Y-35	Y	Y	**N**
4	48	F	27.4	245	299	10.7	8	Y	Y-90	Y-210	Y-44	N	Y	**Y**
5	41	M	32.4	120	147	7.6	10	Y	Y-96	Y-196	N	Y	N	**N**
6	37	F	26.9	149	198	8.9	1	N	Y-88	Y-240	Y-31	N	Y	**Y**
7	55	M	29.4	184	201	9.8	11	Y	Y-94	N	Y-34	N	Y	**Y**
8	69	F	38.4	199	304	14.5	15	N	Y-109	Y-284	Y-29	Y	Y	**Y**
9	45	F	22.4	154	199	8.6	12	Y	N	Y-274	N	Y	Y	**N**
10	52	F	34.7	120	138	7.8	8	N	Y-114	Y-198	Y-31	N	Y	**Y**
11	45	F	29.4	124	134	7.2	6	Y	Y-95	Y-274	Y-28	Y	Y	**Y**
12	52	M	28.4	110	134	6	4	Y	Y-99	Y-221	N	Y	Y	**N**
13	39	F	34.7	85	110	5.8	7	N	Y-119	Y-246	Y- 39	N	Y	**Y**
14	35	M	28.4	178	201	8.4	2	Y	Y-99	Y-274	N	Y	N	**N**
15	45	M	22.7	112	144	6.5	6	Y	N	Y-245	N	Y	Y	**N**
16	56	M	31	154	199	8.7	7	N	Y-101	Y-214	Y-34	N	Y	**Y**
17	68	F	28.7	199	245	11.2	12	Y	Y-93	Y- 188	Y-44	N	Y	**Y**
18	32	M	24.45	114	178	8.8	1	Y	N	Y-172	Y-36	Y	Y	**N**
19	45	M	21.6	152	184	9.4	3	Y	N	Y-184	N	Y	N	**Y**
20	54	M	19.32	99	124	5.1	9	Y	N	Y-199	Y-35	N	Y	**N**
21	46	F	28.47	147	320	17.4	5	Y	Y-98	Y-245	N	N	Y	**Y**

SL NO	AGE	SEX	BMI	DIABETIC				HYPERTENSION	AB DIAME	TGL	HDL	EXERICSE	NV	NLR>2
				FBS	PPBS	HBAIC	DURATION	Y OR N	Y OR N	Y OR N	Y OR N	Y OR N	Y OR N	Y OR N
22	56	M	27.45	158	198	8.4	2	Y	Y-94	Y-178	Y-44	N	Y	**Y**
23	38	F	33.4	132	148	6.4	3	N	Y=119	Y-298	N	N	Y	**Y**
24	44	F	38.4	123	164	7.3	8	N	Y-110	Y-210	Y-39	N	Y	**Y**
25	54	F	27.1	245	336	13.9	11	Y	Y-99	Y-343	Y-44	N	Y	**Y**
26	65	F	28.4	147	204	12.4	17	Y	Y=96	N	N	N	Y	**Y**
27	62	F	32.6	124	178	9.4	5	Y	Y-110	N	N	N	Y	**N**
28	47	M	29.4	164	245	12.4	7	Y	Y-94	Y-202	N	Y	Y	**Y**
29	65	F	33.1	110	138	7.5	12	Y	Y-101	Y-189	N	N	Y	**Y**
30	40	M	21.7	145	187	8.5	4	Y	N	Y-175	Y-35	N	N	**N**
31	58	F	28.6	135	154	7.1	18	Y	Y-91	Y=170	N	N	Y	**Y**
32	51	M	20.4	125	138	7.3	5	Y	N	Y-198	N	N	Y	**N**
33	60	F	33.4	110	136	6.4	4	Y	Y-101	N	N	N	Y	**Y**
34	63	F	21.4	94	125	5.9	9	Y	N	N	Y-39	N	Y	**N**
35	54	M	27.9	212	384	14.8	5	Y	Y-94	172	Y-35	Y	Y	**Y**
36	65	F	25.3	100	202	12	8	Y	N	Y-200	N	N	Y	**N**
37	61	M	37.4	99	121	7.1	12	Y	Y-110	Y-241	N	Y	Y	**Y**
38	48	M	33.8	144	198	12.4	7	Y	Y-98	N	Y-35	Y	Y	**Y**
39	54	F	28.4	154	178	8.6	5	N	Y-90	Y-219	Y-39	N	Y	**Y**
40	36	F	24.6	167	254	12.8	3	N	Y-95	Y-250	Y-35	N	Y	**Y**
41	54	M	24.9	189	269	13.9	8	Y	N	Y-244	Y-27	Y	Y	**N**
42	45	F	29.1	178	289	16.8	8	Y	Y-91	Y-186	Y-37	N	N	**Y**
43	56	M	24.6	110	154	8.4	11	Y	N	Y-187	N	Y	Y	**Y**
44	49	F	33.3	212	298	13.6	6	Y	Y-101	Y-198	Y-34	N	Y	**Y**
45	67	F	22.8	147	245	12.1	12	Y	N	Y-166	N	N	Y	**Y**
46	27	F	31.4	145	210	11.6	1	N	Y-118	Y-177	Y-39	N	Y	**N**

SL NO	AGE	SEX	BMI	DIABETIC				HYPERTENSION	AB DIAME	TGL	HDL	EXERICSE	NV	NLR>2
				FBS	PPBS	HBAIC	DURATION	Y OR N	Y OR N	Y OR N	Y OR N	Y OR N	Y OR N	Y OR N
47	35	M	25.5	158	249	9.4	4	Y	N	Y-167	Y-32	N	Y	**Y**
48	45	F	26.8	145	239	8.9	7	Y	N	Y-189	Y-36	N	Y	**N**
49	57	F	29.1	141	297	14.2	11	Y	Y-95	Y-168	N	N	Y	**Y**
50	48	F	36.5	178	299	15.4	7	N	Y-104	Y-298	Y-35	Y	Y	**Y**
51	55	M	21.5	114	138	6.3	8	N	N	N	N	Y	Y	**N**
52	31	F	28.4	145	214	7.1	4	N	Y-89	N	N	N	Y	**N**
53	36	M	29.4	110	176	8.1	7	Y	N	Y-214	N	N	N	**Y**
54	47	M	27.4	141	204	7.2	8	Y	Y-99	N	Y-34	Y	Y	**N**
55	62	F	22.8	124	210	7.6	5	N	Y-101	Y-188	N	N	N	**N**
56	58	F	24.5	154	187	8.4	6	Y	Y-98	Y-140	Y-27	Y	Y	**Y**
57	49	M	28.4	140	224	7.9	9	Y	N	N	N	Y	Y	**N**
58	65	F	27.5	154	198	8.4	8	N	Y-98	Y-198	Y-37	N	N	**Y**
59	54	M	28.4	145	202	7.9	8	Y	N	N	N	Y	Y	**N**
60	58	M	28.7	178	242	8.4	11	N	Y-104	Y-178	Y-34	Y	N	**Y**
61	69	F	23.4	164	187	7.4	13	N	N	Y-169	N	N	N	**Y**
62	54	M	22.4	144	188	6.6	7	Y	N	N	Y-29	Y	Y	**N**
63	47	M	25.8	148	204	6.9	8	N	Y-91	N	N	Y	Y	**Y**
64	35	F	22.4	110	138	5.8	3	Y	N	Y-161	N	Y	N	**N**
65	67	M	26.3	148	202	7.9	8	Y	N	Y-198	Y-32	Y	N	**N**
66	58	F	24.4	198	304	9.6	7	Y	Y-110	N	N	Y	N	**Y**
67	32	F	22.4	110	178	7.2	1	N	Y-96	Y-187	Y-36	N	Y	**N**
68	49	M	29.4	168	254	8.6	8	N	N	Y-178	N	Y	N	**N**
69	51	M	34.5	204	398	15.9	14	N	Y-108	N	N	Y	N	**Y**
70	63	F	24.6	158	245	7.9	7	Y	N	Y-178	Y	Y	N	**N**
71	55	F	33.4	145	189	8.4	11	N	Y-99	Y-165	N	N	N	**Y**

SL NO	AGE	SEX	BMI	DIABETIC				HYPERTENSION	AB DIAME	TGL	HDL	EXERICSE	NV	NLR>2
				FBS	PPBS	HBAIC	DURATION	Y OR N	Y OR N	Y OR N	Y OR N	Y OR N	Y OR N	Y OR N
72	47	F	27.1	157	245	7.9	9	N	Y-104	N	Y-38	Y	Y	**Y**
73	36	M	31.2	142	289	7.6	6	Y	Y-115	N	N	Y	Y	**Y**
74	58	F	24.6	164	221	8.3	8	Y	N	Y-158	Y-34	N	Y	**N**
75	67	F	27.5	155	259	7.9	11	N	N	N	N	N	Y	**N**
76	55	M	33.6	198	224	8.1	8	Y	Y-108	Y-187	Y-32	Y	N	**N**
77	59	M	29.7	185	287	9.6	9	N	N	Y-184	Y-35	Y	N	**Y**
78	68	F	34.8	224	324	11.8	10	N	Y-98	N	N	Y	N	**Y**
79	35	F	26.5	140	199	8.5	2	Y	N	Y-202	N	Y	N	**Y**
80	60	M	28.4	164	254	7.8	9	Y	N	Y-187	Y-32	N	N	**N**
81	34	F	24.8	98	124	5.6	3	N	N	N	N	Y	N	**N**
82	59	M	28.7	165	212	8.4	11	N	Y-94	Y-224	Y-39	Y	N	**Y**
83	69	M	25.9	135	189	7.2	12	N	N	N	N	Y	N	**Y**
84	48	F	22.7	95	129	5.9	5	Y	N	Y-187	N	Y	N	**N**
85	44	F	27.9	110	138	6.2	7	Y	Y-87	N	Y-37	Y	N	**Y**
86	69	M	28.5	165	250	8.6	7	Y	Y-116	Y-190	Y-30	N	Y	**Y**
87	59	M	29	145	226	7.5	5	N	Y-100	N	N	Y	Y	**N**
88	51	F	32	90	170	6.5	2	N	Y-110	Y-200	Y-35	N	Y	**N**
89	47	F	25	127	256	8	3	Y	N	Y-160	Y-45	Y	Y	**y**
90	67	M	19.45	187	310	9	6	N	N	Y-163	N	N	Y	**Y**
91	58	F	22.6	151	214	6.5	8	Y	N	N	Y-25	N	N	**y**
92	53	M	28	100	269	7	4	Y	Y-100	Y-182	y -30	Y	Y	**N**
93	49	M	26.8	130	279	10	7	N	N	N	y-35	N	Y	**y**
94	50	F	29.5	156	231	8	3	N	Y-96	Y-177	N	N	N	**N**
95	68	M	31	180	267	7	8	Y	Y -128	Y-210	Y-36	Y	N	**Y**
96	46	M	29	152	248	6	4	y	y-100	y-198	N	N	N	**N**

SL NO	AGE	SEX	BMI	DIABETIC				HYPERTENSION	AB DIAME	TGL	HDL	EXERICSE	NV	NLR>2
				FBS	PPBS	HBAIC	DURATION	Y OR N	Y OR N	Y OR N	Y OR N	Y OR N	Y OR N	Y OR N
97	59	F	27.5	139	230	6	7	N	Y-116	Y-221	Y-30	N	Y	**N**
98	65	M	30	120	200	5	5	Y	Y-96	Y-180	Y-28	Y	Y	**Y**
99	46	F	23	116	219	9	8	Y	Y-88	N	Y-30	Y	Y	**N**
100	55	F	28.5	171	335	12	5	N	N	Y-221	N	N	Y	**Y**

KEY TO MASTER CHART

M	MALE
F	FEMALE
Y	YES
N	NO
BMI	BODY MASS INDEX
FBS	FASTING BLOOD SUGAR
PPBS	POSTPRANDIAL BLOOD SUGAR
HBA1C	GLYCOSYLATED HEMOGLOBIN
NV	NONVEG
AB DIAMETER	ABDOMNIAL DIAMETER
TGL	TRIGLYCERIDES
HDL	HIGH DENSITY LIPOPROTEIN
NLR	NEUTROPHIL LYMPHOCYTE RATIO