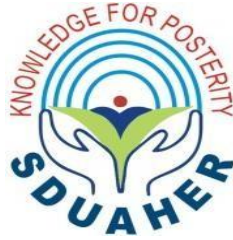


**“A PROSPECTIVE COHORT STUDY OF FATTY LIVER INDEX AND TRIGLYCERIDE GLYCEMIC INDEX AS A MARKERS FOR IDENTIFYING NON ALCOHOLIC FATTY LIVER DISEASE IN TYPE 2 DIABETES PATIENTS”**

**BY**

**DR . SRI MADHURIMA PUTTAGUNTA**



**DISSERTATION SUBMITTED TO  
SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION &  
RESEARCH , TAMAKA, KOLAR, KARNATAKA**

**IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF**

**DOCTOR OF MEDICINE (M.D.)**

**IN**

**GENERAL MEDICINE**

**Under the Guidance of:**

**Dr RAVEESHA A**

**PROFESSOR**

**DEPT OF GENERAL MEDICINE**

**Under the Co-Guidance of:**

**Dr. ANIL KUMAR SAKALECHA,**

**PROFESSOR & HOD,**

**DEPT. OF RADIODIAGNOSIS**



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DATE:  
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SIGNATURE OF THE CANDIDATE  
**Dr SRI MADHURIMA PUTTAGUNTA**  
Postgraduate  
Department of General Medicine  
Sri Devaraj Urs Medical College &  
Research Center, Tamaka, Kolar

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**DR. VIDYASAGAR CR**

Professor & HOD

Department of General Medicine,  
Sri Devaraj Urs Medical College,  
Tamaka, Kolar.

Date:

Place: Kolar

**DR. PRABHAKAR K**

Principal,

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Tamaka, Kolar.

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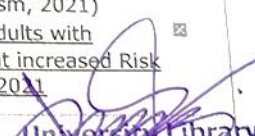
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## **ABBREVIATIONS**

<b>Glossary</b>	<b>Abbreviations</b>
NAFLD	Non alcoholic fatty liver disease
FLI	Fatty liver index
TGY	Triglyceride glyceic index
T2DM	Type 2 diabetes mellitus
IR	Insulin resistance
NASH	Non alcoholic steatohepatitis
DDP-IV	Dipeptidyl Petidase IV Inhibitors
GLP-1	Glucagon like Peptide – 1

## ABSTRACT

Non-alcoholic fatty liver disease (NAFLD) is a prevalent chronic liver disease globally which is related to type 2 diabetes mellitus (T2DM). Early detection of NAFLD among patients having T2DM, early detection of NAFLD, can avoid development to fibrosis, steatohepatitis and cirrhosis. Non-invasive markers like Fatty Liver Index (FLI) as well as Triglyceride Glycemic (TyG) Index have been developed for easy and affordable detection of disease.

### **Objectives:**

"The objective of the above study was to evaluate the performance of FLI and TyG Index for identifying NAFLD in patients with T2DM, determine their diagnostic ability, and test their correlation with elastography results."

### **Methods:**

85 adult T2DM patients visiting the General Medicine Department in R.L. Jalappa Hospital were recruited. Anthropometric and biochemical parameters were recorded and calculated using standard formulas for both FLI and TyG indices. NAFLD was diagnosed through shear wave elastography. The statistical calculations was carried out by SPSS 22.

### **Results:**

Mean value of FLI and TyG index was higher in NAFLD in comparison to non-NAFLD case. Area under ROC curve for FLI and TyG index was 0.538 and 0.554, respectively.

### **Conclusion:**

Findings emphasize feasibility of using FLI and TyG index as initial screening tools in settings where access to imaging modalities is limited. The study did not find statistically significant superiority of either FLI or TyG index in identifying NAFLD among T2DM patients, both indices demonstrated modest diagnostic potential.

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# INTRODUCTION



---

## **INTRODUCTION**

One of the chronic metabolic diseases is T2DM, combination of insulin resistance (IR) and insulin deficiency<sup>1</sup>. NAFLD is characterized by "ectopic fat accumulation" in liver following which, low-grade chronic inflammation develops in the liver<sup>2</sup>. NAFLD is prevalent chronic liver disease which raises risk of atherosclerosis and cardiovascular disease (CVD) along with liver failure. Metabolic syndrome (MS), IR, as well as T2DM are few risk factors linked to NAFLD<sup>3</sup>. For determining NAFLD risk, TyG index is reliable in assessing IR and better marker than FBG, AST/ALT ratio, along with other lipid parameters<sup>4</sup>.

A disorder known as "fatty liver" occurs when the liver's cells build up abnormally high levels of fat. Even though increased alcohol use is common cause of fatty liver (alcoholic fatty liver), alcohol isn't a contributing factor in NAFLD<sup>5</sup>.

About 300 million individuals in China alone suffer from liver illnesses. Triglyceride absorption in hepatocytes that causes the liver weight to rise above 5% is known as NAFLD<sup>6,7</sup>.

NAFLD is categorized as either steatohepatitis (NASH) or fatty liver (also referred to as isolated fatty liver or IFL). Both NASH and IFL have abnormally high levels of fat in liver cells, but NASH also has inflammation in liver, which damages, kills, and replaces the liver cells with scar tissue.

Thus, it's essential to identify people at risk for NAFLD as soon as possible in a straightforward and efficient way. The pathophysiology of NAFLD is yet unknown, though. The most common pathogenesis for NAFLD is that insulin resistance (IR) and an important contributing factor<sup>8</sup>.

In long standing T2DM patients, NAFLD can be one of the complications and early diagnosis along with intervention can prevent development of liver injury in T2DM patients<sup>9</sup>.

Ultrasound is used for detecting NAFLD<sup>10</sup>, but it's not available in many rural areas and not accessible to all groups of people.

NAFLD is frequently diagnosed by imaging methods such hepatic ultrasonography, magnetic resonance imaging (MRI), and abdominal CT. Because of its ease of use and noninvasiveness, hepatic ultrasonography is most widely utilized procedure in medical practice. Abdominal Ultrasound can identify moderate-to-severe hepatic steatosis having high degree of diagnostic accuracy. CT is inappropriate imaging modality for diagnosis of NAFLD due to its limited ability to identify mild degrees of hepatic steatosis along with possibility of radiation exposure<sup>11</sup>.

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Practitioners have included variety of blood biomarkers along with non-invasive algorithms into clinical practice to aid in disease's diagnosis. In addition to SteatoTest and "NAFLD-liver fat score (NAFLD-LFS)", 2 non-invasive scores have produced good findings, which have been confirmed by "proton magnetic resonance spectroscopy (1H-MRS)" for NAFLDLFS and ultrasound for FLI, hepatic steatosis index (HIS), as well as SteatoTest <sup>12</sup>.

FLI and TyG index are simple indices which can be calculated by using values from routine blood tests and they can be as reliable as ultrasound in identifying NAFLD. FLI is employed for identifying and screening fatty liver disease among patients having T2DM. It is estimated on basis of biochemical as well as anthropometric measurements <sup>13</sup>.

Excellent diagnostic accuracy was demonstrated in research performed by Bedogni et al.

where NAFLD's diagnosis was confirmed when FLI-value $\geq$ 60 and value $<$ 30 precluded diagnosis.

Researchers showed that FLI $\geq$ 30 rules out steatosis presence with 87% sensitivity and FLI $\geq$ 60 rules in steatosis presence with 86% specificity, through ultrasound as reference among 216 participants with along with 280 without suspected liver disease. FLI calculation for NAFLD confirmation has only been verified against hepatic ultrasound<sup>14</sup>.

This study is useful to assess and identify index of two in identifying NAFLD, as there is lack of research comparing TyG index as well as FLI.

---

# AIMS & OBJECTIVES



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## **OBJECTIVES**

### **AIM AND OBJECTIVES**

- 1.** To evaluate the role of triglyceride glycaemic index and fatty liver index in identification of non-alcoholic fatty liver disease in type 2 diabetes patients.
- 2.** To analyze triglyceride glycaemic index and fatty liver index and to identify better index of the two."
- 3.** To correlate elastography with triglyceride glycaemic index and fatty liver index

---

# REVIEW OF LITERATURE



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## REVIEW OF LITERATURE

Diabetes has a long history that began thousands of years before the time of Jesus. George Beers discovered a polyuric disorder that mirrored diabetes on ancient Egyptian papyrus circa 150 BC. The disease was initially recognized by Celsius (30 BC–50 AD). Aretaeus was first to employ term "diabetes", which refers to "run through" or "a syphon," in the second century AD. He had given a general description of the condition causing excessive urine production. 19 Diabetes was described as "a wonderful affection, not very frequent among men, being melting down of flesh and limbs into urine" by the Roman physicians Celsus and Aretaeus (30-90AD). Cappadocian physician Aretaeus once described diabetes as disorder in which "patient never stops making water, but the flow is incessant as if from the opening of aqueducts"<sup>15</sup>.

Thomas Willis (1621-75) noted in the 17th century that diabetic urine seemed "as if imbibed with honey and sugar." Mathew Dobson (1735-84) indicated that urine's sweetness was because of sugars, a century after Willis's finding. The term mellitus (mellitus = honey) was initially used by John Rollo to distinguish this polyuric state from others in which the urine lacked flavor (Greek: inspidus). The causes and consequences of diabetes have been described for antiquity. Aricanne, an Arab physician, described gangrene as a result of diabetes about the year 1000 AD.

Pancreatic extracts were created in 1921 by Banting and Best with the intention of lowering the elevated blood sugar levels in dogs with diabetes. In 1922, Leonard Thomson became first patient to receive therapy using pancreatic extract. Long-acting insulin isophane was first established by Hans Christian, Hagedorn, and collaborators. Huisman and Meyering isolated hemoglobin A1c for the first time in 1958 using a chromatographic column. In 1968, Bookchin and Gallop categorized it as a glycoprotein. Samuel Rahbar et al. noted an increase in diabetes in 1969. In 1976, Anthony and his colleagues proposed use of hemoglobin A1c (HbA1c) to assess degree of glucose metabolism control among diabetic patients<sup>16</sup>.

### **Non-alcoholic fatty liver disease:**

First accounts of "fatty liver disease" were in 19th century, when doctors first noted fat deposition in liver during autopsies of undernourished and alcoholic patients. In the second half of the century, fatty liver was more and more identified in obese, diabetic patients. Histological studies came to define fatty liver in terms of the presence of lipid droplets within hepatocytes. Early in the 20th century, clinicians also started to link fatty liver to other more ominous liver outcomes encompassing fibrosis as well as cirrhosis, and associations with diabetes were mentioned. Despite

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these findings, fatty liver was usually considered benign before the mid-20th century. In 1952, Dr. Samuel Zelman documented instances of fatty liver among obese patients without history of alcohol consumption that suggested a non-alcoholic etiology. The medical community was nonetheless divided on whether or not it had clinical significance.

The tide changed in 1980, when Dr. Jurgen Ludwig and coworkers at Mayo Clinic coined term "Non-Alcoholic Steatohepatitis (NASH)". In subsequent decades, more general umbrella term "Non-Alcoholic Fatty Liver Disease (NAFLD)" came into use to cover spectrum from simple steatosis to NASH, fibrosis, as well as cirrhosis.

By 1990s and 2000s, NAFLD emerged as an international focus of interest as hepatic manifestation of MS. During obesity and T2DM epidemics, NAFLD emerged as most prevalent liver disease worldwide. Research demonstrated that NAFLD was not just a liver disease but was linked to augmented cardiovascular risk and all-cause mortality<sup>17,18</sup>.

## **DEFINITION**

Hyperglycemia, which can be caused by anomalies in insulin secretion, action, or both, are characteristics of DM, family of metabolic diseases. Metabolic dysregulation related to DM results in secondary pathophysiological alterations in several organ systems. The rising prevalence of DM worldwide may make it major cause of disease and mortalities in future<sup>19</sup>.

## **EPIDEMIOLOGY**

An important global health concern, T2DM is on rise. As of 2024, nearly 589 million adults between the ages of 20-79 have diabetes, which represents around 11.1% of the adult population worldwide. A staggering 40% plus of them are also unaware that they have it. It is estimated to reach 853 million by 2050, highlighting the necessity for meaningful prevention and control measures. In 2024, diabetes caused 3.4 million deaths, which is one death every six seconds. Interestingly, 47% of the deaths were before the age of 70, indicating the disease's contribution to premature death. The economic impact of diabetes is huge. Global health spending attributable to diabetes accounted for at least USD 1 trillion in 2024, which is 338% higher than the level over the last 17yrs.

As of 2021, India had a total adult population of about 893.9 million, with an estimated 8.3% adult prevalence of diabetes, which amounted to around 74.2 million cases, according to "International Diabetes Federation (IDF)". These statistics highlight tremendous burden of diabetes on India's public health scenario. The IDF further notes that the South-East Asia (SEA) region that comprises India had an estimated 90 million adults between 20-79yrs of age with

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diabetes in 2021. Interestingly, around 46 million of these instances were not diagnosed, indicating a significant lack of diabetes awareness and diagnosis in the region.

There are many various types of DM, which is caused by complex interaction between genetic as well as environmental factors. Diabetic as well as healthcare systems are severely impacted by secondary pathophysiologic variations in several organ systems caused by the metabolic dysregulation related to DM <sup>20</sup>.

### **Classification**

DM is categorised according to pathogenic mechanism causing hyperglycemia.

There are four clinical classes in classification of diabetes.

1. "Type I Diabetes mellitus (T1DM)
2. Type 2 Diabetes mellitus (T2DM)
3. Other specific type of diabetes due to various other causes.
4. Gestational diabetes mellitus (GDM)"

### **Type 2 Diabetes Mellitus**

T2DM has been characterized by IR along with growing insulin secretory deficit. T2DM is accountable for 90-95% of all cases of diabetes. It was previously referred to as "type 2 diabetes, adult onset diabetes, or non-insulin dependent diabetes" <sup>21, 22</sup>.

### **RISK FACTORS OF DIABETES MELLITUS**

Risk factors of T2DM are given below

#### **I. Modifiable Risk factors**

1. Diet
2. Dyslipidemia
3. Hypertension
4. Obesity
5. Physical inactivity

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## **II. Non-Modifiable Risk factors**

1. Genetic factors
2. Family history

Genetics as well as environment are 2 main factors that affect a person's risk of acquiring T2DM.

Modifiable as well as non-modifiable risk factors are linked to T2DM. Obesity, weight increase, along with physical inactivity is among 3 most crucial modifiable risk factors.

### " Type 2 Diabetes Mellitus- Pathophysiology

Beta cells of pancreas produce insulin. Exocytosis, which releases the material from storage within the vacuoles, is mostly caused by food that contains absorbable glucose. Thus, the primary cause of elevated blood glucose levels is eating(23).

Abnormal fat metabolism, insulin resistance, elevated hepatic glucose production, and decreased insulin secretion are all signs of T2DM.

### **Insulin resistance**

IR is reduced biological response to a normal level of circulating insulin. Usually, the cause is defect in the way insulin functions.

### **Loss of beta cell function**

Increasing loss of beta cell function is connected to increased insulin production from beta cells caused by insulin resistance, is crucial for development of fasting hyperglycemia. Selective glucose unresponsiveness, or absence of insulin release in response to glucose, is main anomaly.

Despite IR, glucose tolerance stays relatively normal as pancreatic beta cells make up for this by releasing more insulin in early stages of disease. When compensatory hyperinsulinemia and IR worsen in some individuals, the pancreatic islets are unable to maintain hyperinsulinemic state. Elevated postprandial glucose levels are a later symptom of poor glucose tolerance. Overt diabetes with fasting hyperglycemia, which is caused by persistent reduction in insulin production along with rise in hepatic glucose synthesis, may ultimately lead to beta cell failure.

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## Diagnostic Criteria for type 2 diabetes mellitus

A committee comprising representatives from European Association of Diabetes, American Diabetes Association (ADA), along with IDF has published diagnostic criteria for diabetes (24).

Any one of the following symptoms can be used to identify DM, which is characterized by persistent or recurrent hyperglycemia.

- a) HbA1C, or glycated hemoglobin,  $\geq 6.5\%$  (48mmol/m1)
- b) Fasting plasma glucose level of 7.0mmol (126mg/dl) or more after consuming no calories for at least eight hours
- c)  $\geq 11.1$ mmol//L ( $\geq 200$ mg/dl) of plasma glucose As in glucose tolerance test, two hours following a 75g oral glucose load
- d) Hyperglycaemia symptoms include random plasma glucose levels  $\geq 11.1$ mmol/L (200mg/dl).

If there is no obvious hyperglycaemia, a repeat of any of the tests indicated above should be carried out the next day to confirm a positive result. **Metabolic abnormalities in Diabetes**

Cells absorb less glucose when there is insufficient insulin. The insulin-dependent enzymes' decreased activity, which suppresses glycolysis and promotes gluconeogenesis, results in hyperglycaemia.

### Derangement in protein metabolism

Proteins as well as amino acids are broken down more often to provide the substrate for gluconeogenesis, the process that results in muscular atrophy in diabetics.

### Derangement in lipid metabolism

- a. Higher amounts of free fatty acid in plasma are caused by increased fatty acid breakdown
- b. Depletion of oxaloacetate is caused by activation of gluconeogenesis. Because there is less oxaloacetate accessible, the TCA cycle oxidises more available acetyl CoA.
- c. Ketogenesis is the result of the extra acetyl COA being directed towards ketone body production. Hyperlipidaemia is present, characterised by increased levels of triacylglycerol, cholesterol, as well as NEFA in plasma. Cholesterol production also uses excess acetyl CoA.

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## **Lipid and diabetes mellitus**

Low levels of "high-density lipoprotein (HDL)" cholesterol, elevated triglyceride levels, along with tiny cholesterol-depleted "low-density lipoproteins (LDL)" are all present among individuals having DM. Abnormal metabolism of lipids as well as lipoproteins in T2DM is caused by IR, which is a major part of pathogenesis of diabetic dyslipidemia. There is not much of a difference between insulin-sensitive and resistant people's LDL levels. Consequently, it is inappropriate to determine a diabetic patient's risk of CVD solely by looking at their total cholesterol. In addition, dyslipidaemia and IR, which worsens with elevated glucose intolerance, are present in prediabetics. Women having diabetes are more likely to suffer from CVD than men. VLDL levels rise in response to IR. IR is also related to reduced levels of ApoA1 protein and elevated levels of Apo protein B100, which is believed to be the lipoprotein series protein responsible for atherogenesis. Dyslipidemia may occur during a fasting or postprandial phase. Dyslipidemia during the postprandial period can elevate risk of CVD in those without diabetes <sup>25</sup>.

## **NAFLD IN TYPE 2 DIABETES MELLITUS**

The term "fatty liver," also referred to as "hepatic steatosis," refers to range of early stages of liver cirrhosis development.

"Non-alcoholic fatty liver disease (NAFLD)" is a term employed for describing fatty liver that develops in individuals who have never consumed large amounts of alcohol. NAFLD's natural course includes cirrhosis, steatohepatitis, pure steatosis, and in certain cases, hepatocellular cancer. T2DM, obesity, along with hyperlipidaemia are all closely related to NAFLD.

NASH was initially identified in 1980 in a group of Mayo Clinic patients. Ludwig J, Viggiano Tr, McGill DB, and Ott BJ (1980) reported a pattern of liver damage among nonalcoholic patients that resembled alcoholic hepatitis. To characterize this disease condition, they used the name "non-alcoholic steatohepatitis" (NASH)<sup>26</sup>.

### **Prevalence**

NAFLD is most frequent cause of chronic liver disease, evolving as public health issue that is becoming epidemic in scope. According to histology, the prevalence of NAFLD is 12.2%, with 5% of cases having NASH, and 31% by magnetic resonance spectroscopy(MRS). According to Armstrong et al, 5-7% of people with asymptomatic T2DM had progressed fibrosis <sup>27-29</sup>.

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## **Risk factors**

NAFLD is hepatic manifestation of MS due to strong association with the syndrome. Since degree of liver fat content is linked to all MS components and vice versa, it is demonstrated that all patients with any component of MS have their risk for NAFLD evaluated<sup>30</sup>.

## **Natural history of NAFLD**

Although NAFLD advances slowly, 20% of patients experience fast progression. Every 14yrs for NAFL and every 7yrs for NASH, the progression to Stage1 fibrosis is accelerated when arterial hypertension is present. 11-20% of NASH patients aged 10-15yrs develop cirrhosis along with liver failure<sup>31</sup>.

CVD is considered major cause of mortality in NAFLD, with overall mortality rate increased by 2.2 times. Decompensated liver failure and HCC account for 2% of higher liverrelated mortality risk among patients having NASH (but not NAFL). Individuals having T2DM who have cirrhosis have mortality rate that is more than double that of general population along with individuals who have both T2DM and NAFLD. Additionally, their mortality and cirrhosis rates are higher, and their prognosis is often bad<sup>32</sup>.

NAFLD has been "characterized by pathological ectopic fat buildup and a low-grade chronic inflammatory state in liver, an organ incapable of accumulating fat. Due to IR in hepatic, muscular, as well as adipose tissue, these patients have a five-fold increased risk. Currently, there are no prediction models for onset of T2DM among people having NAFLD," annual surveillance would be practical solution<sup>33,34</sup>.

The existence of T2DM alters or raises the person's risk of acquiring NAFLD. Prediabetes is most likely a predisposing factor to NAFLD and its subsequent development<sup>35</sup>.

## **Non-alcoholic "Fatty liver disease and Diabetes**

In presence of T2DM, cardiovascular event risk in NAFLD increases 1.87 times. In individuals having T2DM, NAFLD has been linked to higher coronary artery calcium score, increased carotid intima-media thickness, early left heart failure, reduced myocardial blood flow<sup>36</sup>.

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Chronic kidney disease (CKD) and retinopathy are two microvascular consequences of diabetes that are known to be exacerbated by NAFLD. These pathological alterations are brought on by production of procoagulant, pro-inflammatory, along with "pro-oxidant mediators, which cause hepatic/systemic IR, atherogenic dyslipidemia, along with release of retinol-binding protein4, fibroblast growth factor-21, as well as fetuin-A by liver. Systemic and hepatic IR is caused by fetuin-A binding and blocking insulin receptor tyrosine kinase in liver as well as skeletal muscle." This hinders transmission of the insulin signal<sup>37,38</sup>.

When the serial biopsies of patients with diabetes or prediabetes were examined, they showed increasing fibrosis. Additionally, it has been proposed that these people are more likely to acquire advanced types of NAFLD, including cirrhosis, advanced fibrosis, NASH, as well as HCC. Patients who have deteriorating metabolic risk factors are more likely to proceed from NAFL to NASH and fibrosis. With a specificity of 90.0% and a sensitivity of 56.8%, Bazick et al. (2015) created a clinical model that was more accurate than NAFLD fibrosis score in predicting NASH as well as advanced fibrosis among NAFLD patients having T2DM<sup>39</sup>.

IR by homeostasis model assessment (HOMA), BMI, HbA1c, waist circumference, along with blood levels of albumin, ferritin, alanine aminotransferase (ALT), and aspartate aminotransferase (AST) were among the factors that this model included. As a result, it may identify 1249 patients who have NASH. Pathophysiological connection between T2DM as well as HCC was further reinforced by elevated levels of inflammatory biomarkers along with hyperinsulinemia, which raised HCC risk. Individuals having T2DM may benefit from elastography as screening method for NAFLD. It is still necessary to determine whether there is a causative association between NAFLD as well as CAD/CKD in T2DM, despite mounting evidence to the contrary<sup>40,41</sup>.

## **Pathophysiology**

NAFLD's primary pathogenic mechanism is IR in liver as well as extrahepatic tissues, encompassing skeletal muscle and adipose tissue, which work in concert to create systemic inflammation, which triggers production of nephrotoxic along with proatherogenic substances. Elevated rate of lipolysis in defective adipose tissue results in raised flux of "free fatty acids (FFAs)" to ectopic tissues, which causes IR as well as apoptosis in liver and muscle. Hepatocyte necroinflammation is thus the outcome of the "lipotoxic state" in NASH<sup>42,43</sup>.

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Triacylglycerol (TAG), which tends to build up in liver, comes from 3 sources: 59% comes from circulating FFAs, 26% comes from *de novo* lipogenesis (DNL), which is process by which carbohydrates are changed into lipids, and remaining 14% comes from diet. When FFAs enter portal circulation, they can either undergo  $\beta$ -oxidation, reesterify to TAG and be flushed out as very LDL, or undergo re-esterification and be retained in the liver. Insulin resistance improves DNL even more. In NAFLD, the rate of gluconeogenesis is higher and the rate of glycogen synthesis is lower. Increased intrahepatic glucose and pyruvate, a byproduct of glycolysis, serve as DNL substrates. Hepatic steatosis is caused by all of the aforementioned factors. Hepatic insulin resistance is exacerbated by elevated FFA flow into liver. Hepatocytes with elevated ceramide levels suppress the function of protein kinase B, which lowers insulin signalling<sup>42,43</sup>.

## Diagnosis and management

### Diagnosis

No history of significant alcohol use, either past or present, exposure to steatogenic drugs, or other liver disease causes, like viral hepatitis, should be present in order to diagnose NAFLD.

- ❖ Liver biopsy is preferred test for precise diagnosis of NAFLD.
- ❖ In NAFLD, liver biopsy indications include:
  1. Patients having NAFLD are more likely to develop progressive fibrosis and steatohepatitis.
  2. NAFLD fibrosis score and metabolic syndrome: those at risk for progressive fibrosis and steatohepatitis.
  3. It is impossible to rule out concurrent chronic liver disorders and competing etiologies for hepatic steatosis in suspected NAFLD.

Numerous ratings, including NAS, steatosis, activity, along with fibrosis score, can be employed to stage steatosis along with fibrosis based on liver biopsy<sup>30</sup>.

- ❖ Non-invasive imaging tests for steatosis include "quantitative fat/water-selective MRI/fibroscan/CT, proton density fat fraction, along with proton MRS. Ultrasound (USG) is the preferable method for first-line diagnosis due to its enhanced echogenicity. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of USG are 84.8%, 93.6%, and 77%, respectively. Unlike MRI, which can identify steatosis as low as <1%," transient elastography (TE) can identify steatosis greater than

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10%. Another benefit of MRI is that, unlike TE, which loses sensitivity in patients having BMI > 35 kg/m<sup>2</sup>, it is unaffected by obesity. A number of steatosis scores, including NAFLD-LFS, FLI, and steato test, predict existence of steatosis but not severity.

However, imaging methods only identify existence of a "fatty liver" and can't differentiate between NASH, simple benign steatosis, as well as extent of fibrosis.

With 2-4 fold increase in serum ALT and AST levels, serum biomarkers and scores can be employed as alternative for diagnosing steatosis in situations when imaging methods are not practical or available (such as in large epidemiological investigations). However, in 78% of people, it may be normal. AST/ALT is often less than 1. However, when fibrosis progresses, it can rise. Additionally, prothrombin time, serum bilirubin, as well as albumin levels are normal, with the exception of cirrhosis, but alkaline phosphatase and GGT levels may be increased.

"Cytokeratin-18 fragments (CK-18)" are generated when caspases cause cell death, can be employed with 82% specificity and 66% sensitivity. It isn't advised in standard clinical practice, nevertheless. Additional biomarkers for NAFLD diagnosis encompass:

- ❖ Additional indicators of cell death (such as intact CK-18 and soluble Fas)
- ❖ Adipokines (like adipocyte fatty acid-binding protein, tumor necrosis factor-alpha [TNF $\alpha$ ], interleukin-6 (IL-6), adiponectin)
- ❖ Metabolic indicators (growth factor receptor 21 and HOMA-IR)
- ❖ Indicators of inflammation, like C-reactive protein [CRP]

Numerous scores, including the NAFLD fibrosis score, improved LFS, Fibro test, BARD score (ALT, AST, Diabetes/Impaired Fasting Glucose, BMI), as well as FIB4 score, can be used to diagnose liver fibrosis. TE, a helpful diagnostic method for NAFLD, measures velocity of 50MHz shearwave as it passes through liver and converts it to stiffness score in kPa. When it comes to predicting fibrosis in NAFLD, its sensitivity, specificity, PPV, NPV, and accuracy are 100%, 73.9%, 77.8%, 100%, and 86.4%, respectively<sup>30</sup>.

Magnetic resonance elastography, Shear wave elastography, and acoustic radiation force impulse are further imaging modalities for fibrosis.

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## Management

Utilization of therapeutic disease-modifying strategies in NAFLD is limited.

The management measures are also utilized for treating T2DM because they improve insulin resistance and glycemia, which has an indirect effect. Only individuals with the highest risk of NAFLD disease development should receive pharmacotherapy. There are few conclusive clinical trials. It is not advised to use some medications, such as ursodeoxycholic acids, to treat NASH or NAFLD. Only effective treatments for T2DM and NAFLD are covered in this debate<sup>44</sup>.

## Lifestyle modification

It has been suggested that in order to cause 500-1000g of weight loss per week, an energy deficit of 500-1000kcal is necessary. In comparison to high-carb, low-fat diet, Mediterranean diet along high protein intake lowers liver fat on H1-MRS. With weight decrease of  $\geq 7\%$  over a 12month period, 25% of people see a regression in NASH, and 40% experience a regression in steatosis. Rapid weight reduction, however, may exacerbate LFT in NAFLD. Avoid foods and drinks that include fructose as well as saturated fats. Additionally, it states that alcohol consumption should be below the danger level, which is less than 30g for males and less than 20g for females. Regularly drinking two to three cups of coffee day is known to lower the chance of developing hepatic fibrosis. It has also been suggested that 150-200min per week of moderately intense aerobic physical activity, divided into three to five sessions, such as stationary cycling, brisk walking, and three 45-minute sessions of weight training, are beneficial. Exercise alone itself can lessen hepatic steatosis, however it is unknown if it can also improve other features of liver histology<sup>33</sup>.

## Statins

Statin safety in NAFLD/NASH was demonstrated by the GREACE study. Statins along with other lipid-lowering medications are safe for dyslipidemia in NAFLD as well as NASH when histology improves. Statin use should be avoided in decompensated cirrhosis, even though it is justified in NASH cirrhosis<sup>45</sup>.

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Risk factor for CVD is NAFLD. Cardiovascular risk is often underestimated in those with T2DM. Cardiovascular risk in case of T2DM as well as NAFLD is typically underestimated by algorithms employed for conventional CVD risk calculation. If predicted 10yrs cardiovascular risk is greater than 15%, a statin is necessary because there is no evidence to the contrary. Apart from its beneficial effects on cholesterol, statins also enhance insulin sensitivity, lower the generation of AGEs, and have anti-inflammatory characteristics that may lessen inflammation as well as steatosis linked to NASH<sup>46</sup>.

### **Omega - 3 Polyunsaturated fatty acid**

High doses of omega-3 polyunsaturated fatty acids (PUFAs) can be employed for treating hypertriglyceridemia, which frequently coexists with NAFLD as well as T2DM. They work by activating FGF21, which then stimulates PPAR  $\alpha$  (peroxisome proliferator-activated receptor alfa), which activates number of genes related to FA oxidation. However, until hypertriglyceridemia is present, PUFAs cannot be thought of having special role in therapy of NAFLD/NASH<sup>47</sup>.

### **Vitamin E**

Oxidative stress is present in T2DM as well as NAFLD. 800 international units per day of vitamin E enhanced liver enzymes, inflammation, steatosis, when given for 96 weeks, and 42% of patients saw a remission of NASH, according to the PIVENS experiment. As a result, it has been regarded as first-line medication for non-diabetic adults having biopsy-proven NASH at dose of 800IU/day. However, until more information proving its efficacy becomes available, it hasn't been advised for T2DM having NASH, NASH cirrhosis, NAFLD without liver biopsy, or cryptogenic cirrhosis<sup>48</sup>.

### **Pentoxifylline**

One nonselective phosphodiesterase inhibitor that helps reduce inflammatory pathways like TNF- $\alpha$  is pentoxifylline. There have been conflicting findings on imaging of hepatic steatosis and plasma aminotransferases; some studies have seen improvement, while others have found none<sup>49,50</sup>.

### **Insulin**

In T2DM patients, exogenous insulin may be beneficial even if IR with hyperinsulinemia is harmful to the liver. Because IR and NAFLD are closely related, there is a greater need for insulin, which may result in weight gain. Human studies reveal a paradoxical enhancement in liver fat,

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which may be associated with enhanced triacylglycerol secretion, enhanced hepatic insulin sensitivity, along with decreased gluconeogenesis, even while insulin increases lipogenesis with decline in *in vitro* lipid oxidation. Insulin is therefore useful in maximising glycaemic control in T2DM along with all stages of NAFLD<sup>51-53</sup>.

### **Metformin**

First-line treatment for T2DM is metformin. Metformin improves hepatic insulin sensitivity while reducing body fat. Protein kinase activation enhances fatty acid oxidation and reduces DNL without appreciably improving hepatic steatosis or inflammation histologically. Application of metformin in NAFLD without diabetes is not licensed. Although there hasn't been proof of a clear enhancement in steatosis or histological characteristics of NASH<sup>54,55</sup>.

### **Sulfonylurea**

Prospective investigations have yet to determine sulfonylurea role in NAFLD having diabetes. Conversely, sulfonylurea-treated T2DM with NAFLD may be more susceptible to fibrosis because of the profibrotic impact of insulin, according to retrospective studies<sup>56</sup>.

### **Thiazolidinediones**

Glitazones activate Peroxisome proliferator-activated receptors (PPAR $\gamma$ ), which results in uptake along with storage of FAs and sensitizes adipose tissue to insulin. Along with the reduction in pro-inflammatory adipokines, there is also an increase in adiponectin, which improves insulin sensitivity by lowering gluconeogenesis and fatty acid influx. They also lead to enhancement in hepatic steatosis along with "restoration of normal adipose tissue biology. In individuals without overt diabetes, PIVENS trial found that pioglitazone enhanced all histological characteristics (except from fibrosis) and resolved NASH more effectively than placebo. In randomized, doubleblind, placebo-controlled research, Cusi et al. found that" pioglitazone reduced NAS in NASH patients having pre-diabetes or T2DM by enhancing inflammation, hepatic steatosis, as well as ballooning without exacerbating fibrosis. Improvements in adipose tissue, skeletal muscle, liver fibrosis, along with insulin sensitivity were also observed; these beneficial effects persisted for 36 months following treatment. In conclusion, it plays role in T2DM-associated biopsy-proven NASH. However, NASH can relapse after treatment, therefore ongoing care is required. However, the FDA has not approved its usage in non-diabetics having NAFLD<sup>57, 58</sup>.

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## **Dipeptidyl Peptidase IV Inhibitors**

Serum levels of DDP-IV are higher among NASH patients than in controls, and histopathological grade is correlated with DDP-IV liver staining. DDP-IV inhibitors stimulate "5'Adenosine monophosphate-activated protein kinase (AMPK)" in animal models of diet-induced obesity, which attenuates lipogenesis by downregulating genes implicated in lipogenesis. In animal models having liver damage, hepatic steatosis along with enhanced insulin sensitivity led to decrease in liver inflammation, which stopped development of fibrosis. In limited, nonrandomized investigation of people having ultrasonographic steatosis, DDP-IV inhibition result in better glycemic control having lower AST as well as ALT. In prospective blinded randomized controlled research, hepatic triglycerides as determined by MRS decreased after 6 months of DDPIV inhibitor treatment<sup>59,60</sup>. There is currently insufficient data to distinguish between the usage of various DDP-IV inhibitors for people who have both diabetes and NAFLD. Patients having severe hepatic impairment must employ it with caution<sup>61</sup>.

## **Glucagon like Peptide – 1 analogs**

Analogs of GLP-1 have been demonstrated in animal trials to ameliorate hepatic steatosis as well as steatohepatitis through weight loss and GLP-1 receptor expression. Since DNL plays part in pathophysiology of NAFLD, GLP-1 agonists directly suppress hepatocyte lipogenesis, improving action of insulin in hepatocytes as well as adipose tissue<sup>60,61</sup>.

Exenatide treatment of hepatocytes with NASH results in reduction of c-Jun N-terminal kinase phosphorylation by increasing peroxisome PPAR $\delta$  expression. Insulin sensitivity rises as a result. Furthermore, PPAR alfa activity increased in protein kinase A-dependent manner due to elevated protein kinase A activity, Akt, as well as AMPK activation. People with NASH who also have diabetes have been reported to benefit from ligarglutide. In comparison to 9% in placebo arm, 39% patients who took liraglutide saw a resolution of NASH at 52 weeks in a placebo-controlled study. Nevertheless, it is too soon to think about using GLP1 analogs for treating NAFLD/NASH particularly<sup>62</sup>.

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## **Sodium Glucose Cotransporter 2 inhibitors**

Sodium glucose cotransporter 2 inhibitors were found to have protective effect on fibrosis, inflammation, as well as steatosis in animal models of NAFLD. Glycosuria can slow progression of steatosis and fibrosis by producing a negative energy balance and causing the substrate to switch to lipids as source of energy expenditure. No human research on SGLT2 inhibitors along with NAFLD have been reported <sup>63</sup>.

## **Bariatric Surgery**

Noncirrhotic NASH that is refractory to medication and lifestyle modifications is an indication for bariatric surgery. Inflammation and fibrosis were observed in 37% and 20% of patients, respectively, but NASH was cleared in 85% patients. Weight loss was blamed for this. Prevalence of MS decreased from 70% to 14%; that is, 85%, 93.8%, and 95.6% of patients, respectively, experienced a remission of hypertension, dysglycemia, and dyslipidemia. Before trying surgery, portal hypertension should be ruled out.

The following are the ways that bariatric surgery helps NAFLD:

1. Lowering ghrelin and raising oxyntomodulin, GLP-1, and pancreatic polypeptide Y (PPY) for improving insulin sensitivity along with reducing appetite.
2. Reducing inflammation via lowering TNF $\alpha$ , CRP, IL1, and IL8.
3. Reducing dyslipidemia
4. Lowering expression of hepatic markers implicated in development of inflammation and fibrosis and raising adiponectin levels.
5. Reduction in IR
6. Encouraging the reduction of body weight <sup>64,65</sup>.

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## Guidelines for follow up

Condition	Frequency of monitoring
NAFL patients without worsening of metabolic risk factors	Once in every 2-3 years
NASH and/or those with fibrosis	Annually
NASH with cirrhosis	Once in 6 months
NASH with high risk of progression	Liver biopsy after 5-year follow-up
NASH patients with fibrosis and hypertension	Closer monitoring because of a higher risk of disease progression
NASH cirrhosis	Screen for gastroesophageal varices and HCC

NASH: Nonalcoholic steatohepatitis, NAFL: Nonalcoholic fatty liver, HCC: Hepatocellular carcinoma

In systemic review and meta-analysis carried out by Wang et al. in December 2022 relationship of TyG index and "metabolic dysfunction associated fatty liver disease (MAFLD)" was investigated. This investigation is performed with —Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)" statement. This system introduces "evidence-based minimum set of items for reporting in systematic reviews as well as meta-analyses. In his metaanalysis, total of 20 investigations with 165725 MAFLD participants had been included." Inclusion criteria included patients diagnosed with NAFLD/MAFLD and exclusion criteria included in vitro studies, insufficient literature, review articles, literatures. Study concluded that TyG index can diagnose as well as predict MAFLD with good accuracy <sup>66</sup>.

In a retrospective investigation performed by Liu J et al. in Shandong provincial hospital, in June 2021 they evaluated association between TyG index and NAFLD. Their study size included 11,424 subjects who were diagnosed with NAFLD. Study period included 21 months and they evaluated association between TyG index with NAFLD progression as well as improvement. The study population excluded patients having missing abdominal ultrasound data, missing basic information, patients having alcoholic fatty liver, patient with tumors and hepatitis. They concluded that triglyceride glycaemic index is significant indicator for NAFLD's risk appraisal in clinical practice <sup>67</sup>.

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In meta-analysis, study carried out by Castellana et al. four data bases were searched until January 2021. The subjects were grouped in Fatty liver index classes <30, 30-60, >60. For pooling data, random-effects model was employed. In this study they concluded FLI demonstrated "adequate performance in stratifying risk of NAFLD. Findings provided only evidence of discriminatory performance in excluding or diagnosing this disorder" <sup>68</sup>.

In research performed by Yu et al., they explored diagnostic value of TgY along with its related parameters in MAFLD. This is cross-sectional study which included residents who attended medical checkup at First Hospital of Nanping city. This study included 2605 subjects and study was conducted between 2015 to 2017. The investigation indicated that TgY index efficiently identifies MAFLD <sup>69</sup>.

In investigation performed by Lajeunesse-Trempe et al. from August 2005 to January 2006 in Kenya which was published on August 2023, they aimed to evaluate the validity of FLI in identifying NAFLD. This is community based cross-sectional investigation and it included 1473 individuals in the study. The participant's anthropometrical, clinical, biochemical as well as life style data were obtained for study. The study concluded that FLI is simple and valid scoring system for employing among rural as well as urban adults of Kenya <sup>70</sup>.

In research performed by Li-Wei Chen et al., data was collected from August 2013 to August 2016. This was community-based study and it included 1371 subjects to study the application of FLI in screening subjects with NAFLD. The exclusion criteria of this study included men consuming alcohol more than 30g/day and women consuming alcohol more than 20g/day, hepatitis B infection, underlying genetic and metabolic diseases affecting liver, corticosteroid use, gastric bypass surgery. This study concluded that FLI can be used in screening for NAFLD <sup>71</sup>.

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# MATERIALS & METHODS



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## MATERIALS AND METHODS

A prospective investigation was performed at Department of Internal Medicine, R L JALAPPA HOSPITAL-Tertiary care centre, Tamaka, Kolar. This research was conducted from May 2023 to October 2024. All patients presenting with T2DM to Department of General medicine were included in study. Clearance from institution ethics committees was obtained before conducting study. Informed consent was obtained before including study subjects in study. Sample size was evaluated as follows:

### Sample size:

Sample size was assessed by employing proportion of adverse outcome in subjects who were ventilated was 67.7% from investigation by Wei Li et al. through "formula

$$\text{Sample Size} = \frac{Z_{1-\alpha/2}^2 P(1-P)}{d^2}$$

$Z_{1-\alpha/2}$  denotes standard normal variate (at 5% type 1 error ( $P<0.05$ ) it is 1.96 and at 1% type1 error ( $P<0.01$ ) it is 2.58)." P-values $<0.05$  are regarded significant in most investigations hence, 1.96 has been employed in formula.

"P= Expected proportion in population based on previous studies or pilot studies d= Absolute error or precision P = 67.7% or 0.677 q = 32.3% or 0.323 d = 10% or 0.10"

Employing above values at 95% Confidence level, sample size of 85 subjects had been included in study.

### Inclusion Criteria:

1. Patients aged above 18yrs.
2. Subjects with T2DM

### Exclusion Criteria:

- Patient having past history of autoimmune hepatic disease, hepatitis virus infection, liver cirrhosis along with other chronic hepatic diseases
- Patients with history of hypertension, alcohol consumption greater than 140 g/ week

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## Methodology:

1. This investigation will be conducted after obtaining ethical clearance from institutional ethical committee as well as consents from study subjects.
2. 85 individuals fulfilling inclusion and exclusion criteria were included.
3. Detailed history and examination was done and recorded
4. The patient underwent all the necessary investigations with fasting blood glucose level, fasting triglyceride levels and liver function tests along with GGT, 2 ml blood is collected from patient in fasting state in plain vacutainer and their values were assessed
5. TyG index was evaluated by employing formula

"TyG index formula- $\ln$  [fasting triglycerides (mg/dL)  $\times$  fasting plasma glucose (mg/dL)/2]  
Values of fasting glucose level and" fasting triglyceride levels were adjusted in above formula and triglyceride value is obtained

6. FLI was evaluated by FLI-calculator which employs WAIST CIRCUMFERENCE , BMI, GGT as well as TRIGLYCERIDES

"Formula- FLI =

$(e^{0.953 \times \log_e(\text{triglycerides})} + 0.139 \times \text{BMI} + 0.718 \times \log_e(\text{GGT}) + 0.053 \times \text{waistcircumference} - 15.745) / (1 +$

$e^{0.953 \times \log_e(\text{triglycerides})} + 0.139 \times \text{BMI} + 0.718 \times \log_e(\text{GGT}) + 0.053 \times \text{waistcircumference} - 15.745) \times 100.$ " And FLI-scores  $\geq 60$  demonstrates presence of Fatty liver.

7. Ultrasound scan was done to identify fatty liver changes and it was correlated with FLI score. Ultrasonography was done by employing 1-5.0MHZ high-frequency curvilinear transducer(C1-5) in PHILIPS Affinity 70 ultrasound machine examination was done by using shear wave elastography (Elast PQR technique)

Sample box has been positioned on liver's B-mode image and elastography measurements had been obtained by pressing button. Region of interest (ROI) is placed 1.5-2.0cm beneath Glisson's capsule for avoiding reverberation artefacts. Multiple measurements in same location are made. Median of 10 valid measurements will be obtained. Liver stiffness values were expressed in m/s.



Figure depicting Multifrequency Ultrasound Philips affinity 70G with probes

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### **Statistical analysis:**

Microsoft excel data sheet was employed for entering data and subsequently analyzing via SPSS-22 version software. "Categorical data was represented in form of frequencies as well as proportions.

Chi-square test was employed as test of significance. Continuous data was indicated as mean and standard deviation (SD). Independent t-test was employed as test of significance for identifying mean difference. P-value<0.05 was regarded statistically significant."

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# RESULTS



**"Table 1. Distribution of the study subjects according to age group"**

Age group	Frequency	Percentage (%)"
31-40yrs	2	2.4
41-50yrs	15	17.6
51-60yrs	25	29.4
61-70yrs	41	48.2
71-80yrs	2	2.4
Total	85	100

**Chart 1. "Distribution of the study subjects according to age group"**

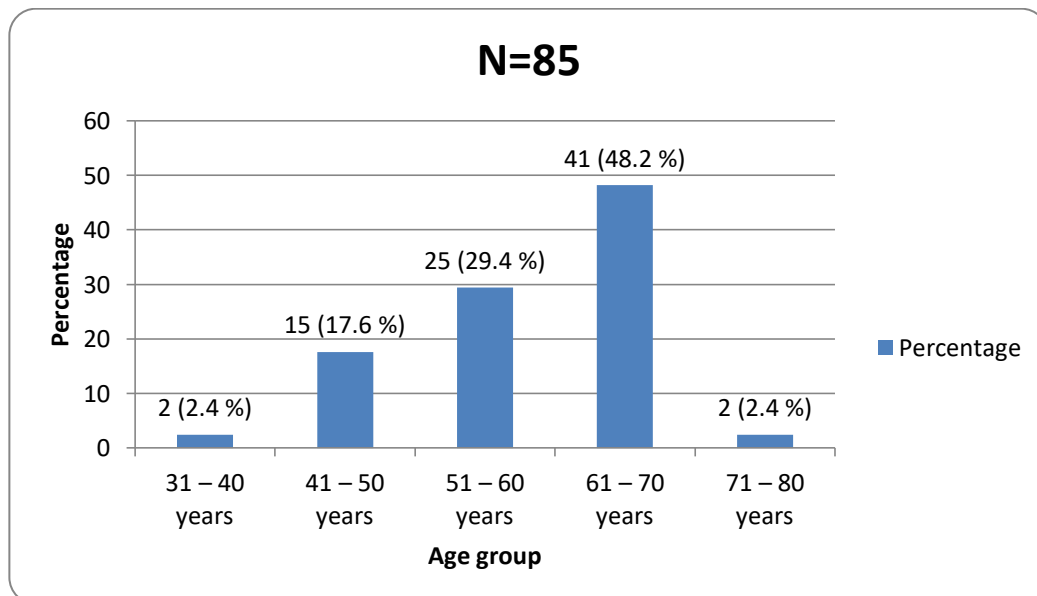


Chart 1 suggests the distribution of subjects in the study according to age group. Subjects were divided in accordance to their age into 31-40yrs which showed about 2.4% of cases, 41-50yrs which showed 17.6% of cases, 51-60yrs with cases of 29.4, 61-70yrs with 48.2% of cases and 7180yrs with 2.4% of cases. The above data suggests that more participants in the study belong to age group of 61-70yrs

**"Table 2. Distribution of the study subjects according to Sex**

Sex	Frequency	Percentage(%)
Male	56	65.9
Female	29	34.1
Total	85	100

**Chart 2. Distribution of the study subjects according to Sex**

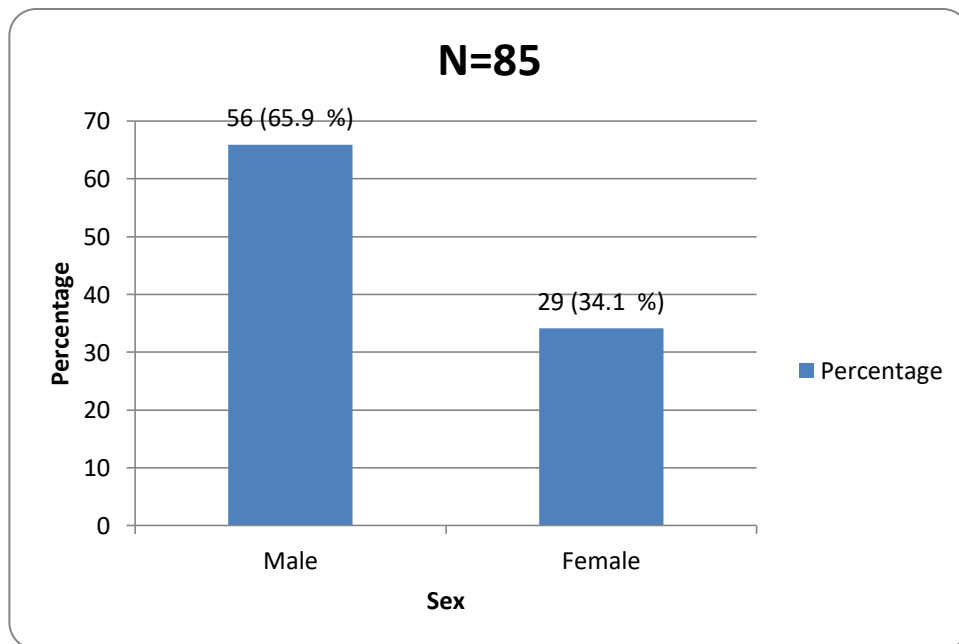


Chart 2 represents total number of male and female patients included in study. Out of 85 participants, 56 were males and 29 were females. From above data, 65.9% were males and 34.1 were females.

**Table 3. „Distribution of the study group according to Body Mass Index**

BMI	Frequency	Percentage(%)
18.5-24.9"	12	14.1
25-29.9	49	57.6
30-34.9	21	24.7
35-39.9	1	1.2
More than 40	2	2.4
Total	85	100

**Chart 3. "Distribution of the study group according to Body Mass Index"**

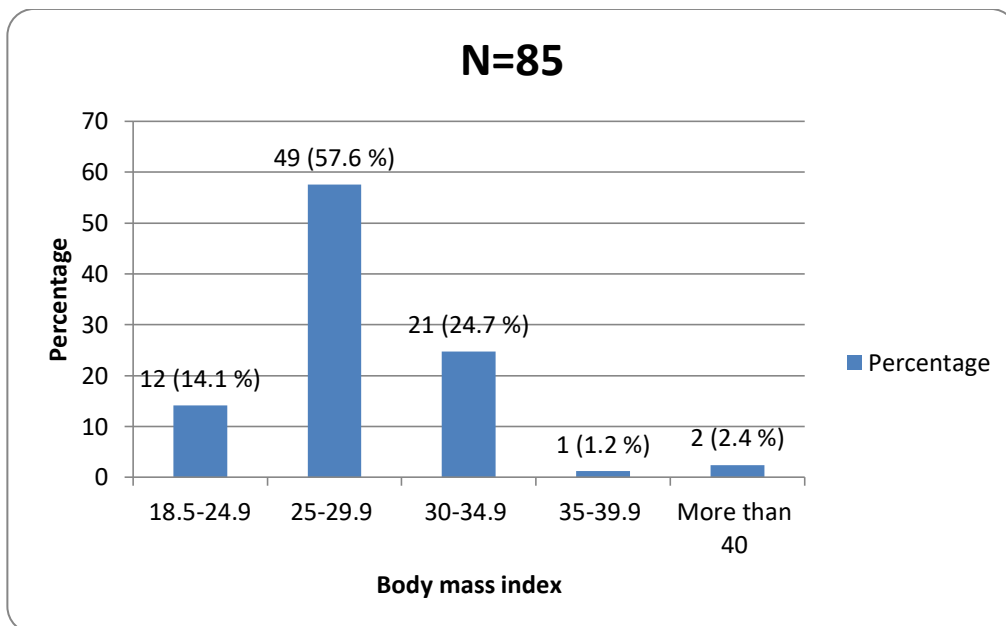


chart 3 represents grouping of study subjects according to BMI. 14.1% of study group belong between BMI of 18.5-24.9, 57.6% belong to 25-29.9 BMI that is over-weight , 24.7% of study group belong to 30-34.9 BMI which suggests obese class 1, 1.2% of population belong to 35-39.9 BMI group , which means obese class 2 and 2.4% belong to more than 40 BMI that indicates obese class 3.

**Table 4. "Distribution of the study subjects according to Fatty liver index"**

Mean $\pm$ SD	NAFLD	Non NAFLD	P value
Fatty liver index	59.1 $\pm$ 11.3	57.8 $\pm$ 18.6	0.780

**Chart 4. Distribution of the study subjects according to Fatty liver index**

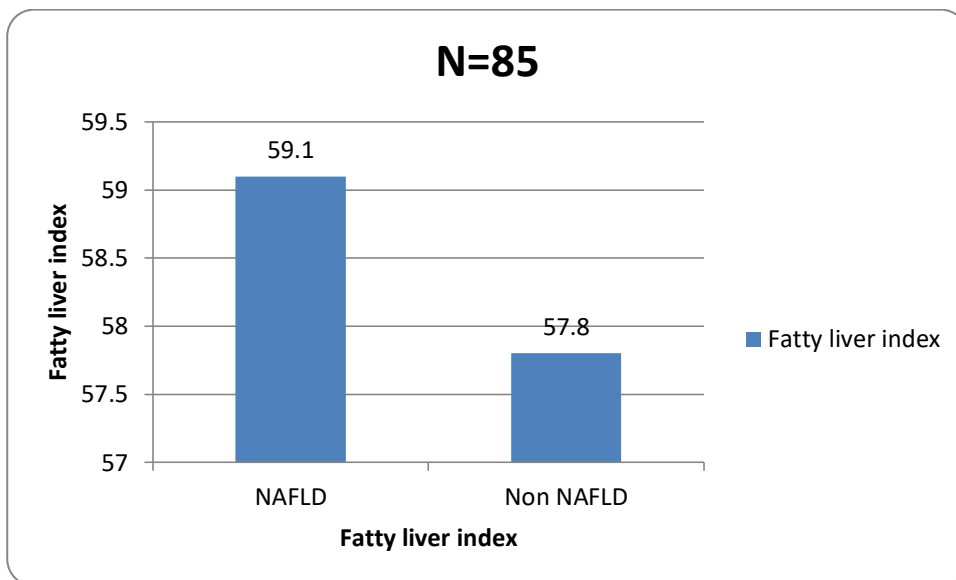
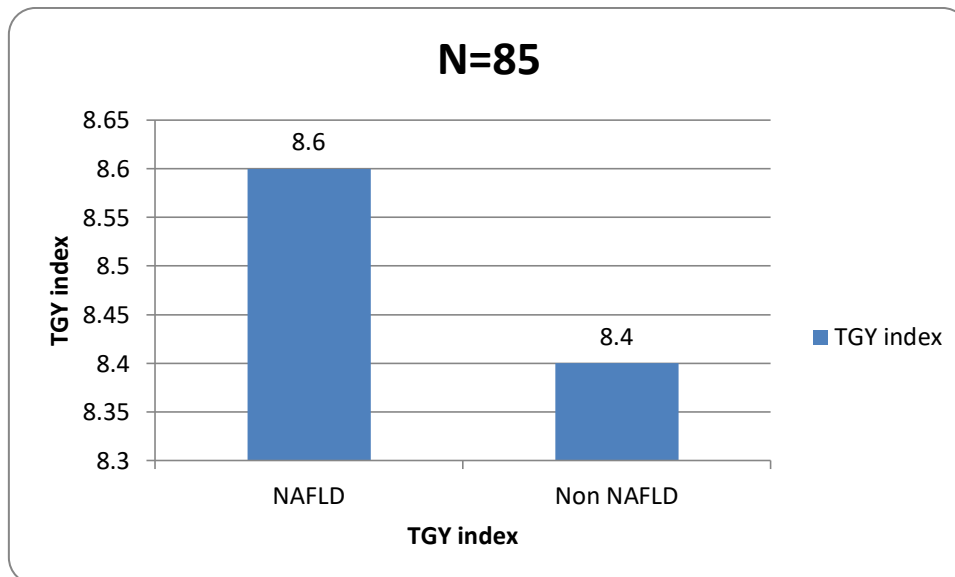


chart 4 represents the distribution of subjects to NAFLD and subjects without the pathology according to FLI. 59.1 $\pm$ 11.3 cases were NAFLD cases and remaining were not. The P-value is 0.780 which suggests that it was found to be statistically insignificant.

**Table 5. "Distribution of the study subjects according to TGY index**

Mean ± SD	NAFLD	Non NAFLD	P value
TGY index	8.6 ± 0.9	8.4 ± 1.14	0.483

**Chart 5. Distribution of the study subjects according to TGY index**



According to chart 5, study subjects were divided into NAFLD and subjects that doesn't have NAFLD. Mean value of  $8.6 \pm 0.9$  have NAFLD and mean value of  $8.4 \pm 1.14$  subjects doesn't have NAFLD. P-value being 0.438 was considered statistically insignificant.

**Table 6. Distribution of the cases according to elastography**

Mean ± SD"	NAFLD	Non NAFLD	P value
Elastography score	7.8 ± 1.3	7.9 ± 1.28	0.874

**Chart 6. Distribution of the cases according to elastography**

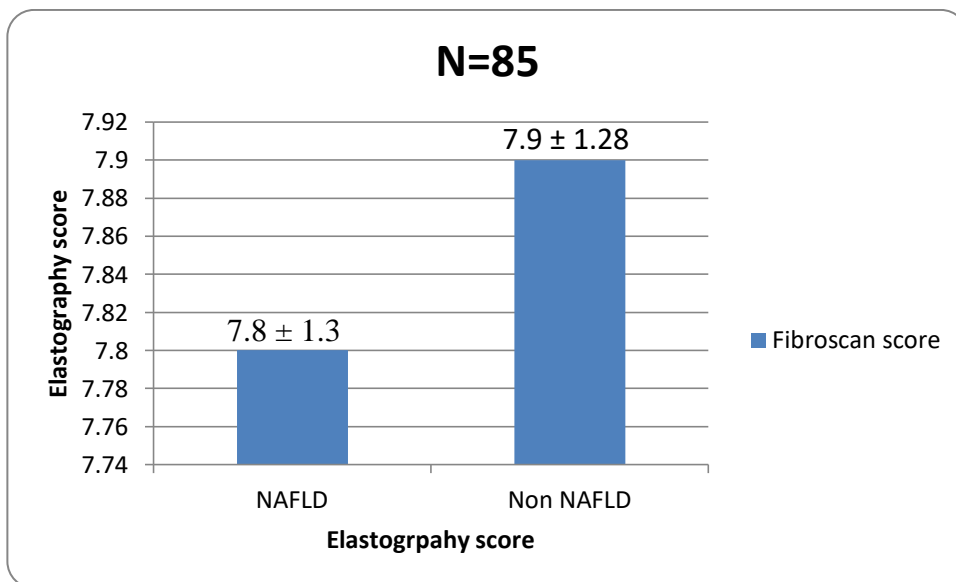


chart 6 divides study subjects into cases having NAFLD and cases with no disease based on elastography findings. The mean value of 7.8 suggests cases belong to NAFLD group and mean value of 7.9 suggests cases without disease. The P-value of the data was 0.874 which suggests it was observed to be statistically insignificant.

**Table 7. Distribution of the cases according to elastography values**

Elastography values	Frequency	Percentage(%)
F0 – F1	26	30.6
F <sub>2</sub>	51	60.0
F <sub>3</sub>	8	9.4
Total	85	100.0

**Chart 7. Distribution of the cases according to elastography values**

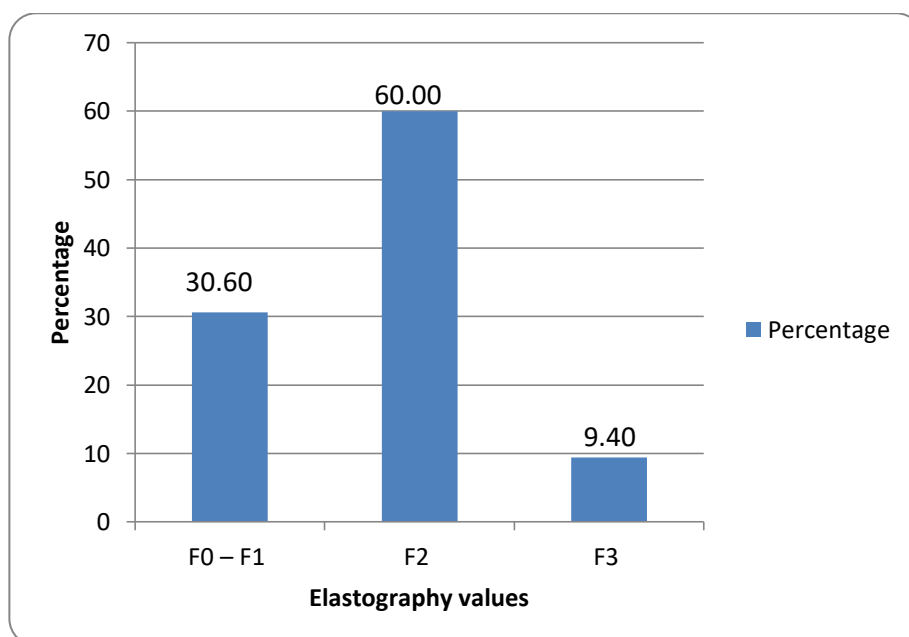


chart 7 represents grouping of study subjects according to elastography scan score. 30.6% of study group belongs to F<sub>0</sub> – F<sub>1</sub> group which range from 2-7kPa, which indicates no scarring. 60.0% of study subjects belong to F<sub>2</sub> group which suggests early stages of scarring indicating mild fibrosis of liver, score range from 7.5-10kPa which suggests moderate scarring indicating severe fibrosis of liver and 9.4% of study subjects belong to F<sub>3</sub> group which range from 10-14kPa which indicates severe scarring.

**Table 8. Distribution of the subjects according to HbA1c Levels**

Mean $\pm$ SD	NAFLD	Non NAFLD	P value
HbA <sub>1c</sub>	8.4 $\pm$ 0.8	8.5 $\pm$ 1.2	0.677

**Chart 8. Distribution of the subjects according to HbA1c Levels**

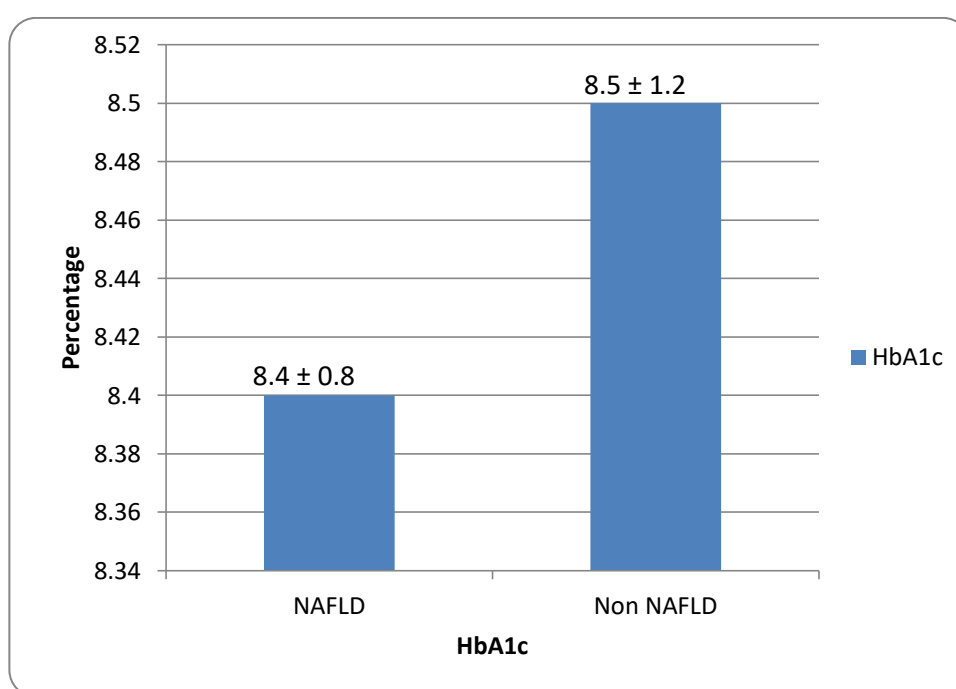
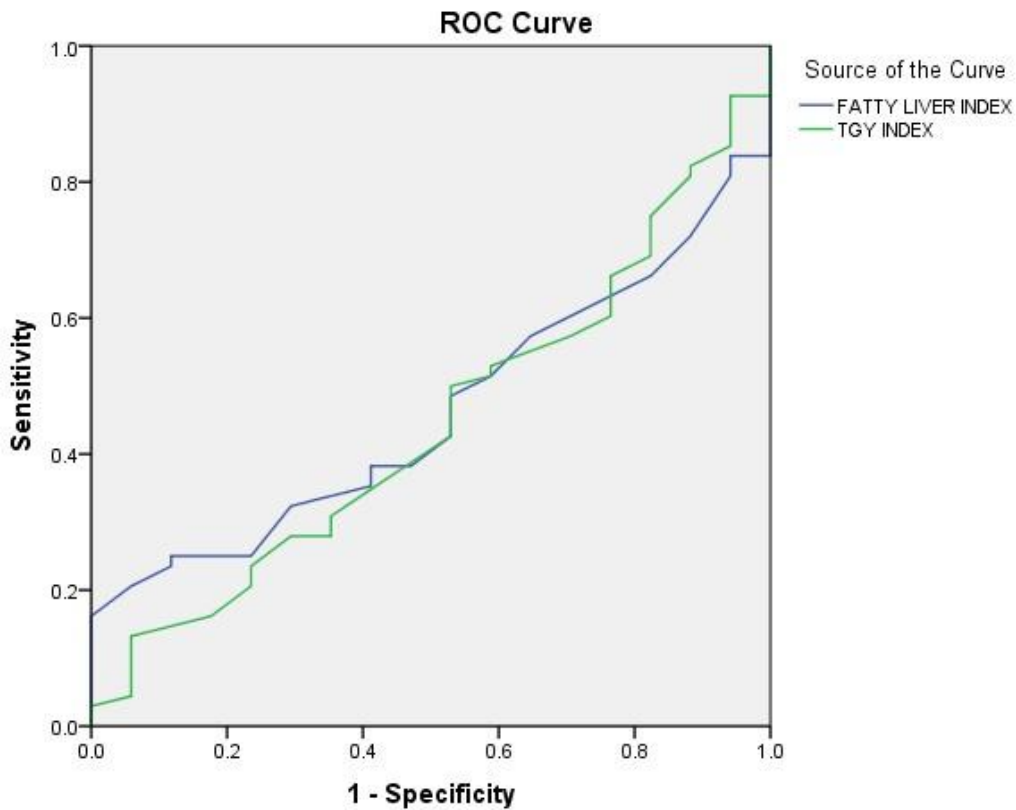


chart 8 suggests the mean values of HbA1C of subjects with NAFLD and subjects without pathology. Mean-value of HbA1C was found to be 8.4 in NAFLD cases and mean-value of HbA1C was found to be 8.5 in subjects without pathology and P-value was found to be 0.677 which suggests statistically insignificant.

**Chart 9. ROC curve of Fatty live and TGY index**



Diagonal segments are produced by ties.

**Table 9. Area under curve of Fatty liver index and TGY index**

"Area Under the Curve

Test Result Variable(s)	Area	Std. Error <sup>a</sup>	Asymptotic Sig. <sup>b</sup>	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
FATTY LIVER INDEX	.538	.066	.625	.409	.668
TGY INDEX	.554	.073	.489	.411	.698

The test result variable(s): FATTY LIVER INDEX, TGY INDEX has at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased.

a. Under the nonparametric assumption

b. Null hypothesis: true area = 0.5"

AUC was 53.8% for FLI in current investigation and AUC for TGY index was 55.4%.

**Table 10. "Cut off value of fatty liver index and TGY index**

Test Result Variable	Positive if greater than or equal to	Sensitivity	Specificity"
Fatty liver index	27	100	0
	34	83.9	0
	39.5	82.4	5.9
	42.5	80.9	5.9
	46	72.1	11.8
	48.5	66.2	17.6
	54.5	57.4	35.3
	57.5	48.5	47.1
	60.5	42.6	47.1
TGY Index	3.95	100	0
	5.175	97.1	0
	6.06	92.6	0
	7.95	85.3	5.9
	7.85	86.8	5.9
	8.01	82.4	11.8
	8.36	66.2	23.5
	8.47	57.4	29.4
	8.65	50.0	47.1

Table 10 suggests that fatty liver index level at 27 suggests 100% sensitivity for identification of the disease and triglyceride glyceic index level at 3.95 indicates 100% sensitivity of the score in identifying non alcoholic fatty liver disease. FLI of 54.5 had a sensitivity of 57.4% and specificity was 35.3% and at a level of 60.5, the sensitivity was 42.6% and specificity was 47.1%. At the level of TGY index, at the level of 8.47, the sensitivity was 57.4% and specificity was 59.4% and at the level of 8.65, sensitivity was 50.0% and specificity was 47.1%.

**Table 11. Distribution of the NAFLD and Non NAFLD cases according to Fatty liver index and TGY index**

	Fatty Liver Index	TGY index
NAFLD	59.1 ± 11.3	8.6 ± 0.9
Non NAFLD	57.8 ± 18.6	8.4 ± 1.14

**Chart 10. Distribution of the NAFLD and Non NAFLD cases according to Fatty liver index and TGY index**

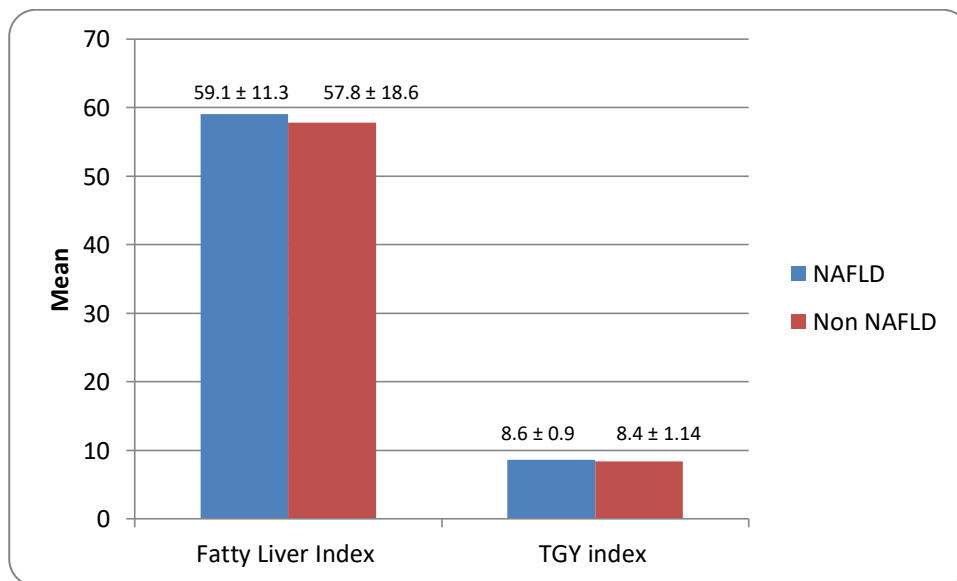


Chart 10 indicates the mean TGY index and FLI. The mean TGY index for NAFLD cases is 8.6 and for non NAFLD cases is 8.4 and the mean FLI score for NAFLD cases is 59.1 and non NAFLD cases was 57.8.

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# IMAGES



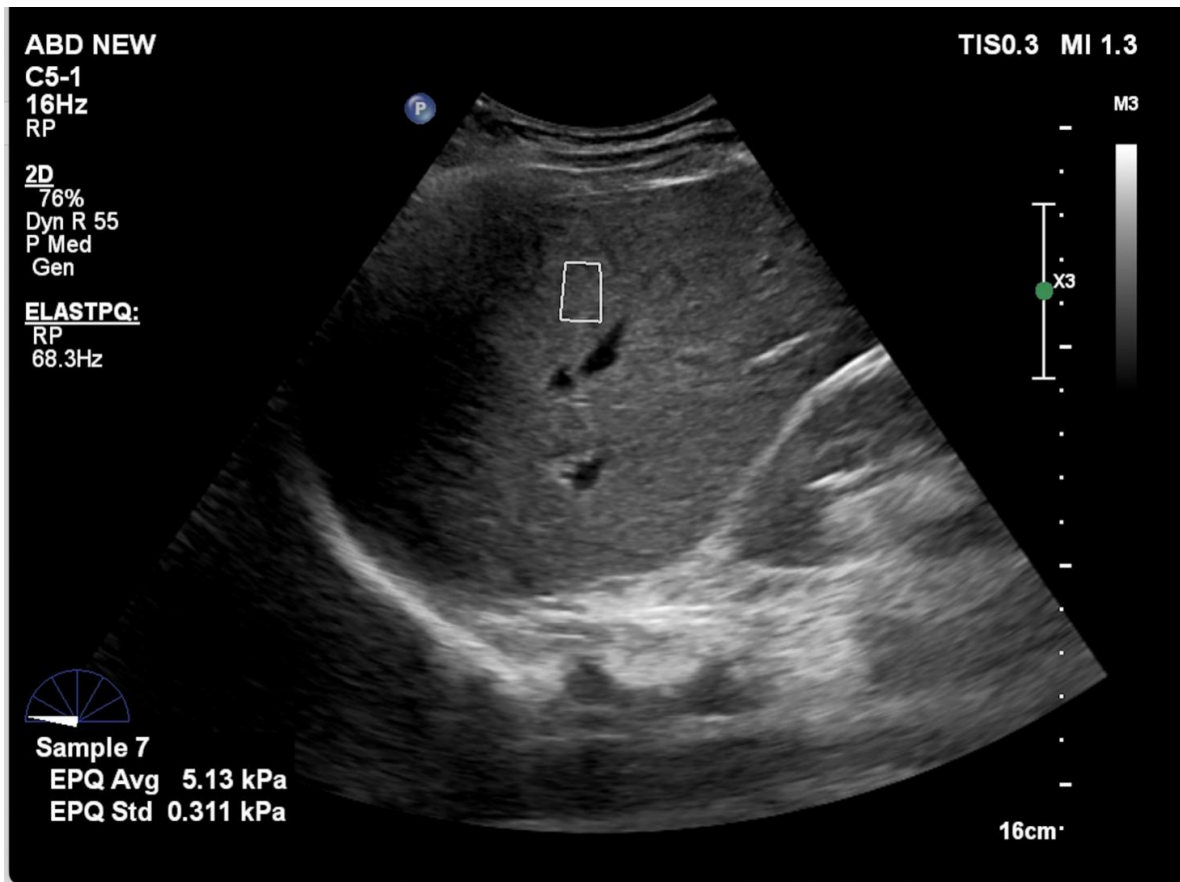
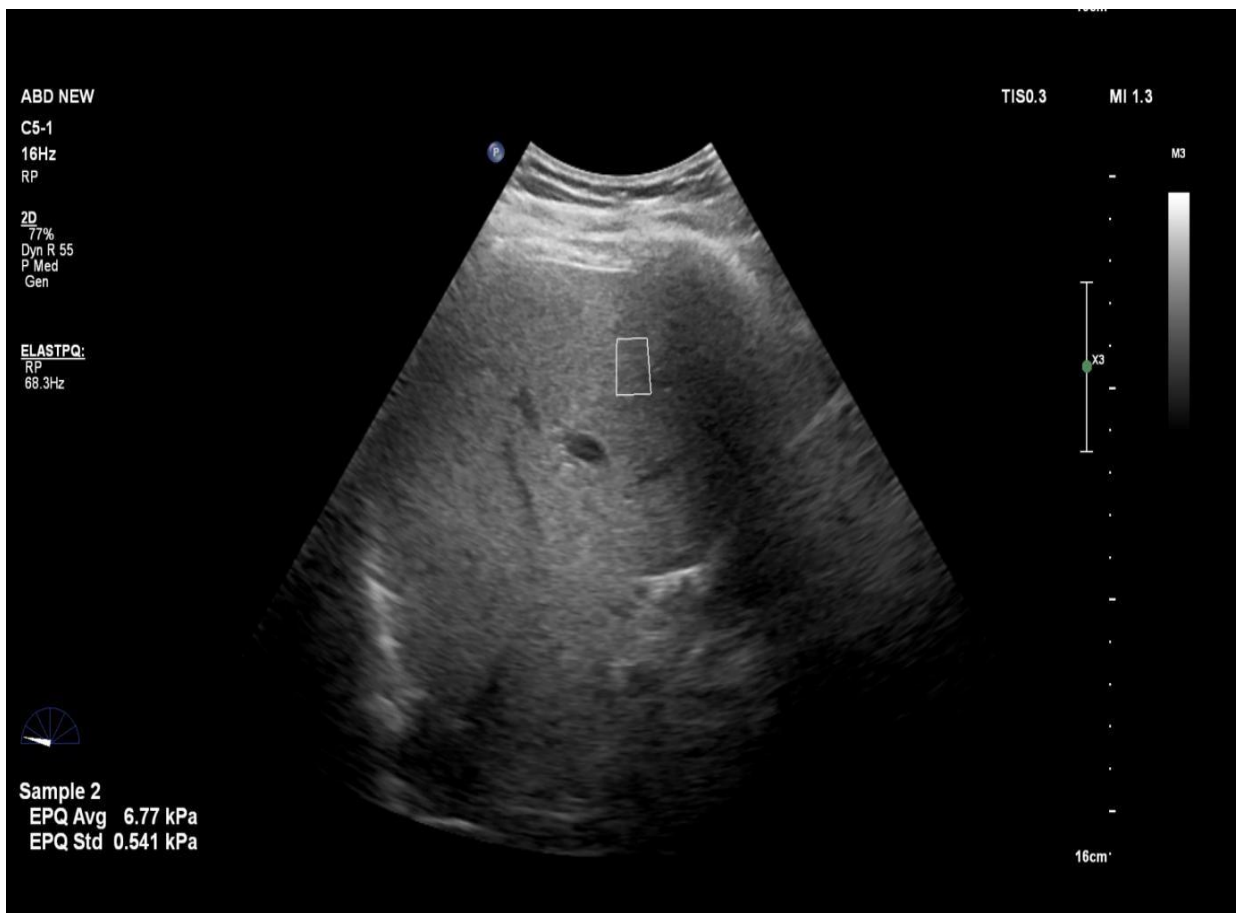


Figure 1 elastography score of 5.13kPa , which suggests no fatty liver changes



**Figure 2 shows fatty liver in a type 2 diabetes mellitus patient ,with a elastography score of 6.77kPa which suggests fibrosis stage F1 disease**



Figure 3 shows fatty liver in a type 2 diabetes mellitus patient ,with a elastography score of 6.97kPa which suggests fibrosis stage F2 disease.

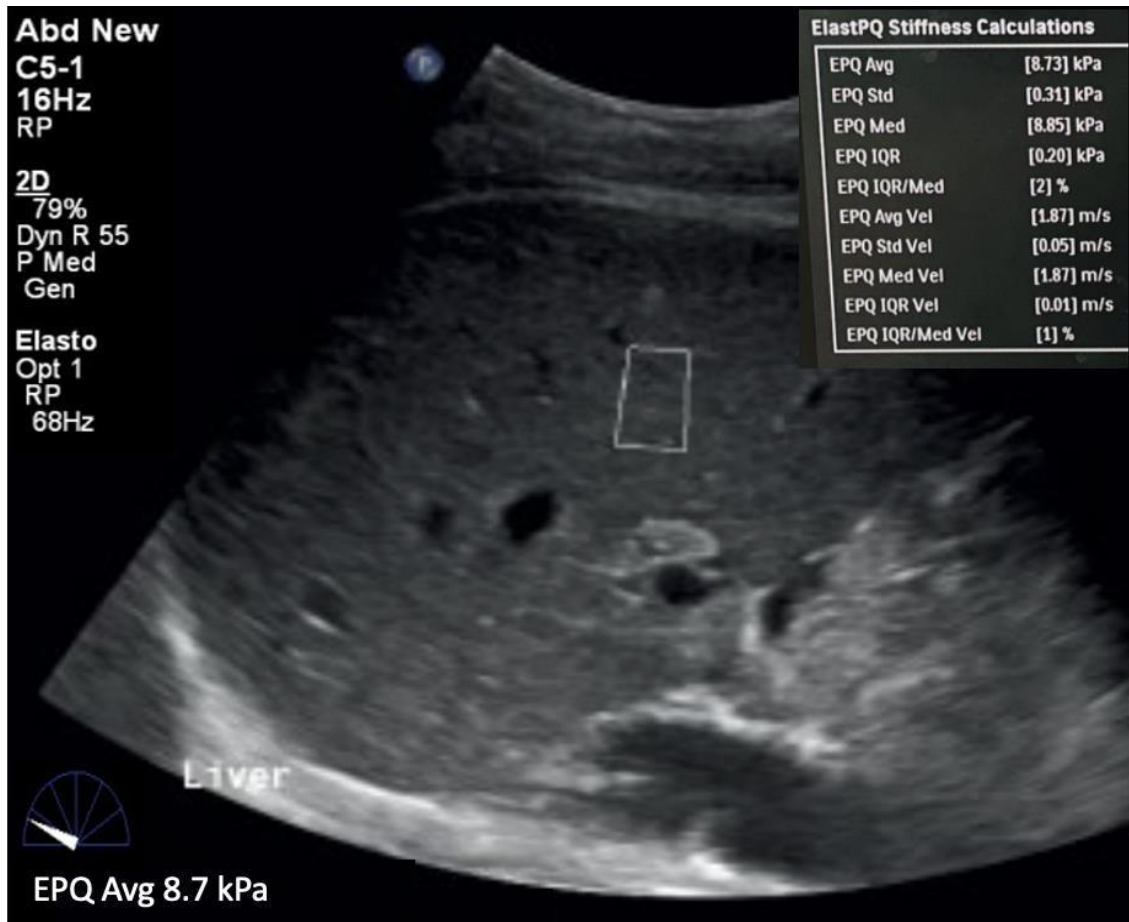


Figure 4 shows fatty liver in a type 2 diabetes mellitus patient ,with a elastography score of 8.7 kPa which suggests fibrosis stage F3 disease.

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# DISCUSSION



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## DISCUSSION

NAFLD is spectrum of hepatic disorders ranging from simple steatosis to NASH, fibrosis, as well as cirrhosis. It is rising in prevalence worldwide alongside obesity and diabetes pandemics. T2DM has a close bidirectional association with NAFLD, and estimated 70% of T2DM patients are said to have NAFLD <sup>78</sup>. Early diagnosis of NAFLD among diabetic individuals is essential to avoid hepatic and cardiovascular complications.

Although imaging techniques such as elastography are widely employed, their use in large-scale screening is limited availability. Therefore, non-invasive markers such as FLI and TyG have emerged as possible markers for NAFLD risk stratification. Research objective was to determine efficiency of FLI along with TyG as surrogate markers for NAFLD diagnosis in patients having T2DM in prospective cohort.

### Age group

In this study, approximately 48.2% of the patients were between ages of 61-70yrs, 29.4% were between ages of 51-60yrs, and 17.6% were between ages of 41-50yrs. Mean age group in this study was 57.72. This was in contrast to outcomes reported by Kitazawa et al where most cases were aged between 50-59yrs <sup>72</sup>. In research by Seo et al, mean age of all patients was 51.7yrs <sup>73</sup>. In research conducted by Kurniwati et al, mean age of cases without hepatic steatosis was 59.53yrs and 54.97yrs in cases with hepatic steatosis <sup>74</sup>. In contrast, research by Li et al reported that mean age of non-NAFLD cases was 53yrs and that of NAFLD cases was 49.5yrs <sup>67</sup>. This age profile does imply that NAFLD is possibly more common or more likely to be diagnosed in older people. Age has uniformly been demonstrated as a non-modifiable risk factor for NAFLD, and investigations have reported that its prevalence rises with increasing age, with the likely cause being prolonged exposure to metabolic risk factors encompassing IR, T2DM, obesity, as well as dyslipidemia <sup>44,75</sup>.

Additionally, physiological alterations like enhanced visceral adiposity, sarcopenia, and mitochondrial dysfunction during aging contribute to hepatic fat deposition and fibrosis development <sup>76,77</sup>. Younossi et al. indicated statistically significant increase in prevalence of NAFLD in patients over 60yrs versus younger age groups, highlighting the need for focused screening in older populations <sup>78</sup>. Thus, the age profile seen in this study supports significance of early detection as well as lifestyle modification interventions directed at high-risk older adults.

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## Gender

In current investigation, most study participants were males constituting 65.9% of the cases, while females made up about 34.1%. Similar outcomes were reported in investigation by Li et al where 60.4% of the non NAFLD cases and 71.3% of the NAFLD cases were males<sup>67</sup>. In a study by Kurniawati et al, 33.3% of the cases without hepatic steatosis and 66.7% with hepatic steatosis were males.<sup>81</sup> In research by Seo et al, most cases were males<sup>73</sup>. In research by Kitazawa et al, majority of the cases were male<sup>72</sup>. This male dominance aligns with outcomes of other investigations that indicate NAFLD is more common in males, particularly during the earlier years of life.

This gender disparity has been partially explained by hormonal effects—specifically the protective effect of estrogen in premenopausal women, which can decrease hepatic fat content and IR<sup>79, 80</sup>. A big population-based study from China reported that male gender was strongly related to greater risk of NAFLD after managing age along with BMI<sup>81</sup>. Thus, the present study's observed male predominance might result both from biological as well as behavior risk profiles that are responsible for putting men at risk of the disease.

## Body Mass Index

In this study, 14.1% of the cases had normal BMI, whereas 85.9% cases exhibited BMI>25kg/m<sup>2</sup>.

Mean BMI for NAFLD groups was 28kg/m<sup>2</sup> and mean BMI for non-NAFLD group was 28.35kg/m<sup>2</sup>. In research by Li et al, mean BMI in non-NAFLD cases was 23.7kg/m<sup>2</sup> and in NAFLD cases it was 26.7kg/m<sup>2</sup><sup>67</sup>. In research by Kurniawati et al, mean BMI was 24.08kg/m<sup>2</sup> in cases without hepatic steatosis and 27.79 kg/m<sup>2</sup> in cases with hepatic steatosis<sup>74</sup>. In research by Seo et al, mean BMI was 24.4kg/m<sup>2</sup> and increased with increase in FLI<sup>73</sup>. In research by Kitazawa et al, mean BMI was 21.6kg/m<sup>2</sup> in patients who are non-obese and without FLI proven NAFLD, 23.8kg/m<sup>2</sup> in non-obese patients and with FLI proven NAFLD, and 25.7kg/m<sup>2</sup> in Obese patients without FLI proven NAFLD and 27.4kg/m<sup>2</sup> in Obese patients with FLI proven NAFLD<sup>72</sup>.

This finding is in alignment with established association of elevated BMI with NAFLD. Obesity, particularly central or visceral obesity, has central role in NAFLD pathogenesis by mechanisms related to IR, inflammation, as well as adipokine dysregulation<sup>44</sup>. Enhanced BMI is strong predictor of hepatic steatosis as well as fibrosis progression<sup>82</sup>. Younossi et al. reported that those with BMI>25kg/m<sup>2</sup> were much more likely to have NAFLD regardless of other metabolic risk factors<sup>78</sup>. NAFLD may even occur in lean people, although frequently with varying metabolic profiles and possibly varying genetic susceptibility, as noted in Asian populations<sup>80</sup>. High

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prevalence of increased BMI in this study highlights importance of the delivery of focused lifestyle and weight management interventions to reduce NAFLD risk and development.

### **Fatty Liver index**

In NAFLD cases, mean FLI was 59.1, while in non-NAFLD cases, it was 57.8. There was statistically insignificant difference in mean FLI among groups with p-value of 0.78. In research by Kitazawa et al, mean FLI was 41.3 in non-obese with FLI--NAFLD and 59.5 in obese with FLI-NAFLD<sup>72</sup>. These findings indicate that FLI is capable of separating groups when both obesity and fatty liver condition are taken into account. Further studies also support effectiveness of FLI in prediction of NAFLD. Bedogni et al., who first came up with the FLI, reported it to be a good index with AUC of 0.84 for prediction of hepatic steatosis, suggesting cut-offs of <30 to exclude and >60 to include fatty liver<sup>14</sup>. Nevertheless, investigation by Lee et al demonstrated that FLI performed more predictively in overweight and obese patients, whereas its capacity was restricted in lean NAFLD patients<sup>83</sup>. Collectively, these results indicate that while FLI is a valuable instrument, its performance as a diagnostic tool will depend on the population characteristics and can be optimized with the addition of other indices or imaging modalities.

### **TGY Index**

The mean TGY index was 8.6 for NAFLD cases and 8.4 for non-NAFLD cases. There was statistically insignificant difference in mean TGY index between NAFLD cases as well as nonNAFLD cases with p-value of 0.48. Similar outcomes were reported in investigation by Li et al, non NAFLD cases had TyG index of 8.89 and NAFLD cases had TyG of 9.42<sup>67</sup>. In research by Kurniawati et al, mean TyG index was 8.9 in cases without hepatic steatosis and 9.31 in cases with hepatic steatosis<sup>74</sup>. This implies that even though TyG index rises with hepatic steatosis, there is significant overlap between groups, particularly when additional metabolic risk factors are equally prevalent. Research by Zhang et al pointed out that TyG index was predictor of NAFLD in T2DM patients independently, but stressed necessity of using it in combination with other clinical or biochemical markers to enhance predictive power<sup>84</sup>. Therefore, although TyG index is significant marker for indicating underlying metabolic derangement, its independent diagnostic performance can be different based on population characteristics and comorbidities.

### **ELASTOGRAPHY**

According to this study, the average elastography score for NAFLD cases was 7.8, while it was 7.9 for non-NAFLD cases. There was statistically insignificant difference in mean elastography scores between NAFLD and non-NAFLD cases with p value of 0.87. Transient elastography, is

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mainly employed to measure liver stiffness along with controlled attenuation parameter (CAP) for assessment of hepatic steatosis as well as fibrosis. Absence of marked difference in score between two study groups could be due to several factors such as both groups being at an early stage of disease, insufficient resolution to detect mild steatosis or fibrosis, or inconsistency in CAP cut-off values for use in NAFLD diagnosis. Various studies have reported that CAP values increase with increasing hepatic fat content. Sasso et al. reported that CAP values correlated well with histologically confirmed steatosis grades, suggesting CAP threshold of 248dB/m for detecting steatosis $\geq$ S1 with good accuracy<sup>85</sup>. Similarly, Eddowes et al. indicated that diagnostic accuracy of elastography in several centers by demonstrating excellent sensitivity and specificity of NAFLD when suitable CAP and liver stiffness measurement (LSM) cut-offs were utilized<sup>86</sup>. Diagnostic overlap and variability between operators could restrict accuracy in particular groups, such as individuals with diabetes or increased BMI, which stressed the influence of metabolic confounders on the accuracy of transient elastography findings. Thus, although elastography is still noninvasive and significant tool in assessment of liver disease, its capacity to distinguish between early NAFLD and metabolically comparable non-NAFLD subjects might be restricted without supporting clinical or biochemical information.

### **HbA<sub>1c</sub>**

The mean HbA<sub>1c</sub> was 8.4% in NAFLD cases and 8.5% in non-NAFLD cases, according to current investigation. There was insignificant difference in mean HbA<sub>1c</sub> levels between 2 groups having p-value of 0.677. Mean HbA<sub>1c</sub> in non NAFLD cases was 8.4 and 8.7 in cases with NAFLD<sup>67</sup>. In research by Kurniawati et al, mean HbA<sub>1c</sub> was 7.55 in cases without hepatic steatosis and 8.7 in cases with hepatic steatosis.<sup>81</sup> In investigation by Kitazawa et al, mean HbA<sub>1c</sub> level was 5.7 in Non obese without FLI-NAFLD, 5.6 in FLI-NAFLD, 5.7 in obese without FLI-NAFLD and 5.7 in obese with FLI-NAFLD<sup>72</sup>. This finding indicates that glycemic control as expressed by HbA<sub>1c</sub> does not have a direct or independent association with incidence of NAFLD among individuals having T2DM. Although insulin resistance is a classic promoter of hepatic steatosis, evidence has been put forward by numerous studies to support that HbA<sub>1c</sub> in isolation could not be considered an adequate measure of hepatic fat deposition<sup>87,88</sup>. This is probably so since HbA<sub>1c</sub> reflects long-term glycemic control but fails to account for the intricate interaction of other metabolic conditions like dyslipidemia, obesity, or hepatic IR, which also play essential part in NAFLD pathogenesis<sup>89</sup>. Thus, although poor glycemic control is recognized risk factor for development of liver fibrosis in NAFLD, presence of fatty liver itself might not always be accompanied by increased HbA<sub>1c</sub> levels, especially in a metabolically uniform population like that of T2DM.

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## **Correlation with elastography**

There was insignificant association between elastography and patients' BMI (p-value of 0.79), TGY index (p value of 0.083), or fatty liver index (p value of 0.15). There is mixed evidence on the association between BMI and liver stiffness measurement (LSM) from elastography. In morbidly obese patients, an association of elevated BMI with raised liver stiffness has been reported, indicative of a direct relationship between BMI and severe fibrosis<sup>90</sup>. In contrast, another study by Khamseh noted moderate correlation ( $r=0.31$ ,  $p<0.001$ ) between BMI as well as LSM, which implies that, although BMI is likely to affect LSM, it is not independent of other determinants<sup>91</sup>. Such inconsistencies illustrate the intricate relationship and imply that determinants other than BMI affect liver stiffness.

## **Predictive accuracy**

In this study, the fatty liver index's AUC was 53.8%. Sensitivity and specificity was 57.4% and 35.3% at FLI level of 54.5. In a study Kruniawati et al, at the cut off level for TGY was 9.334, sensitivity of TGY index was 0.816 and specificity of 0.806<sup>74</sup>. A study by Dehnavi et al indicated that AUC was 0.85 for FLI in diagnosing NAFLD when optimal cut-off was 26.2, yielding sensitivity of 83% and specificity of 70%<sup>92</sup>. Another study by Vamja et al indicated AUC of 0.92 with sensitivity and specificity of 96% and 92.5%, respectively, at a cut-off of 60<sup>93</sup>.

In this study, the AUC for TGY index was 55.4%. For TGY index level, the sensitivity was 57.4% and the specificity was 59.4% at the 8.47 level, while the sensitivity and specificity were 50.0% and 47.1% at the 8.65 level. Research by Wang et al indicated AUC of 0.811 for TyG index for predicting NAFLD, and higher values correlate with higher risk<sup>94</sup>. A systematic review demonstrated that TyG index had AUC of 0.75, sensitivity of 73%, along with specificity of 67% in diagnosing MAFLD<sup>66</sup>.

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# CONCLUSION



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## CONCLUSION

The present prospective cohort study was designed for evaluating and comparing utility of 2 biochemical indices—Fatty liver index and triglyceride glycemic index—in identifying non alcoholic fatty liver disease among patients having Type 2 diabetes mellitus. Given increasing burden of both Type 2 diabetes mellitus and non alcoholic fatty liver disease globally, especially in developing countries like India, early identification as well as management of non alcoholic fatty liver disease among diabetics is imperative to reduce morbidity, mortality, and healthcare burden.

Demographically, majority of the study population were elderly males aged 61-70yrs, with BMI above 25kg/m<sup>2</sup>, aligns with existing literature that identifies age, gender, and BMI as critical risk factors for non alcoholic fatty liver disease in diabetics. These findings underline the significance of targeted screening in this demographic group.

Importantly, the findings emphasize the feasibility of using Fatty liver index and triglyceride glycemic index as initial screening tools in resource-limited settings where imaging accessibility is constrained. These indices are calculated from routinely available blood tests and anthropometric measurements, making them convenient and cost-effective tools for primary care physicians and endocrinologists to assess risk and prioritise further evaluation.

Given the increasing recognition of non alcoholic fatty liver disease as hepatic component of metabolic syndrome and its strong relationship with Coronary vascular diseases, early detection among diabetics assumes even greater clinical relevance. It isn't merely liver condition but a multisystem metabolic disorder with implications for cardiac, renal, and endocrine health. Thus, deploying indices like fatty liver index and Triglyceride glycemic index in outpatient diabetic care can improve holistic patient assessment.

To conclude, while this study did not find statistically significant superiority of either fatty liver index or Triglyceride glycemic index in identifying non alcoholic fatty liver disease among Type 2 diabetic patients, both indices demonstrated modest diagnostic potential. Given their simplicity, non-invasiveness, and accessibility, they hold promise as first line screening tools. Integration of these indices into clinical algorithms may support early identification and management of non alcoholic fatty liver disease, thus averting progression to more severe liver conditions encompassing Non alcoholic steatohepatitis, cirrhosis, or hepatocellular carcinoma..

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# LIMITATIONS



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## LIMITATIONS

Sample size included in this study included only 85 patients. This modest number limits the statistical power to detect subtle yet potentially clinically meaningful differences between NAFLD as well as non-NAFLD groups. A larger cohort could have strengthened the analysis, improved the precision of the estimates, and facilitated more robust subgroup analyses.

Research was performed at single tertiary care center, which may not be representative of broader population. Patients attending tertiary care facilities often present with more advanced disease or comorbidities, potentially introducing selection bias. Multi-centric studies involving diverse geographic and socioeconomic backgrounds would enhance external validity.

The study relied on elastography for diagnosing NAFLD and estimating fibrosis, respectively. While ultrasonography is widely employed because of its non-invasiveness and cost-effectiveness, it lacks sensitivity in detecting early or mild steatosis and can't distinguish between simple steatosis, steatohepatitis (NASH), as well as fibrosis. Similarly, elastography, although useful in assessing liver stiffness, is less accurate in obese individuals and does not provide histological insights. The absence of liver biopsy, which remains gold standard for NAFLD diagnosis and staging, is a significant limitation.

Future research addressing these limitations can pave way for more definitive clinical guidelines regarding utility of FLI and TyG in NAFLD's screening and management.

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# RECOMMENDATIONS



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## RECOMMENDATIONS

In light of study's findings and corroborating evidence from existing body of literature, several practical recommendations can be made for improving clinical application of non-invasive indices encompassing FLI and TyG index in screening and management of NAFLD amongst individuals having T2DM.

1. Integration of FLI and TyG indices into routine screening protocols for diabetic patients is strongly advised. These indices, derived from easily obtainable clinical as well as laboratory parameters, may serve as preliminary tools for identifying high-risk individuals who would benefit from confirmatory imaging or referral to specialized care.
2. There is a pressing need to validate and possibly recalibrate cut-off values for both FLI and TyG indices according to regional and ethnic variations. Differences in body composition, dietary patterns, genetic predisposition, and lifestyle behaviours may influence the performance of these indices. Establishing population-specific thresholds will improve diagnostic accuracy and clinical applicability.
3. These indices should be incorporated into broader NAFLD risk stratification algorithms alongside other metabolic parameters like HbA1c, BMI, lipid profile, blood pressure (BP), along with duration of diabetes. Such integrative approaches can enhance predictive power and aid in tailored risk-based patient management strategies.
4. Patient awareness and education initiatives are vital. Individuals with T2DM should be informed about potential risk of NAFLD along with importance of regular liver health assessment. Making self-assessment tools such as FLI and TyG calculators available through digital platforms may empower patients to engage actively in disease prevention and monitoring.

In summary, while FLI and TyG indices do not replace definitive diagnostic methods such as liver biopsy or advanced imaging, they provide a practical, economical, and accessible means of identifying at-risk individuals.

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# SUMMARY



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## SUMMARY

This study, titled “A Prospective Cohort Study of Fatty Liver Index and Triglyceride Glycemic Index as Markers for Identifying Non-Alcoholic Fatty Liver Disease in Type 2 Diabetes Patients,” was conducted at RL Jalappa Hospital, Tamaka, Kolar, between May 2023 and October 2024. Research objective was to compare efficacy of 2 indices—FLI and TyG—in diagnosing NAFLD among T2DM.

85 subjects with T2DM were included in study. These patients underwent through anthropometric as well as biochemical measures, and values were analyzed comparing with elastography score to determine presence of NAFLD. FLI was calculated using serum triglycerides, waist circumference, GGT, along with BMI. TyG was calculated using fasting triglycerides and fasting plasma glucose.

Findings revealed no differences between both the NAFLD and non-NAFLD subjects statistically when comparing FLI and TyG indices. FLI in NAFLD cases was  $59.1 \pm 11.3$ , compared to  $57.8 \pm 18.6$  in non-NAFLD cases ( $p=0.780$ ). TyG index was similarly non-significant, with  $8.6 \pm 0.9$  for NAFLD cases and  $8.4 \pm 1.14$  for non-NAFLD ( $p=0.483$ ). Elastography also did not yield significant differences across groups.

However, despite these statistical outcomes, a closer look at the area under the ROC curve indicated slight diagnostic potential: 53.8% for FLI and 55.4% for TyG index. These figures suggest a limited yet potentially valuable utility in screening settings where ultrasonography is inaccessible. The study also stratified the population by demographic features. The majority were aged between 61-70yrs and had a  $BMI > 25$ , indicating a typical high-risk profile for NAFLD. Males predominated the sample, comprising 65.9% of the participants. This study enriches the limited body of comparative literature on FLI and TyG index as screening tools for NAFLD in T2DM patients. While neither index demonstrated statistically significant predictive accuracy, both showed moderate sensitivity and specificity at certain thresholds. Notably, at a FLI cut-off of 54.5, sensitivity was 57.4% and specificity 35.3%, while at TyG cut-off 8.47, sensitivity was 57.4% and specificity 59.4%.

While ultrasound remains standard for NAFLD detection, these indices, derived from simple, non-invasive blood and anthropometric parameters, offer accessible alternatives for risk stratification in resource-limited settings.

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# ANNEXURES



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## INFORMED CONSENT FORM

Date:

I, Mr/Mrs \_\_\_\_\_, have been explained in my own vernacular language that I/We will be included in **A PROSPECTIVE COHORT STUDY OF FATTY LIVER INDEX AND TRIGLYCERIDE GLYCEMIC INDEX AS A MARKERS FOR IDENTIFYING NON ALCOHOLIC FATTY LIVER CHANGES IN TYPE 2 DIABETES PATIENTS**

Hereby I/We give my valid written informed consent without any force or prejudice for recording the observations of haematological and clinical parameters. I have been explained in detail about the study being conducted. I have read the patient information sheet and I have had the opportunity to ask any question. Any question that I have asked, have been answered to my satisfaction. I provide consent voluntarily to allow myself as a participant in this research. I hereby give consent to provide history, undergo physical examination, undergo investigations and provide its results and documents etc to the doctor / institute etc. All the data may be published or used for any academic purpose.

\_\_\_\_\_

Name of Patient/Guardian

(Relation with patient)

\_\_\_\_\_

(Signature of Patient / Attendant)

(Signature & Name of Research doctor)

## ರೋಗಿಯ ಮಾಹಿತಿ ಹಾಳೆ

ಅಧ್ಯಯನದ ಶೀರ್ಷಿಕೆ: ಎ ಪ್ರಾಸ್ಟೆಕ್ಟಿವ್ ಕೊಹಾರ್ಟ್ ಸ್ಟಡಿ ಆಫ್ ಫ್ಯಾಟಿ ಲಿವರ್ ಇಂಡೆಕ್ಸ್ ಅಂಡ್ ಟ್ರೈಗ್ಲಿಸೆರೈಡ್ ಗ್ಲೈಸಿಮಿಕ್ ಇಂಡೆಕ್ಸ್ ಅಸ್ ಎ ಮಾರ್ಕರ್ ಫಾರ್ ಐಡೆಂಟಿಫೈಯಿಂಗ್ ನಾನ್ ಆಲ್ಕೋಹಾಲಿಕ್ ಫ್ಯಾಟಿ ಲಿವರ್ ಡಿಸೀಸ್ ಇನ್ ಟೈಪ್ 2 ಡಯಾಬಿಟಿಸ್ ಪೇಷಂಟ್ಸ್ ಅಧ್ಯಯನ ಮಾಡಲು.

ಪ್ರಧಾನ ತನಿಖಾಧಿಕಾರಿ: ಡಾ. ಮಧುರಿಮಾ ಪುಟ್ಟಗುಂಟ / ಡಾ.ರವೀಶಾ ಎ

ಶ್ರೀ ದೇವರಾಜ್ ಅರಸ್ ಮೆಡಿಕಲ್ ಕಾಲೇಜಿನಲ್ಲಿ ಸಾಮಾನ್ಯ ಔಷಧಿ ವಿಭಾಗದಲ್ಲಿ ಸ್ನಾತಕೋತ್ತರ ವಿದ್ಯಾರ್ಥಿ ಡಾ. ಮಧುರಿಮಾ ಪುಟ್ಟಗುಂಟ, “ಎ ಪ್ರಾಸ್ಟೆಕ್ಟಿವ್ ಕೊಹಾರ್ಟ್ ಸ್ಟಡಿ ಆಫ್ ಫ್ಯಾಟಿ ಲಿವರ್ ಇಂಡೆಕ್ಸ್ ಅಂಡ್ ಟ್ರೈಗ್ಲಿಸೆರೈಡ್ ಗ್ಲೈಸಿಮಿಕ್ ಇಂಡೆಕ್ಸ್ ಅಸ್ ಎ ಮಾರ್ಕರ್ ಫಾರ್ ಐಡೆಂಟಿಫೈಯಿಂಗ್ ನಾನ್ ಆಲ್ಕೋಹಾಲಿಕ್ ಫ್ಯಾಟಿ ಲಿವರ್ ಡಿಸೀಸ್ ಇನ್ ಟೈಪ್ 2 ಡಯಾಬಿಟಿಸ್ ಪೇಷಂಟ್ಸ್” ಎಂಬ ಅಧ್ಯಯನವನ್ನು ನಡೆಸಲಿದ್ದೇನೆ. ಮುಂದಿನ ದಿನಗಳಲ್ಲಿ ಫ್ಯಾಟಿ ಲಿವರ್ ಉಲ್ಬಣಗೊಳ್ಳುವಿಕೆಯ ಮತ್ತಷ್ಟು ನಿರ್ವಹಣೆಗೆ ಉಪಯುಕ್ತವಾಗಿದೆ. ಯಕೃತ್ತಿನ ಕಾರ್ಯ ಪರೀಕ್ಷೆಗಳಿಗೆ ಅಗತ್ಯವಾದ ಹಣವನ್ನು ನನ್ನ ಸ್ವಂತ ವೆಚ್ಚದಲ್ಲಿ ಮಾಡಲಾಗುತ್ತದೆ ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸುವ ಪ್ರತಿಯೊಬ್ಬ ರೋಗಿಗಳಿಂದ ಯಕೃತ್ತಿನ ಕಾರ್ಯ ಪರೀಕ್ಷೆ ಮತ್ತು ಸಕ್ಕರೆಯ ಮಟ್ಟ ಅಂದಾಜು ಮಾಡಲು ರಕ್ತವನ್ನು ಎಳೆಯಲಾಗುತ್ತದೆ. ಈ ಅಧ್ಯಯನವನ್ನು ಡಾ.ರವೀಶಾ ಎ, ಮಾರ್ಗದರ್ಶನದಲ್ಲಿ ಮಾಡಲಾಗುವುದು

ಎಲ್ಲಾ ಡೇಟಾವನ್ನು ಗೌಪ್ಯವಾಗಿಡಲಾಗುತ್ತದೆ ಮತ್ತು ಸಂಸ್ಥೆಯು ನಿರ್ದಿಷ್ಟಪಡಿಸಿದ ಉದ್ದೇಶಕ್ಕಾಗಿ ಮಾತ್ರ ಬಳಸಲಾಗುತ್ತದೆ. ಈ ಅಧ್ಯಯನದಲ್ಲಿ ನಿಮ್ಮ ಭಾಗವಹಿಸುವಿಕೆಗೆ ನೀವು ಒಪ್ಪಿಗೆ ನೀಡಲು ಮುಕ್ತರಾಗಿದ್ದೀರಿ. ಯಾವುದೇ ಕಾರಣಗಳನ್ನು ನೀಡದೆ ನೀವು ಯಾವುದೇ ಸಮಯದಲ್ಲಿ ಅಧ್ಯಯನದಿಂದ ನಿಮ್ಮನ್ನು ಹಿಂತೆಗೆದುಕೊಳ್ಳಬಹುದು. ನೀವು ಭಾಗವಹಿಸಲು ನಿರಾಕರಿಸುವುದರಿಂದ ಈ ಸಂಸ್ಥೆಯಲ್ಲಿ ಯಾವುದೇ ಪ್ರಸ್ತುತ ಅಥವಾ ಭವಿಷ್ಯದ ಆರೈಕೆಗೆ ನೀವು ಪೂರ್ವಾಗ್ರಹ ಮಾಡುವುದಿಲ್ಲ.

ಯಾವುದೇ ಸ್ಪಷ್ಟೀಕರಣಗಳು ಅಗತ್ಯವಿದ್ದರೆ ನೀವು ನನ್ನನ್ನು ಈ ಮೊಬೈಲ್ ಸಂಖ್ಯೆಯಲ್ಲಿ ಸಂಪರ್ಕಿಸಲು ಮುಕ್ತರಾಗಿದ್ದೀರಿ - 9963309797

ಪ್ರಧಾನ ತನಿಖಾಧಿಕಾರಿಯ ಹೆಸರು ಮತ್ತು ಸಹಿ

ದಿನಾಂಕ-

ರೋಗಿಯ ಅಥವಾ ರೋಗಿಯ ವೀಕ್ಷಕರ ಸಹಿ

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## PATIENT INFORMATION SHEET

**Study title : A PROSPECTIVE COHORT STUDY OF FATTY LIVER INDEX AND TRIGLYCERIDE GLYCEMIC INDEX AS A MARKERS FOR IDENTIFYING NONALCOHOLIC FATTY LIVER CHANGES IN TYPE 2 DIABETES PATIENTS**

Principal investigator: Dr Madhurima Puttagunta /Dr.Raveesha A

I Dr. Madhurima Puttagunta , Post graduate student in Department of general medicine at Sri Devraj Urs Medical College, will be conducting a study titled “**A PROSPECTIVE COHORT STUDY OF FATTY LIVER INDEX AND TRIGLYCERIDE GLYCEMIC INDEX AS A MARKERS FOR IDENTIFYING NON ALCOHOLIC FATTY LIVER CHANGES IN TYPE 2 DIABETES PATIENTS**” .This study will be useful to identify risk of non-alcoholic fatty liver changes in type 2 diabetes patients with simple triglyceride glycaemic index test and also fatty liver index will be useful to conform presence of fatty liver even in areas where ultrasound is not present. 2 ml of blood will be drawn for estimation of fasting blood glucose and fasting triglyceride levels , from each of the participating patients in this study. Participants in this study will under ultrasound scan. This study will be done under the guidance of Dr.RAVEESHA A, Professor of Department of GENERAL MEDICINE .

All the data will be kept confidential and will be used only for purpose specified by the institution. You are free to provide consent for the participation of yourself in this study. You can also withdraw yourself from the study at any point of time without giving any reasons whatsoever. Your refusal to participate will not prejudice you to any present or future care at this institution. All the expenses will be borne by the principal investigator

In case of any clarifications are needed you are free to contact me on this mobile number - 9963309797

Name and Signature of the Principal Investigator

Date-

Patient or patient bystanders Signature

## ರೋಗಿಯ ಮಾಹಿತಿ ಹಾಳೆ

ಅಧ್ಯಯನ ಶೀರ್ಷಿಕೆ: ಟೈಪ್ 2 ಮಧುಮೇಹ ರೋಗಿಗಳಲ್ಲಿ ಆಲೋಹಾಲ್ಯುಕ್ತವಲ್ಲದ ಕೊಬ್ಬಿನ ಯಕೃತ್ತಿನ ಬದಲಾವಣೆಗಳನ್ನು ಗುರುತಿಸುವ ಗುರುತುಗಳಾಗಿ ಕೊಬ್ಬಿನ ಯಕೃತ್ತಿನ ಸೂಚ್ಯಂಕ ಮತ್ತು ಟ್ರೈಗ್ಲಿಸರೈಡ್ ಗ್ಲೈಸೆಮಿಕ್ ಸೂಚ್ಯಂಕದ ನಿರೀಕ್ಷಿತ ಸಹ-ಅಧ್ಯಯನ

ಪ್ರಧಾನ ತನಿಖಾಧಿಕಾರಿ: ಡಾ. ಮಧುರಿಮಾ ಪುಟ್ಟಗುಂಟ / ಡಾ. ರವೀಶ್ ಎ

ಶ್ರೀ ದೇವರಾಜ್ ಉರ್ಸ್ ವೈದ್ಯಕೀಯ ಕಾಲೇಜಿನಲ್ಲಿ ಜನರಲ್ ಮೆಡಿಸಿನ್ ವಿಭಾಗದಲ್ಲಿ ಸ್ನಾತಕೋತ್ತರ ವಿದ್ಯಾರ್ಥಿನಿ ಡಾ. ಮಧುರಿಮಾ ಪುಟ್ಟಗುಂಟ ಅವರು "ಟೈಪ್ 2 ಮಧುಮೇಹ ರೋಗಿಗಳಲ್ಲಿ ಆಲೋಹಾಲ್ಯುಕ್ತವಲ್ಲದ ಕೊಬ್ಬಿನ ಯಕೃತ್ತಿನ ಬದಲಾವಣೆಗಳನ್ನು ಗುರುತಿಸುವ ಗುರುತುಗಳಾಗಿ ಕೊಬ್ಬಿನ ಯಕೃತ್ತಿನ ಸೂಚ್ಯಂಕ ಮತ್ತು ಟ್ರೈಗ್ಲಿಸರೈಡ್ ಗ್ಲೈಸೆಮಿಕ್ ಸೂಚ್ಯಂಕದ ನಿರೀಕ್ಷಿತ ಸಹ-ಅಧ್ಯಯನ" ಎಂಬ ಶೀರ್ಷಿಕೆಯ ಅಧ್ಯಯನವನ್ನು ನಡೆಸಲಿದ್ದಾರೆ. ಈ ಅಧ್ಯಯನವು ಟೈಪ್ 2 ಮಧುಮೇಹ ರೋಗಿಗಳಲ್ಲಿ ಆಲೋಹಾಲ್ಯುಕ್ತವಲ್ಲದ ಕೊಬ್ಬಿನ ಯಕೃತ್ತಿನ ಬದಲಾವಣೆಗಳ ಅಪಾಯವನ್ನು ಗುರುತಿಸಲು ಉಪಯುಕ್ತವಾಗಿರುತ್ತದೆ. ಮಧುಮೇಹ ರೋಗಿಗಳಿಗೆ ಸರಳ ಟ್ರೈಗ್ಲಿಸರೈಡ್ ಗ್ಲೈಸೆಮಿಕ್ ಸೂಚ್ಯಂಕ ಪರಿಶೀಲನೆ ಮತ್ತು ಕೊಬ್ಬಿನ ಪಿತ್ತಜನಕಾಂಗ ಸೂಚ್ಯಂಕವು ಅಲ್ಪಾಸೌಂಡ್ ಇಲ್ಲದ ಪ್ರದೇಶಗಳಲ್ಲಿಯೂ ಸಹ ಕೊಬ್ಬಿನ ಪಿತ್ತಜನಕಾಂಗದ ಉಪಸ್ಥಿತಿಯನ್ನು ಪರಿಶೀಲಿಸಲು ಉಪಯುಕ್ತವಾಗಿರುತ್ತದೆ. ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸುವ ಪ್ರತಿಯೊಬ್ಬ ರೋಗಿಯಿಂದ ಉಪವಾಸ ರಕ್ತದಲ್ಲಿನ ಗ್ಲೂಕೋಸ್ ಮತ್ತು ಉಪವಾಸ ಟ್ರೈಗ್ಲಿಸರೈಡ್ ಮಟ್ಟವನ್ನು ಅಂದಾಜು ಮಾಡಲು 2 ಮಿಲಿ ರಕ್ತವನ್ನು ತೆಗೆದುಕೊಳ್ಳಲಾಗುತ್ತದೆ. ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸುವವರು ಅಲ್ಪಾಸೌಂಡ್ ಸ್ಯಾನ್‌ಗೆ ಒಳಗಾಗುತ್ತಾರೆ. ಈ ಅಧ್ಯಯನವನ್ನು ಜನರಲ್ ಮೆಡಿಸಿನ್ ವಿಭಾಗದ ಪ್ರಾಧ್ಯಾಪಕರಾದ ಡಾ.ರವೀಶ್ ಎ ಅವರ ಮಾರ್ಗದರ್ಶನದಲ್ಲಿ ಮಾಡಲಾಗುತ್ತದೆ.

ಎಲ್ಲಾ ಡೇಟಾವನ್ನು ಗೌಪ್ಯವಾಗಿಡಲಾಗುತ್ತದೆ ಮತ್ತು ಸಂಸ್ಥೆಯು ನಿರ್ದಿಷ್ಟಪಡಿಸಿದ ಉದ್ದೇಶಕ್ಕಾಗಿ ಮಾತ್ರ ಬಳಸಲಾಗುತ್ತದೆ. ಈ ಅಧ್ಯಯನದಲ್ಲಿ ನಿಮ್ಮ ಭಾಗವಹಿಸುವಿಕೆಗೆ ನೀವು ಒಪ್ಪಿಗೆ ನೀಡಲು ಸ್ವತಂತ್ರರು. ಯಾವುದೇ ಕಾರಣಗಳನ್ನು ನೀಡದೆ ನೀವು ಯಾವುದೇ ಸಮಯದಲ್ಲಿ ಅಧ್ಯಯನದಿಂದ ಹಿಂದೆ ಸರಿಯಬಹುದು. ಭಾಗವಹಿಸಲು ನಿಮ್ಮ ನಿರಾಕರಣೆಯು ಈ ಸಂಸ್ಥೆಯಲ್ಲಿನ ಯಾವುದೇ ಪ್ರಸ್ತುತ ಅಥವಾ ಭವಿಷ್ಯದ ಆರೈಕೆಗೆ ನಿಮ್ಮನ್ನು ಹಾನಿಗೊಳಿಸುವುದಿಲ್ಲ. ಎಲ್ಲಾ ವೆಚ್ಚಗಳನ್ನು ಪ್ರಧಾನ ತನಿಖಾಧಿಕಾರಿ ಭರಿಸುತ್ತಾರೆ

ಯಾವುದೇ ಸ್ಪಷ್ಟೀಕರಣಗಳ ಅಗತ್ಯವಿದ್ದರೆ ನೀವು ಈ ಮೊಬೈಲ್ ಸಂಖ್ಯೆ - 9963309797 ನಲ್ಲಿ ನನ್ನನ್ನು ಸಂಪರ್ಕಿಸಬಹುದು

ಪ್ರಧಾನ ತನಿಖಾಧಿಕಾರಿಯ ಹೆಸರು ಮತ್ತು ಸಹಿ

ದಿನಾಂಕ-

ರೋಗಿ ಅಥವಾ ರೋಗಿಯ ಪಕ್ಕದಲ್ಲಿರುವವರ ಸಹಿ

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**PROFORMA**

<b>NAME</b>	
<b>AGE</b>	
<b>GENDER</b>	
<b>DATE OF ADMISSION</b>	
<b>Risk factor :</b> <b>1. SMOKER (Y/N)</b> <b>If Yes , number of pack years</b>  <b>1. Drinking</b> <b>If yes , quantity of daily consumption (Y/N)</b>	
<b>CORMORDBIDITES</b> <b>TYPE 2 DIABETES</b> <b>(Y/N)</b>	
<b>DURATION OF STAY IN HOSPITAL</b>	

**INVESTIGATIONS**

**1.COMplete HEMOGRAM**

DATE	HB	RBC	PCV	MCV	WBC	PLATLETS

**2. SERUM ELECTROLYTES AND RFT**

DATE	UREA	CREAT	SODIUM	POTASSIUM	MAGNESIUM

- 2. Liver function tests**
- 3. urine routine**
- 4. Fasting blood glucose, Post prandial blood glucose**
- 5. Albumin creatinine ratio**
- 6. Fasting triglyceride levels**
- 7. Fasting insulin level**
- 8. Uric Acid**
- 9. Lipid profile**
- 10.HBA1C**

Sl no	AGE OF PATIENT	SEX OF PATIENT	NAFLD	BMI OF PATIENT	FATTY LIVER INDEX	TGY INDEX	Hb A1c	ELASTOGRAPHY SCORE	CORRELATION
1	55	Male	Yes	28	80.00	8.90	10.40	9.00	Yes
2	64	Male	Yes	30	89.00	8.51	11.00	8.20	Yes
3	72	Female	Yes	40	100.00	8.03	9.20	9.20	Yes
4	45	Female	No	23	35.00	8.93	7.40	5.60	No
5	58	Male	Yes	25	63	8.32	7	5.2	No
6	40	Female	Yes	23	68	9.91	9	8.2	Yes
7	48	Male	Yes	28	95	8.91	10.2	6.7	Yes
8	45	Female	Yes	28	78	9.6	9	7.9	Yes
9	50	Male	Yes	30	32	8.45	10	5.5	No
10	49	Male	Yes	25	55	8.6	7.9	8.3	Yes
11	63	Male	No	24	62	8	8.4	8.4	Yes
12	63	Male	Yes	26	58	8	6.9	8.6	Yes
13	50	Male	Yes	29	83	9.32	7.1	7.9	Yes
14	49	Male	Yes	28	61	8.9	9	9.1	Yes
15	45	Female	Yes	25	32	8.91	7.2	5.4	No
16	55	Female	Yes	26	28	8.95	7.9	7.9	Yes
17	69	Male	No	32	71	8.95	7.9	7.9	Yes
18	55	Male	Yes	29	83	9.32	10	8.7	Yes
19	40	Female	Yes	28	61	8.4	8.9	7.7	Yes
20	59	Female	Yes	25	39	8.22	9.5	8.6	Yes
21	61	Male	Yes	32	71	8.5	7	7.8	Yes
22	45	Male	Yes	29	82	8.8	9	10	Yes
23	54	Female	No	24	78	9.4	7.3	6.5	No
24	75	Male	Yes	28	60	9.3	11	6.8	Yes
25	62	Male	No	30	50	8.9	7.4	8.4	Yes
26	68	Male	Yes	29	29	8.4	6.8	6.6	No
27	64	Female	Yes	24	45	8.5	8.4	6.9	Yes
28	65	Male	Yes	25	40	8	9	6	No
29	62	Male	No	30	45	8.6	7	7.1	Yes
30	64	Male	Yes	28	55	9.6	8.5	7.9	Yes
31	63	Female	Yes	32	67	9.5	6.3	10	Yes
32	52	Male	No	25	67	8.9	7.9	8.4	Yes
33	54	Male	Yes	27	45	8.3	7.5	6.6	No
34	56	Male	Yes	30	47	8.1	6.9	6.9	Yes
35	62	Male	Yes	22	68	8.9	9.1	8.4	Yes
36	48	Female	No	31	57	8.1	9.6	8.7	Yes
37	54	Male	Yes	29	54	8.9	8.9	11	Yes
38	56	Male	Yes	28	30	8.9	8.6	9.8	Yes
39	62	Male	No	27	55	8.9	8.9	7.9	Yes
40	68	Female	Yes	28	45	7.9	7.9	6.9	Yes
41	52	Male	Yes	26	68	5.4	7.4	8	Yes
42	45	Male	No	32	69	9.4	8.6	5.6	No
43	53	Female	Yes	29	50	8.8	9.6	7.6	Yes

Sl no	AGE OF PATIENT	SEX OF PATIENT	NAFLD	BMI OF PATIENT	FATTY LIVER INDEX	TGY INDEX	Hb A1c	ELASTOGRAPHY SCORE	CORRELATION
44	56	Male	Yes	29	70	8.4	10	7.9	Yes
45	62	Male	No	32	69	8.5	9.9	8.9	Yes
46	68	Male	Yes	23	66	9.5	6.8	9	Yes
47	64	Female	Yes	29	47	8.8	8.9	9	Yes
48	63	Male	No	30	67	8.5	8.6	8.4	Yes
49	62	Male	Yes	25	45	8.5	9.6	6.6	No
50	68	Male	Yes	24	47	7.8	10	6.9	Yes
51	64	Female	No	30	68	5.8	8.5	8.4	Yes
52	65	Male	Yes	45	78	9.4	6.3	7.2	Yes
53	62	Male	Yes	35	60	8.3	7.9	8.4	Yes
54	64	Female	Yes	30	50	8.9	11	6.6	No
55	63	Male	Yes	29	29	9.1	7.4	6.9	Yes
56	52	Male	Yes	26	28	8.3	6.8	9	Yes
57	54	Female	Yes	32	71	8.9	9.6	5.6	No
58	56	Male	Yes	29	83	8.7	8.9	7.6	Yes
59	62	Male	Yes	29	61	9.67	8.6	7.9	Yes
60	48	Female	Yes	25	45	8.95	10	8.7	Yes
61	54	Male	Yes	27	47	8.32	8.9	11	Yes
62	56	Female	Yes	30	68	5.4	9.5	9.8	Yes
63	62	Male	Yes	22	57	4.95	7	8.7	Yes
64	68	Female	Yes	24	54	9.32	9	7.7	Yes
65	52	Male	Yes	26	55	6.32	7.3	8.6	Yes
66	45	Male	Yes	27	88	8.1	7.9	7.9	Yes
67	53	Female	Yes	28	82	8.9	7.4	6.9	Yes
68	56	Male	Yes	26	78	8.1	9.6	8	Yes
69	62	Male	Yes	26	60	6.9	8.9	5.6	No
70	68	Female	Yes	32	50	8.45	8.6	6.5	No
71	64	Male	Yes	29	29	9.6	7.9	6.8	Yes
72	63	Female	Yes	32	67	8.4	7.5	8.4	Yes
73	62	Male	Yes	29	50	9.8	6.9	6.6	No
74	68	Male	Yes	28	29	9.4	9.1	8.2	Yes
75	64	Female	Yes	30	33	8.8	10	9.2	Yes
76	62	Male	Yes	29	61	9.67	8.6	7.9	Yes
77	48	Female	Yes	25	45	8.95	10	8.7	Yes
78	54	Male	Yes	27	47	8.32	8.9	11	Yes
79	56	Female	Yes	30	68	5.4	9.5	9.8	Yes
80	62	Male	Yes	22	57	4.95	7	8.7	Yes
81	68	Female	Yes	24	54	9.32	9	7.7	Yes
82	52	Male	Yes	26	55	6.32	7.3	8.6	Yes
83	45	Male	Yes	27	88	8.1	7.9	7.9	Yes
84	68	Female	Yes	32	50	8.45	8.6	6.5	No
85	64	Male	Yes	29	29	9.6	7.9	6.8	Yes