"STUDY OF CLINICAL PROFILE OF PATIENTS OF NON ALCOHOLIC FATTY LIVER DISEASE AND ITS ASSOCIATION WITH METABOLIC SYNDROME"

By

REG. NO. BG0116008

Dissertation

Submitted to the

KLE Academy of Higher Education and Research,

Belagavi, Karnataka.

In partial fulfilment

of the requirements for the degree of

M.D.

in

GENERAL MEDICINE

DEPARTMENT OF GENERAL MEDICINE,

JAWAHARLAL NEHRU MEDICAL COLLEGE,

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APRIL - 2019

KLE ACADEMY OF HIGHER EDUCATION AND RESEARCH, BELAGAVI, KARNATAKA

DECLARATION BY THE CANDIDATE

I hereby declare that this dissertation entitled **"STUDY OF CLINICAL PROFILE OF PATIENTS OF NON ALCOHOLIC FATTY LIVER DISEASE AND ITS ASSOCIATION WITH METABOLIC SYNDROME"** is a bonafide and genuine research work carried out by me at Jawaharlal Nehru Medical College, Nehru Nagar, Belagavi – 590010.

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ENDORSEMENT

This is to certify that the dissertation entitled **"STUDY OF CLINICAL PROFILE OF PATIENTS OF NON ALCOHOLIC FATTY LIVER DISEASE AND ITS ASSOCIATION WITH METABOLIC SYNDROME"** is a bonafide research work done by **(REG. NO. BG0116008)** at Jawaharlal Nehru Medical College, Nehru Nagar, Belagavi – 590010.

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ABBREVATIONS

ALP	Alkaline Phosphatase
ALT	Alanine Aminotransferase
APO C3	Apolipoprotein C3
AST	Aspartate Aminotransferase
ATPIII	Adult Treatment Panel III
BMI	Body mass index
CAD	Coronary artery disease
CC	Cryptogenic Cirrhosis
CK 18	Cytokeratin 18
CT	Computed Tomography
DM	Diabetes Mellitus
EMA	Anti-Endomysial antibodies
FFA	Free Fatty Acids
FPG	Fasting Plasma Glucose
GTT	Glucose Tolerance Test
HCC	Hepatocellular Carcinoma
HOMA-IR	Homeostasis Model Assessment for Insulin Resistance
HTG	Hepatic triglyceride
HTN	Hypertension
IFG	Impaired Fasting Glucose
IGT	Impaired Glucose Tolerance
IKK-β	Inhibitor of nuclear factor kappa-B kinase beta
IR	Insulin resistance
IRS-1	Insulin Receptor Substrate-1
LFTs	Liver Function Tests
MRE	Magnetic Resonance Elastography

MS	Metabolic syndrome
NAFLD	Non-alcoholic fatty liver disease
NASH	Non-Alcoholic Steatohepatitis
PCOS	Polycystic Ovarian Syndrome
PPG	Post-Prandial Glucose
T2DM	Type 2 Diabetes Mellitus
TG	Triglycerides
TTG	Anti-tissue transglutaminase
VLDL	Very Low Density Lipoprotein
WHO	World Health Organization

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ABSTRACT

BACKGROUND AND OBJECTIVES: Non-alcoholic fatty liver disease (NAFLD) is considered to be the commonest liver problem in the western world and is increasingly being recognized as a major cause of liver-related morbidity and mortality. It is known to be associated with various metabolic abnormalities, but not much information regarding association between the metabolic disease and the severity of fatty liver is available.

METHODS: 100 consecutive patients aged >18 years attending the outpatient and inpatient of department of medicine, Jawaharlal Nehru medical college and hospital from January 2017-18, were included according to the inclusion and exclusion criteria. Relevant clinical, anthropometric, biochemical and radiological data was recorded. The study was an observational and analytical study of patients diagnosed as NAFLD. All patients diagnosed as NAFLD were investigated for metabolic syndrome according to the NCEP ATP 3 criteria and a relationship between NAFLD and metabolic syndrome was studied.

RESULTS: 53% of patients of NAFLD had metabolic syndrome and statistical significance was found in waist circumference, blood pressure, triglycerides and fasting glucose.

CONCLUSION: There is higher prevalence of all the components of metabolic syndrome in cases of NAFLD. Its early detection will help in modifying the disease course, delaying complications and will also play a major role in preventive cardiology.

INTRODUCTION

1. INTRODUCTION

Non-alcoholic fatty liver disease encompasses the entire spectrum of fatty liver disease in individuals without significant alcohol consumption, ranging from fatty liver to steato-hepatitis and cirrhosis.

Non-alcoholic fatty liver disease (NAFLD), is now considered to be the commonest liver problem in the western world affecting 15-40% of the general population.[1] Non-alcoholic fatty liver disease is increasingly being recognized as a major cause of liver-related morbidity and mortality.[2,]

Because of its potential to progress to cirrhosis and liver failure, interest in this disease is increasing among researchers and clinicians in the relevant basic and clinical science fields.

The pathologic picture of non-alcoholic fatty liver disease, ranging from simple steatosis to steatohepatitis, advanced fibrosis and cirrhosis, resembles that of alcohol induced liver disease.[3] Nonalcoholic steato-hepatitis that is characterised by hepatic steatosis, liver cell injury, hepatic inflammation, fibrosis and necrosis is believed to be an intermediate stage of non-alcoholic fatty liver disease.[2]

It has been suggested that fatty liver disease can be considered to be the hepatic consequence or component of metabolic syndrome or a cluster of metabolic disorders. This disease is often associated with obesity, type 2 diabetes mellitus, dyslipidaemia and hypertension. Each of these abnormalities carries a cardiovascular disease risk and together they are often categorized as the insulin resistance syndrome or the metabolic syndrome.[5-9]

The third report of the national cholesterol education program expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (adult treatment panel III [ATP III])

recommended the use of 5 variables for diagnosing the metabolic syndrome, namely waist circumference, serum triglyceride level, serum high-density lipoprotein (HDL) cholesterol level, blood pressure, and fasting plasma glucose level.[10]

The frequent association of non alcoholic fatty liver disease with individual components of the metabolic syndrome is now well known. However, it is unknown whether the risk for this disease is increased in patients with the metabolic syndrome. This is important because the metabolic syndrome is an emerging problem worldwide and its prevalence is likely increasing.

This work was designed to study the clinical profile of patients of NAFLD with varying degrees of severity as diagnosed by ultrasonography and evaluate the cross-sectional relationship between the non-alcoholic fatty liver disease and the metabolic syndrome along with its individual components, as defined by the modified NCEP ATP III criteria.

OBJECTIVES OF THE STUDY

2. OBJECTIVES OF THE STUDY

1.To study the clinical profile of patients of non alcoholic fatty liver with varying degrees of severity as diagnosed by ultrasonography.

2. To study the correlation between non alcoholic fatty liver disease and metabolic syndrome along with its individual components.

REVIEW OF LITERATURE

3. REVIEW OF LITERATURE

NAFLD is an emerging chronic liver disease that may lead to liver cirrhosis and hepatic cellular carcinoma. It is defined as the abnormal accumulation of lipids primarily in the form of triglycerides in individuals who do not consume significant amount of alcohol (< 20g of ethanol/day).[11]

It is characterized by a spectrum of disease varying from simple steatosis through steato-hepatitis with fibrosis and scarring, which can lead to cirrhosis.[12] It is a multifactorial disease and is the hepatic manifestation of metabolic syndrome, it is now the most common chronic liver disease in many developed countries. NAFLD is expected to become an even more serious public health issue because of increased prevalence of obesity and aging. The disease can be associated with other co-morbidities and affects 80% of diabetes, 57 to 74% of obese people.[13]

The term non alcoholic steato-hepatitis (NASH) was first introduced in 1980 by Ludwig et al, he described liver histology changes resembling alcoholic hepatitis in 20 patients with no history of alcohol abuse. He also found the disease was more common in women. Most of the patients were obese and had obesity associated diseases such as diabetes and cholelithiasis.[14]

History:

Non-alcoholic fatty liver disease (NAFLD) was recognized by Zelman, and Westwater and Fainer as early as five decades ago.[15,16] For a longtime, 'fatty liver' was ignored, and was considered to be a fanciful appendage that ultrasound reports were tagged with by the ultrasonologist.

All this changed approximately one-quarter of a century ago when Ludwig et al at Mayo described the histological findings of fatty liver and coined the term 'non-alcoholic steatohepatitis (NASH), and gave the entity a modicum of respectability.[17]

Definitions:

Non-alcoholic Fatty Liver Disease (NAFLD): Indicates the presence of fatty infiltration of the liver, defined as fat exceeding 5%–10% of liver weight and frequently taken as fat in >5%–10% macrosteatotic hepatocytes in biopsy specimens. Encompasses the entire spectrum of fatty liver disease in individuals without significant alcohol consumption, ranging from fatty liver to steatohepatitis and cirrhosis.

Non-alcoholic Fatty Liver (NAFL): Presence of hepatic steatosis with no evidence of hepatocellular injury in the form of ballooning of the hepatocytes or no evidence of fibrosis. The risk of progression to cirrhosis and liver failure is minimal.

Non-alcoholic steatohepatitis (NASH): Presence of hepatic steatosis and inflammation with hepatocyte injury (ballooning) with or without fibrosis. This can progress to cirrhosis, liver failure and rarely liver cancer.

NASH Cirrhosis: Presence of cirrhosis with current or previous histological evidence of steatosis or steatohepatitis.

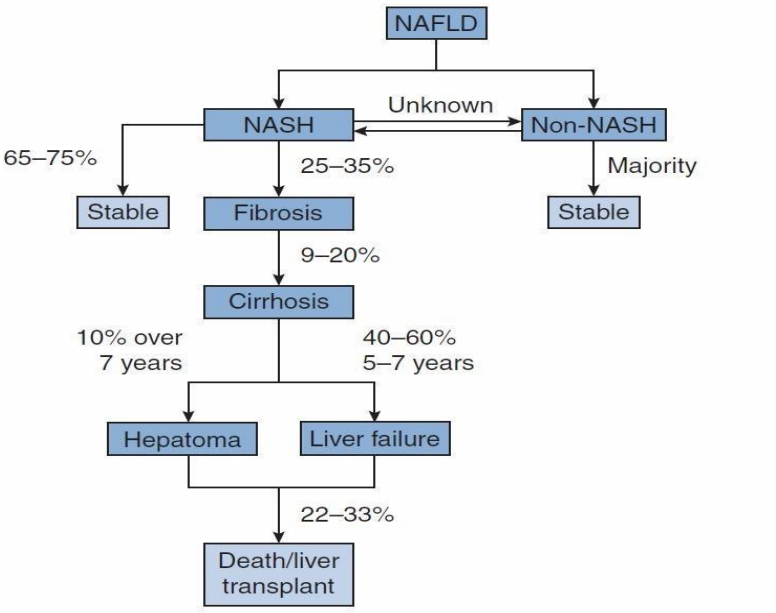
Cryptogenic Cirrhosis: Presence of cirrhosis with no obvious etiology. Patients with cryptogenic cirrhosis are heavily enriched with metabolic risk factors such as obesity and metabolic syndrome.

Global scenario:

The reported prevalence of NAFLD varies widely depending on the population studied and the definition used. In the Dallas Heart Study, when assessed by MR spectroscopy the prevalence of NAFLD in the general population was 31%.[18] The prevalence of suspected NAFLD when estimated using aminotransferases alone without imaging or histology ranged between 7% and 11%, but aminotransferases can be normal in individuals with NAFLD.[19] In summary, estimates of the worldwide prevalence of NAFLD ranges from 6.3% to 33% with a median of 20% in the general population, based on a variety of assessment methods.[19] The prevalence of NASH cirrhosis in the general population is not known. Many recent studies have reported that female gender is a risk factor for fatty liver disease.[19] For example, in a study of 26,527 subjects undergoing medical check-ups, the prevalence of NAFLD was 1% in men and 16% in women.[20] Compared to non-Hispanic whites, Hispanic individuals have significantly higher and non- Hispanic blacks have significantly lower prevalence of NAFLD.[18,21,22.] The prevalence of NAFLD in American Indian and Alaskan-Native populations appears lower, ranging from 0.6% to 2.2%, although the lack of histologic definition makes it likely that is an underestimate.[23,24]

Figure 1: Risk Factors Associated with NAFLD

Conditions with established association	Conditions with emerging association*
Obesity	Polycystic ovary syndrome
Type 2 diabetes mellitus	Hypothyroidism
Dyslipidemia	Obstructive Sleep apnea
Metabolic syndrome**	Hypopituitarism
	Hypogonadism
	Pancreato-duodenal resection



Natural History: Figure 2: Natural history of NAFLD progression

Natural history of Non-alcoholic fatty liver disease is quite variable. There are some inherent draw backs in studying natural history of NAFLD. [25,26] Firstly there is no definitive laboratory test for diagnosis. Various studies published have different definitions. The evolution of hepatic histologic changes in patients with NAFL and NASH has been investigated by several studies, but these generally included smaller number of patients and had relatively modest duration of follow-up.[19,27] Nonetheless, it is generally agreed that patients with simple steatosis have very slow, if any, histological progression, while patients with NASH can exhibit histological progression to cirrhotic-stage disease.[19,27] The long term outcomes of patients with NAFLD and NASH have been reported in several studies. Their findings can be summarized as follows; (a) patients with NAFLD have increased overall mortality compared to matched control populations, (b) the most common

cause of death in patients with NAFLD, NAFL and NASH is cardiovascular disease, and (c) patients with NASH (but not NAFL) have an increased liver-related mortality rate. Another piece of indirect evidence that supports the progressive nature of NASH is in the features of cryptogenic cirrhosis which is closely related to NAFLD.[28,29] Patients with cryptogenic cirrhosis have disproportionately high prevalence of metabolic risk factors (T2DM, obesity, metabolic syndrome) typical of patients with NAFLD, their liver biopsies frequently show one or more features of NASH, and studies have demonstrated the loss of histological features of NASH with the development of cirrhosis.[19,27,28,29] Patients with NAFLD are at increased risk for HCC, but this risk is likely limited to those with advanced fibrosis and cirrhosis.[30,31,32]

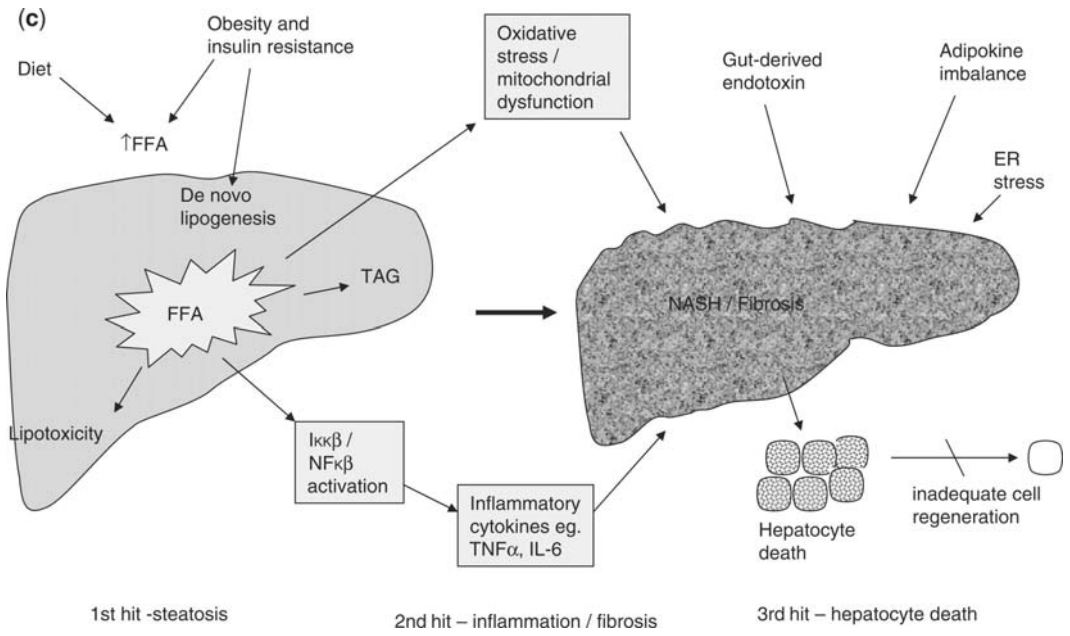
Pathogenesis:

The pathogenesis of NAFLD is currently not well understood. It has been hypothesized that this involves complex interactions of genetics and environmental factors. The early 'two-hit' model of NASH had proposed that the 'first hit' involve accumulation of lipids specially triglycerides (TG) inside the hepatocyte.[33] The lipid- rich environment inside the hepatocyte then provides the setting for oxidative stress constituting the 'second hit' that triggers hepato cellular injury, inflammation, and fibrosis.

Recently an alternative hypothesis has been proposed; the metabolites of fatty acids induce hepatocellular injury in NASH rather than the fatty acids themselves. The 'lipotoxicity' model of NASH suggests that the accumulation of triglyceride in the liver is not a cause of liver injury but rather which may paradoxically be protective. This excessive or inappropriate peripheral lipolysis, and excessive de novo lipogenesis, which exceeds the liver's ability to burn the fat or convert it to triglyceride which can be secreted. The flux of free fatty acids from the liver forms metabolites that cause hepato cellular injury in the form of stress to the endoplasmic reticulum, inflammation, apoptosis, and necrosis. Other contributors to the pathogenesis of NASH include mitochondrial

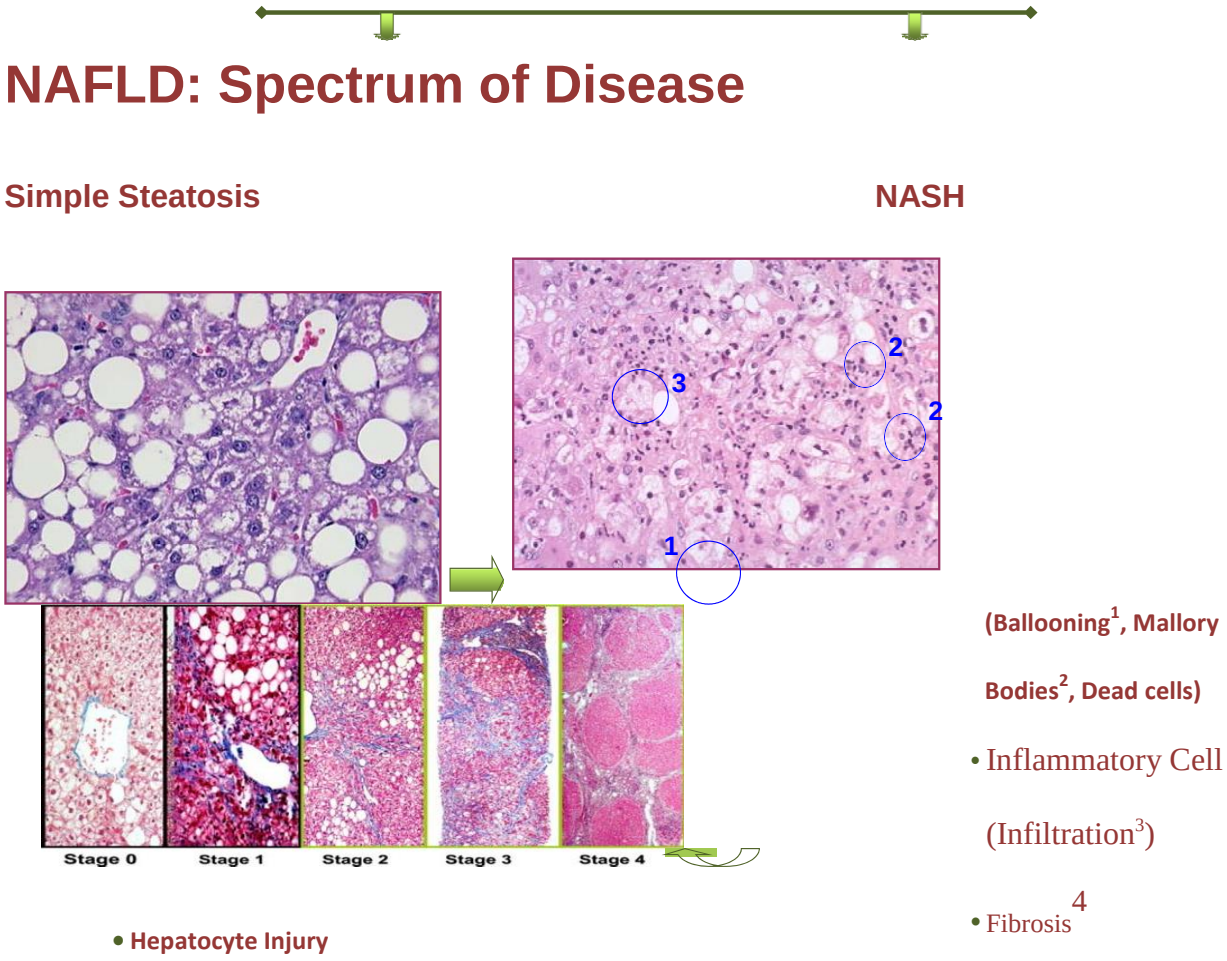
dysfunction,[34,35] impaired adenosine triphosphate (ATP) production,[36]hypoxia due to impaired blood flow,[37,38] gut-derived endotoxin and ethanol,[39,40] and dysregulation of adipokine [41,42] and cytokine production. While the exact etiology of NAFLD and NASH is unclear, insulin resistance appears to be central to the pathogenesis of NASH by allowing inappropriate levels of lipolysis from the adipose tissue and impairing peripheral glucose disposal. Besides insulin resistance, NAFLD is also closely associated with other characteristics of the metabolic syndrome including central obesity, hypertension and hyperlipidaemia. The obesity epidemic and increasing prevalence of the metabolic syndrome is predicted to be paralleled by an increasing prevalence of NAFLD in the future.

Figure 3: Pathogenesis of NAFLD



Pathology:

Figure 4: Histologic spectrum of NAFLD



Liver biopsy features include steatosis polymorph nuclear and/or mononuclear hepatocyte ballooning and necrosis, Mallory hyaline, glycogenated nuclei, mega mitochondria and fibrosis indistinguishable from alcoholic liver disease.

Steatosis in NASH is typically macro vesicular and inflammation of steatohepatitis is predominantly lobular, whereas intense portal inflammation with interface activity is more potent in other causes e.g. chronic viral, autoimmune or drug induced hepatitis.[43] However, interestingly

children with non-alcoholic steatohepatitis may have portal infiltrate which predominates over lobular inflammation.[33] Neutrophilic cells in lobular inflammatory infiltrate are a distinguishing feature of steatohepatitis and differentiate from earlier forms of acute and chronic hepatitis. Balloon degeneration is a recognized form of liver cell injury and is a significant feature of NASH. Mallory's hyaline is a characteristic finding of alcoholic hepatitis and its presence ranges from 90% to 95%.[44,45] Mallory hyaline presence is not mandatory for making a histological diagnosis of NASH. Mallory hyaline is absent or sparse in children with steatohepatitis.[33] In some patients of burnt out cirrhosis, features of steatosis and necroinflammatory activity may be absent.[44]
The pattern of fibrosis in NASH is initial collagen deposition is peri-venular and peri-sinusoidal spaces of zone [19]. In certain areas chicken wire fibrosis may be observed. This pattern is different from portal based fibrosis seen in other forms of chronic liver disease. Finding of fibrosis in NASH denotes a more severe and advanced liver disease.

Diagnosis:

Many times NAFLD is diagnosed incidentally as more than half of the patients are asymptomatic. One fourth to half patients may complain of right upper quadrant pain and equal no of patients may complain of fatigue. At times cirrhosis or its complications may be the initial presentation. Majority of the patients have normal physical examination. 25-50% may have clinically identifiable hepatomegaly. Mild to modest ALT, AST elevation is found in 25-50% of patients, remaining patients have normal liver enzymes. [46,47,48] The diagnosis of NAFLD requires that (a) there is hepatic steatosis by imaging or histology, (b) there is no significant alcohol consumption, (c) there are no competing etiologies for hepatic steatosis, and (d) there are no co-existing causes for chronic liver disease. Common alternative causes of hepatic steatosis are significant alcohol consumption, hepatitis C, medications, parenteral nutrition, Wilson's disease, and severe malnutrition.

Assessment of NAFLD:

All NAFLD patients should be assessed as follows:

Careful history: This is mandatory especially history of alcohol consumption to rule out alcoholic liver disease.

- Anthropometric evaluation: In any patient with NAFLD, one must measure height (in meters), weight (in kilogram), BMI (kg/m2) and waist circumference (cm). The patient should then be classified as: Overweight: body mass index (BMI) ≥23 but < 25 Kg/m2 or Obese (BMI > 25 Kg/m2); Central obesity should be as diagnosed by using the following Asia- Pacific criteria. Abnormal waist circumference is > 90 cm (men) and >80 cm (women).49,50
- Blood pressure should be measured not only because hypertension is common in NAFLD patients, but also because this is a criterion for metabolic syndrome.
- Biochemical tests: This must include serum bilirubin, serum AST, ALT, fasting sugar, and fasting lipid profile.
- Hematological tests: Complete blood count.
- Serological and immunological tests: Anti-HCV and HBsAg are essential in the workup of a NAFLD patient.
- Glycaemic profile and Insulin sensitivity: fasting blood glucose
- Abdominal ultrasound: the liver should be evaluated particularly with reference to the liver echogenicity in comparison to the echogenicity of kidney and spleen, vascular blurring and deep attenuation of ultrasound signal in order to classify hepatic steatosis: Fatty Liver is diagnosed in the presence of 2 of the following 3
    - Bright hepatic echo texture as compared to kidney and spleen
    - Blurring of hepatic veins
    - Loss of deep echo-discontinuous diaphragm.

Ultrasonographically hepatic steatosis can be classified as:

- Grade 1(mild): Normal visualization of diaphragm/intrahepatic vessels,
- Grade-2 (moderate): Impaired visualization of diaphragm/intrahepatic vessels,
- Grade 3(severe): Poor visualization of diaphragm/intrahepatic vessels.

The sensitivity of US in detecting steatosis varies between 60% and 94%. Optional non-invasive imaging modalities are abdominal CT scan, liver biopsy, MR Spectroscopy, MR elastography and fibroscan. Non-contrast enhanced CT is the most accurate CT technique to detect and characterize hepatic steatosis. [51] Magnetic resonance imaging provides an accurate and rapid assessment of hepatic steatosis to a lower limit of 3%. MRS provides a sensitive, quantitative, non-invasive method to measure HTGC (hepatic triglyceride content).[52] An MR equivalent of transient elastography (TE) has recently demonstrated excellent diagnostic accuracy with sensitivity and specificity of 98% and 99% respectively for detecting all grades of fibrosis.[53] Transient elastography (Fibroscan) is a non- invasive method of assessing liver fibrosis which can be performed at the bedside or in the outpatient clinic,it employs ultrasound-based technology to measure liver stiffness and had shown good results in patients with NAFLD.[54] Liver biopsy remains the gold standard for evaluating the degree of hepatic necro- inflammation and fibrosis, liver biopsy should be considered in situations when there is a diagnostic uncertainty,

Management:

The management of patients with NAFLD consists of treating liver disease as well as the associated metabolic co-morbidities such as obesity, hyperlipidaemia, insulin resistance and T2DM. As patients with NAFLD without steatohepatitis have excellent prognosis from a liver standpoint, treatments aimed at improving liver disease should be limited to those with NASH.

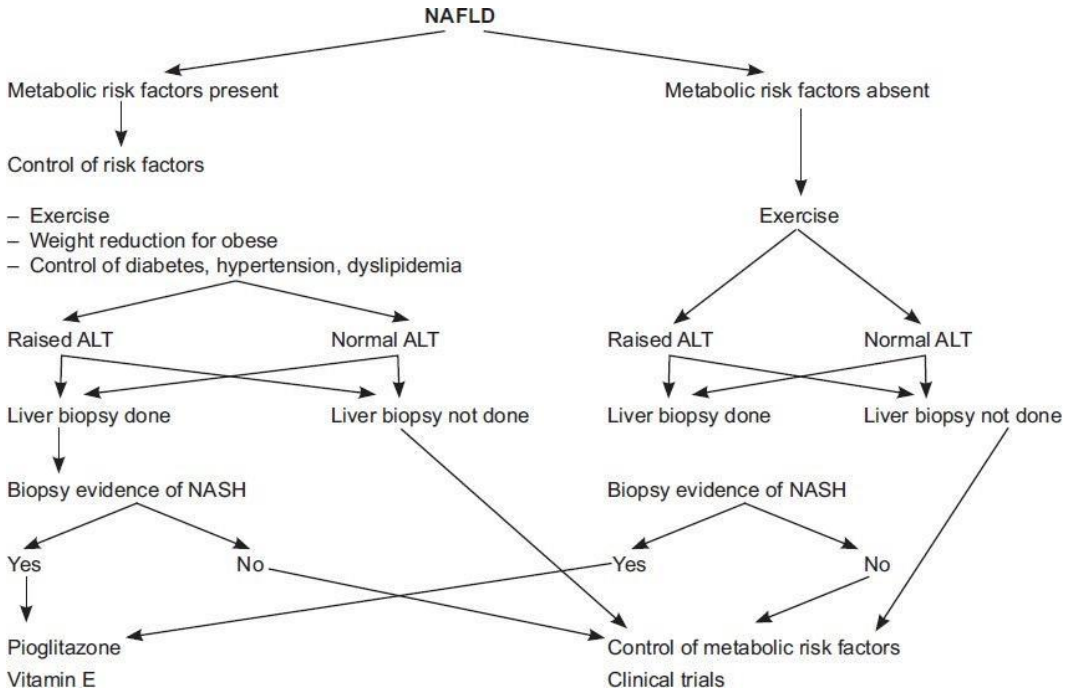


Figure 5: Management algorithm in patients with NAFLD

Lifestyle Intervention:

Currently life style modifications including dietary restrictions and exercise should be recommended as cornerstone of the therapy. Many studies indicate that lifestyle modification may reduce aminotransferases and improve hepatic steatosis.[55,56] Study from India shows Life style modification improves insulin resistance and liver histology in patients with NAFLD, [57] and also helps in normalizing serum aminotransferase level in patients of NASH.[58] The general recommendations for the diet are individualized to achieve energy deficit of 500 to 1000 kcal per day depending on the patients BMI, reduced saturated fat and total fat less than 30% of the total energy intake, reduced refined sugars and increase soluble fibre intake. Physical activities recommended 60 minutes per day at least 3 days a week and progressively increase the exercise to five times a week. [48,59] The degree of hepatic fat reduction was proportional to the intensity of the lifestyle intervention and generally required a body weight loss between ~5 to

10%.[56,60] The effect of exercise without dietary modification on hepatic steatosis was investigated in four studies using MR spectroscopy.[61-64] Exercise programs consisted of 2–3 sessions a week of 30–60 minutes over a period of 6 to 12 weeks. In all but one study liver fat content diminished without a significant change in body weight.[65] Pharmacological and surgical methods of weight loss should be used in morbidly obese patients or moderately obese patients with significant risk factors.

Pharmacotherapy

Metformin is in the class of medication called the biguanides and is a widely used oral medication for the treatment of type 2 diabetes. There are numerous studies assessing the effects of metformin in NASH[66-73] but except two none of them had shown improvement of liver histology.[67,70] A study from India shows metformin is effective in achieving biochemical response in patients with NAFLD not responding to lifestyle interventions.

However a recent meta analysis concluded that 6–12 months of metformin plus lifestyle intervention did not improve aminotransferases or liver histology, compared with lifestyle intervention alone, independently of metformin dose or the presence of diabetes. Currently there is weak support for evidence based recommendations of metformin use however it can be used for the management of patients with pre-diabetes (or polycystic ovarian syndrome) for prevention of diabetes. Thiazolidinediones (TZDs) currently in clinical use include rosiglitazone and pioglitazone. Several studies investigated the effect of pioglitazone and rosiglitazone on aminotransferases and liver histology in adults with NASH[74-79] and shows improvement except one[79] which shows improvement in liver histology only. TZDs appear to have a promising role in the treatment of NASH but there has been considerable debate about the long-term safety of TZDs regarding cardiovascular disease, congestive heart failure (CHF), bladder cancer and bone loss. Oxidative stress is considered to be a key mechanism of hepatocellular injury and disease progression in subjects with NASH, vitamin E is an anti-oxidant and has been investigated to treat

NASH.[80-83] Vitamin E is associated with a decrease in aminotransferases in subjects with NASH, causes improvement in steatosis, inflammation and ballooning and resolution of steatohepatitis in adults with NASH, but it has no effect on hepatic fibrosis. In the largest clinical trial (PIVENS)[83] reported to date, the pure form of α-tocopherol was orally administered at a dose of 800 IU/day for 96 weeks, the primary endpoint i.e. improvement of liver histology was achieved in a significantly greater number of participants receiving vitamin E compared to placebo (42% vs 19%, $p<0.001$, number needed to treat=4.4). One concern with vitamin E is the controversial issue of whether it increases all-cause mortality. Several studies[84-87] investigated UDCA (conventional and high doses) to improve aminotransferases and steatosis in patients with NAFLD and liver histology in patients with NASH. Notably, a single large multicentre RCT convincingly showed that UDCA offers no histological benefit over placebo in patients with NASH. Several other agents like pentoxifylline (PTX), omega-3 fatty acids, S- adenosylmethionine (SAM), alphaglycosidase inhibitor, incretin analogs, obeticholic acid, statins, bile acid sequestrants, angiotensin-converting enzyme inhibitors (ACEI) or angiotensin-II receptor blockers (ARBs) have been used in some Preliminary studies but there are no evidence for their use in clinical practice. Bariatric surgery for the weight loss has been shown to be effective in improving NASH. Two meta-analyses[88,89] evaluated the effect of bariatric surgery on the liver histology in patients with NAFLD. The metaanalysis by Mummadi et al.,[88] showed that steatosis, steatohepatitis, and fibrosis appear to improve or completely resolve after bariatric surgery. However, a recently published Cochrane review[89] concluded that lack of randomized clinical trials or quasi-randomized clinical studies prevents definitive assessment of benefits and harms of bariatric surgery as a therapeutic approach for patients with NASH.

Metabolic Syndrome

Metabolic syndrome is a cluster of cardio -metabolic conditions generally triggered by an expansion of the adipose visceral tissue.[90] Metabolic syndrome is a clinical syndrome

characterized by the constellation of various components namely obesity, type 2 diabetes, dyslipidemia, and hypertension. In 1988, Reaven proposed the term 'syndrome X' to define the contemporary presence of altered glucose regulation, hypertriglyceridemia, low HDL-cholesterol and hypertension and a syndrome carrying a high risk of cardiovascular mortality. The MS is probably much wider and most subjects have evidence of additional metabolic disorders (elevated uric acid, impaired fibrinolysis and endothelial dysfunction). Obesity namely central obesity, type 2 diabetes, hyperlipidemia and hypertension are all characterized by elevated insulin concentrations which predict the development of the metabolic disorder. Accordingly, DeFronzo and Ferrannini proposed the term 'insulin-resistance syndrome' to define this clustering of diseases. The first attempt to define MS came from World Health Organization (WHO), their criteria, partly based on the assessment of insulin sensitivity are scarcely applicable to the general population. New criteria were defined by the European Group for Insulin Resistance in 1999, limiting the syndrome to non-diabetic subjects, but the critical problem of IR was not addressed. Only in 2001, the third Report of the National cholesterol education expert panel on detection, evaluation and treatment of high blood cholesterol in adults [Adult Treatment Panel III (ATPIII)] provided a working definition of MS, based on a combination of five categorical and discrete variables, easily measurable in clinical practice. According to ATP III criteria, MS is defined by the presence of at least three out of five components namely, central obesity, diabetes mellitus, hypertension, low HDL and high triglycerides. The limits for individual components are usually derived from the guidelines of the International Societies or the statements of World Health Organization. A fasting plasma glucose (FPG) of >126 mg/dl on more than one occasion, a random plasma glucose of >200 mg/dl in a symptomatic patient or a 2 h plasma glucose [post-prandial glucose (PPG)] of >200 mg/dl on glucose tolerance test (GTT) is defined as diabetes mellitus. Fasting plasma glucose of >110 mg/dl and <126 mg/dl is defined as impaired fasting glucose (IFG) and 2 h plasma glucose after ingestion of 75 g oral glucose between 140 mg/dl and

200 mg/dl as impaired glucose tolerance (IGT). In the lipid profile, HDL<40 mg/dl in males and<50 mg/dl in females and serum triglycerides (TG) >150 mg/dl are taken as abnormal.[91]

Asia-Pacific/Indian Modifications for Metabolic Syndrome

Even at lower BMI, Asians have been found to have a high percentage of body fat compared to white Caucasians and Blacks. At a given percentage of body fat, BMI values of Asians including Asian-Indians were 3 kg/m^2 lower than those in white Caucasians. This is partly explained by the body build (trunk to leg-length ratio), low muscularity, adaptation to chronic calorie deprivation, and ethnicity. More importantly, the morbidity and mortality associated with higher body fat occur more frequently at lower BMI in Asians than in white Caucasians. A study from Delhi showed that about 66% of men and 88% of women classified as non-obese based on the international cut-off of BMI had one or more cardiovascular risk factors. Based on these data, it has been suggested that the BMI limits for overweight and obesity should be lower for Asians-Indians. Recommendations for BMI are as follows: Normal 18–22.9 kg/m^2, overweight 23–24.9 kg/m^2, and obesity ≥ 25 kg/m^2. A high prevalence of abdominal obesity is seen in Asians, including Asian-Indians even when the BMI is <25 kg/m^2. Similarly, Asians have been found to have more intra- abdominal adipose tissue than Caucasians, in spite of having smaller waists. Lower cut-offs (waist circumference ≥ 90 cm in males and ≥ 80 cm in females) are also recommended for identifying abdominal obesity in Asians. Hence, while defining MS in Asian-Indians, it is recommended to use the Asia-Pacific/Indian cut-offs for abdominal obesity.[91]

Association between Non-alcoholic Fatty Liver Disease and Metabolic Syndrome

The MS and NAFLD share similar associations such as diabetes, hypertriglyceridemia and obesity. Since metabolic risk factors are so common in patients with NAFLD, there is evidence now to show that NAFLD may actually be a hepatic manifestation of MS. Nearly 90.0% and 33.0% NAFLD subjects have at least one feature and all features of the MS. Majority of the patients with NAFLD are obese and resultantly get nearly five-fold higher risk of developing steatosis.

MATERIALS AND METHODS

4.MATERIALS AND METHODS:

All the patients suspected for non alcoholic fatty liver disease are thoroughly examined with detail history of right hypochondriac abdomen pain, fatigue, history of diabetes mellitus, hypertension, alcoholism history and drug history. Patients height, weight, waist circumference, blood pressure was recorded and body mass index will be calculated. Clinical examination and laboratory investigations including ultrasonography of the abdomen was conducted and their association with metabolic syndrome.

Metabolic syndrome was diagnosed as per NCEP ATP 3 criteria (three or more of the following)

1. Elevated waist circumference (asian indian criteria)

a. Men — Equal to or greater than 90 cm

b. Women — Equal to or greater than 80 cm

2. Elevated triglycerides: Equal to or greater than 150 mg/dL

3. Reduced HDL cholesterol:

a. Men — Less than 40 mg/dL

b. Women — Less than 50 mg/dL.

4. Elevated blood pressure: Equal to or greater than 130/85 mm Hg or use of medication for hypertension

5. Elevated fasting glucose: Equal to or greater than 100 mg/dL (5.6 mmol/L) or use of medication for hyperglycemia.

Statistical Methods: Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean ± SD (Min-Max) and results on categorical measurements are presented in Number (%). Student t test has been used to find the significance of study parameters on continuous scale between two groups (Inter group analysis) on metric parameters. Leven1s test for homogeneity of variance has been performed to

assess the homogeneity of variance.

Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups, Non-parametric setting for Qualitative data analysis. Fisher Exact test used when cell samples are very small.

Pearson correlation between study variables is performed to find the degree of relationship.[92-95]

Significant figures

+ Suggestive significance (P value: $0.05<P<0.10$)

* Moderately significant (P value:$0.01<P \leq 0.05$)

** Strongly significant (P value : $P \leq 0.01$)

Statistical software: The Statistical software namely SPSS 18.0, and R environment ver.3.2.2 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc**.**

Ethical Clearance: Ethical clearance has been obtained from " Ethical clearance committee" of the institution.

Sample Size of Estimation

Based on in a study done by Rakesh Gaharwar et al, Sushma et al " STUDY OF CLINICAL PROFILE OF PATIENTS OF NON ALCOHOLIC FATTY LIVER DISEASE AND ITS ASSOCIATION WITH METABOLIC SYNDROME" (2015) 51.4% of patients of NAFLD had metabolic syndrome. Based on this study i have calculated my sample size using the formula **$N= 4PQ/ d^2$.**

Where,

P= Prevalence (from previous studies)

Q= 100-P

d= Allowable error (20%)

Substituting this values we get N= 94.5

Henceforth i have chosen 100 as my sample size.

RESULTS

5.RESULTS

A total of 100 cases of NAFLD, who met the inclusion and exclusion criteria were studied.

Study design: An observational clinical study

Age in years	No. of patients	%
<20	1	1.0
20-30	18	18.0
31-40	35	35.0
41-50	24	24.0
51-60	15	15.0
61-70	5	5.0
71-80	2	2.0
Total	100	100.0

Table 1: Age distribution of patients studied

In our study the mean age of the study population was 42.01±12.48 years . We observed that maximum number of patients were in the age group of 31 to 40 years (35%), 24% were in the age group between 41 to 50 years and it was also observed that NAFLD was less prevalent in the age group between 60 to 80 years.

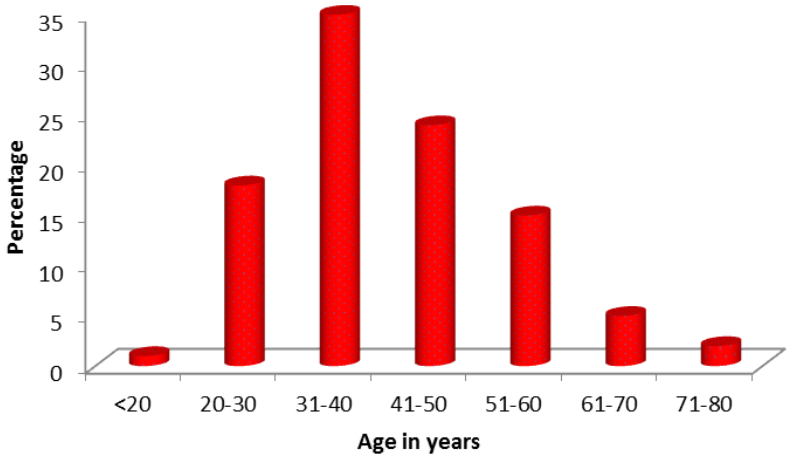


Table 2: Gender distribution of patients studied

Gender	No. of patients	%
Female	50	50.0
Male	50	50.0
Total	100	100.0

Our study comprised of equal ratio of male and female patients.

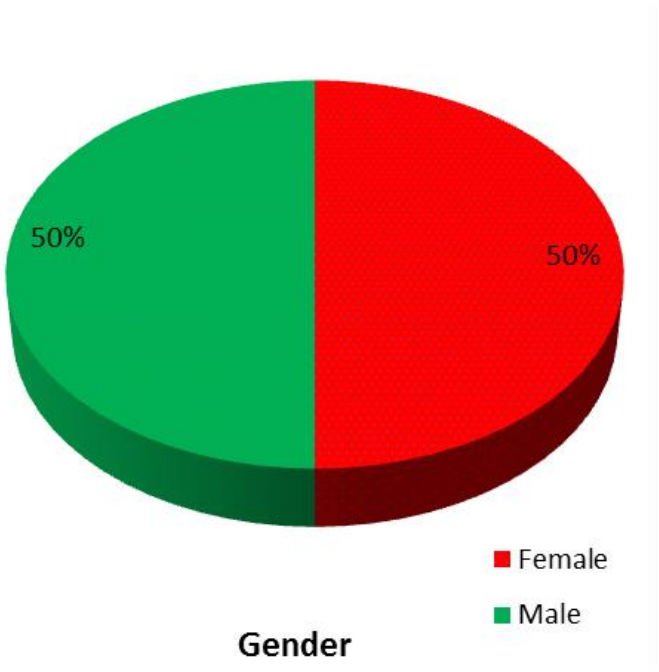


Table 3: Age and gender distribution of patients studied

Age in years	Gender		Total
	Female	Male	
<20	1(2%)	0(0%)	1(1%)
20-30	6(12%)	12(24%)	18(18%)
31-40	17(34%)	18(36%)	35(35%)
41-50	14(28%)	10(20%)	24(24%)
51-60	7(14%)	8(16%)	15(15%)
61-70	4(8%)	1(2%)	5(5%)
71-80	1(2%)	1(2%)	2(2%)
Total	50(100%)	50(100%)	100(100%)

31% of females studied were in the age group of 30 to 50 years, 30% of males were in the age group of 20 to 40 years. We observed both genders had higher prevalence of NAFLD between the age group of 31 to 40 years.

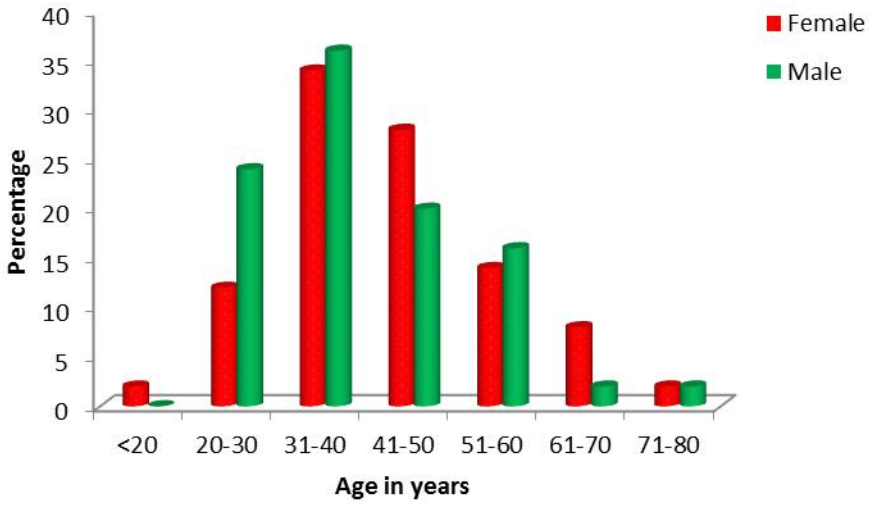


Table 4: Symptom distribution of patients studied

ASYMPTOMATIC	SYMPTOMATIC
35%	65%

In our study 35% out of 100 patients of NAFLD were asymptomatic while 65 patients were symptomatic. (Table 4). Abdominal pain and fatigue was present in 55% and 52% patients respectively.

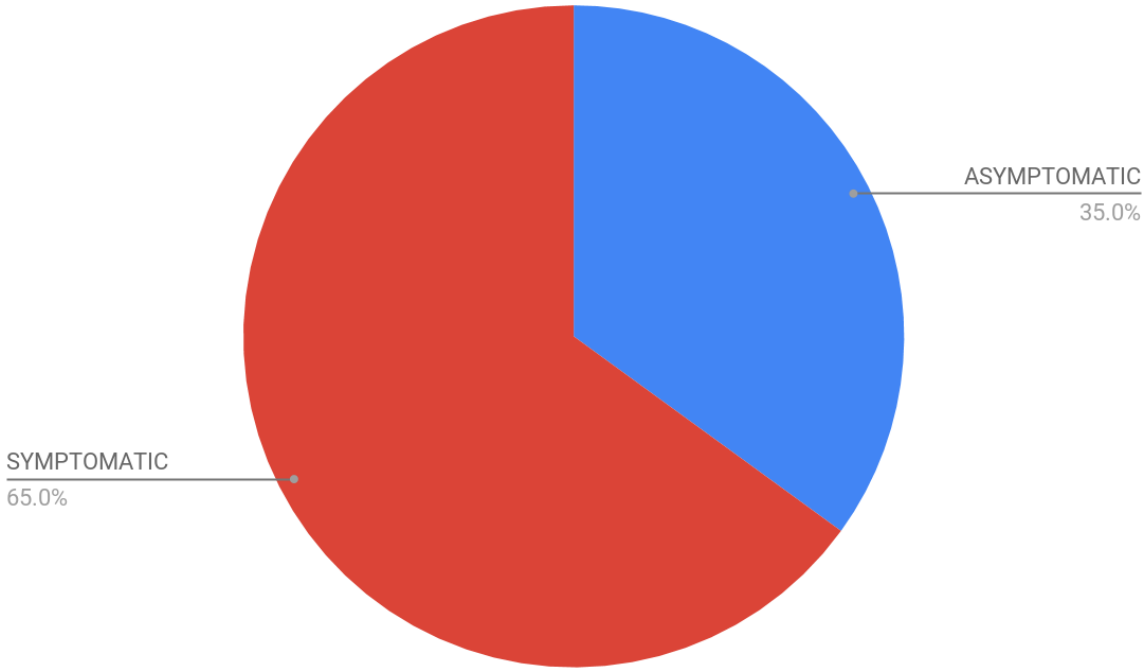


Table 5: Waist circumference distribution of patients studied

Waist Circumference	No. of patients	%
<90	40	40.0
90-110	39	39.0
>110	21	21.0
Total	100	100.0

We observed that out of 100 cases with NAFLD, 39% of cases had waist circumference between 90 to 100 cams and 21% had waist circumference >100 cm**s**

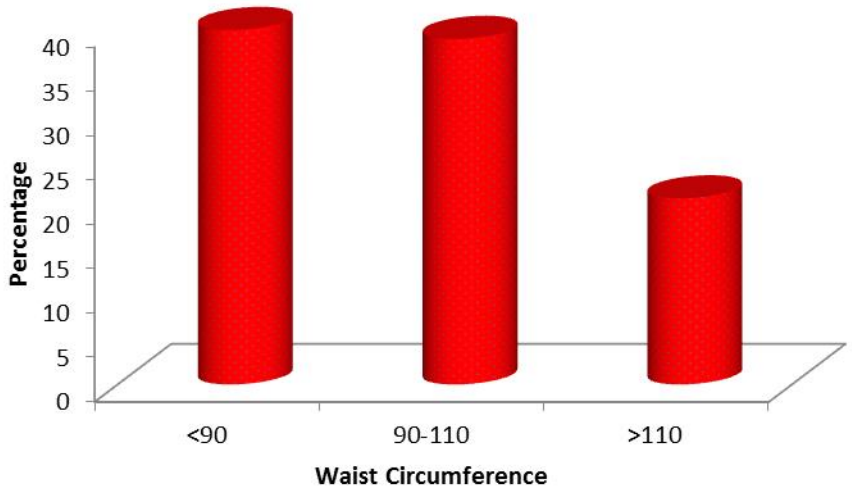
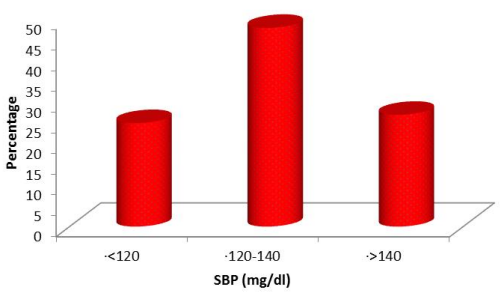


Table 6: Blood pressure distribution of patients studied

	No. of patients (n=100)	%
SBP (mg/dl)		
· <120	25	25.0
· 120-140	48	48.0
· >140	27	27.0
DBP (mm Hg)		
· <80	37	37.0
· 80-100	59	59.0
· >100	4	4.0

Out of 100 patients with NAFLD, 48% of patients were found to be have pre hypertension with systolic blood pressure of 120 to 140 mmHg and 27% of patients were found to have hypertension with SBP > 140 mm/Hg.

59% of patients in our study were found to have diastolic blood pressure between 80 to 100 mmHg.



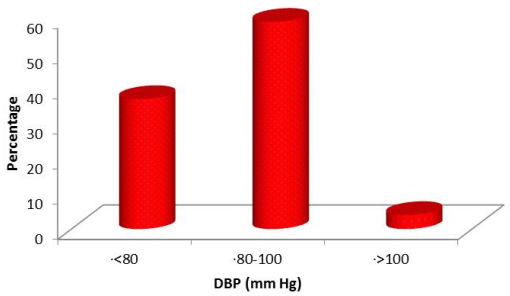


Table 7: FBS (mg/dl) distribution of patients studied

FBS (mg/dl)	No. of patients	%
<100	48	48.0
100-126	14	14.0
>126	38	38.0
Total	100	100.0

Out of 100 patients with NAFLD 14% had impaired fasting sugars (100-126mg/dl) and 38% had diabetes mellitus.

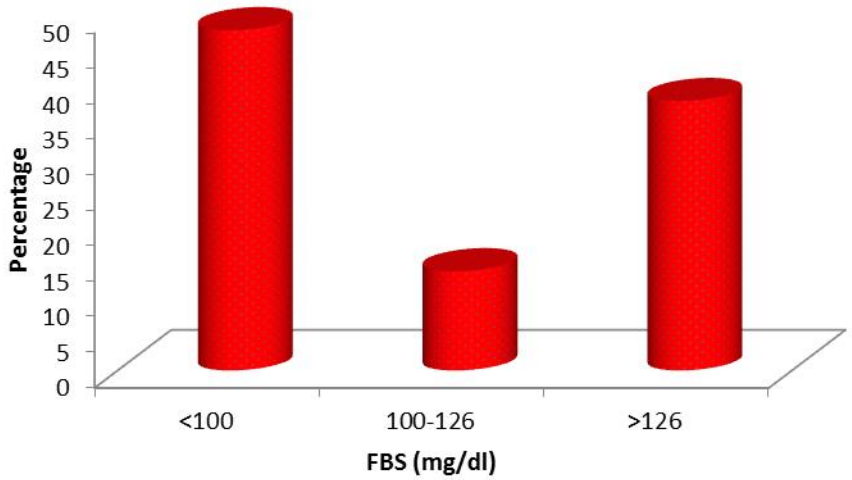
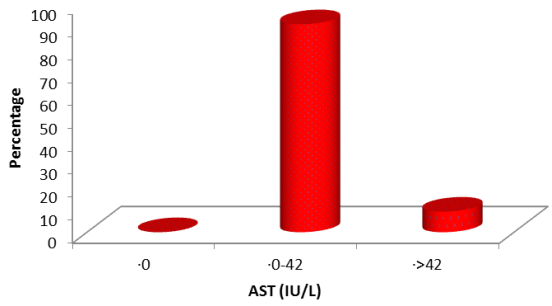


Table8 : Enzyme distribution of patients studied

	No. of patients (n=100)	%
AST (IU/L)		
· 0	0	0.0
· 0-42	91	91.0
· >42	9	9.0
ALT (IU/L)		
· 0	0	0.0
· 0-48	85	85.0
· >48	15	15.0

Out of 100 patients with NAFLD, 91% and 85% of patients were found to be have AST and ALT within normal limits. However 9% and 15% of patients were found to have raised AST and ALT.



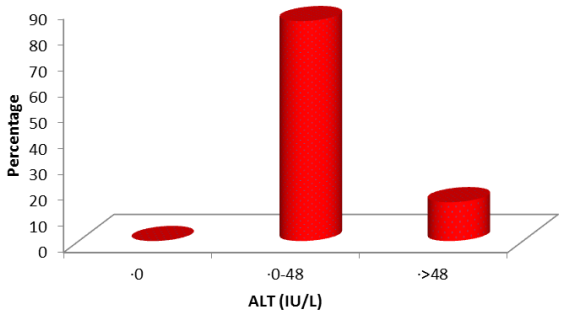


Table 9: TGL distribution of patients studied

	No. of patients (n=100)	%
TGL (mg/dl)		
· <150	41	41.0
· 150-500	57	57.0
· >500	2	2.0

We observed that 57% of cases of NAFLD in our study had TGL equal to or greater than 150 mg/dL .

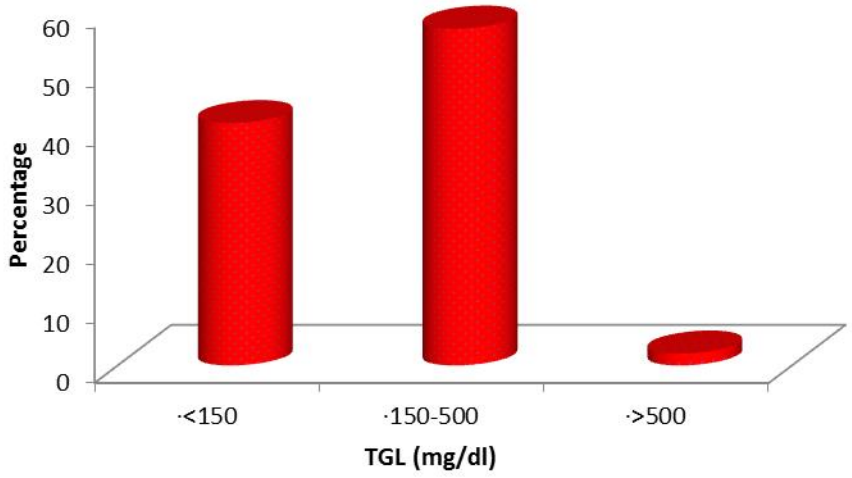
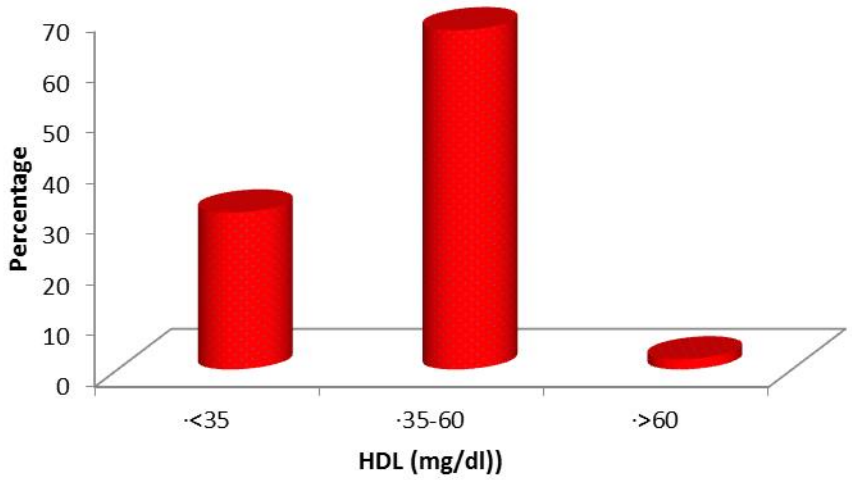


Table 10 : HDL distribution of patients studied

	No. of patients (n=100)	%
HDL (mg/dl)		
· <35	31	31.0
· 35-60	67	67.0
· >60	2	2.0



In our study we observed that 31% of NAFLD cases had HDL of <35 mg/dl and 67% had HDL between 35-60 mg/dl

Table 11: Incidence of Metabolic Syndrome distribution of patients studied

Metabolic Syndrome	No. of patients	%
NAFLD without metabolic syndrome	47	47.0
NAFLD with metabolic syndrome	53	53.0
Total	100	100.0

It was evidently obtained that, among 100 cases with NAFLD, 53% of cases were fulfilling the criteria for metabolic syndrome.

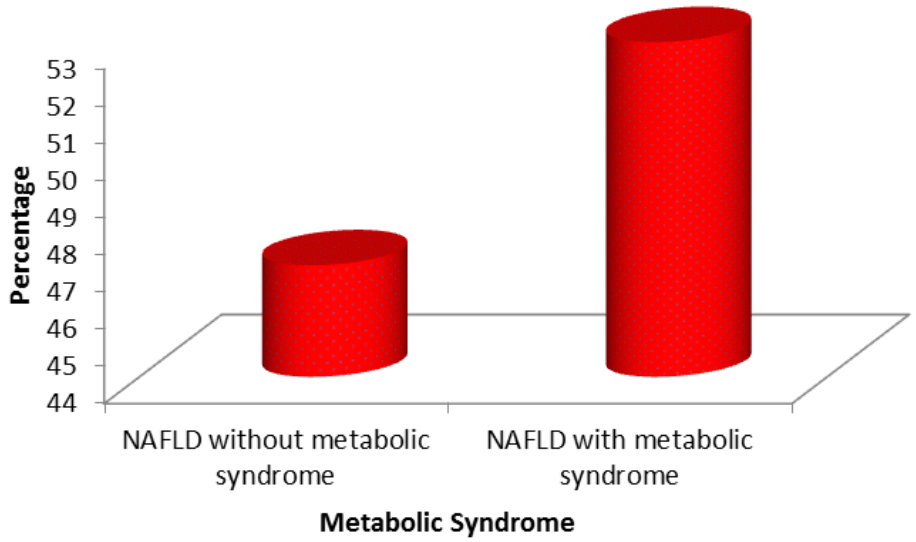


Table 12: Comparison of age in relation to incidence of metabolic syndrome of patients studied

variables	Metabolic Syndrome		Total	P value
	NAFLD without metabolic syndrome	NAFLD with metabolic syndrome		
Age in years	38.89±11.89	44.77±12.44	42.01±12.48	0.018*

In our study we observed that 44.77±12.44 was the mean age in cases of NAFLD with metabolic syndrome when compared to 38.89±11.89 in cases without metabolic syndrome.

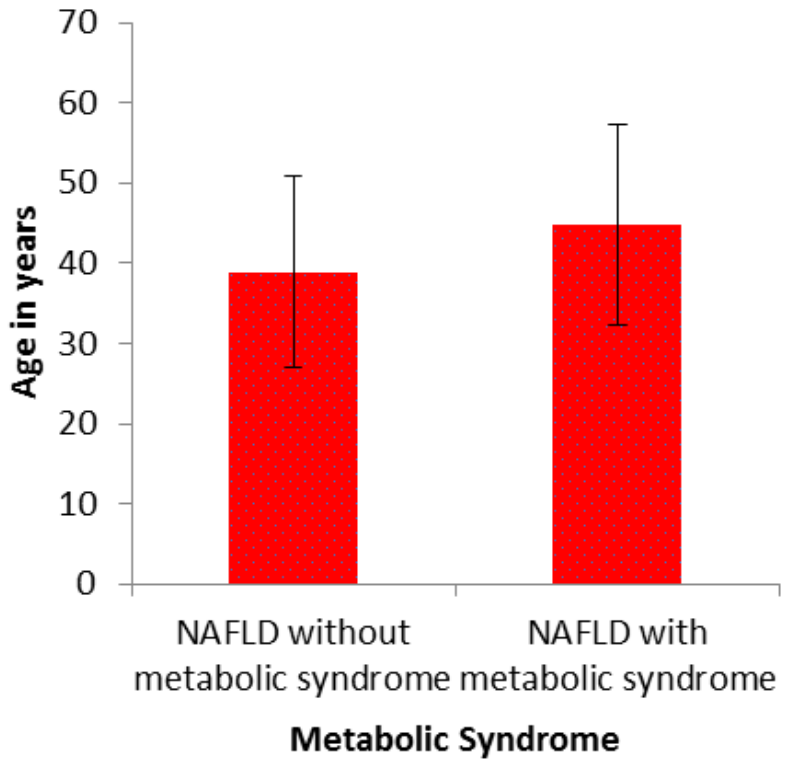


Table 13: Comparison of waist circumference in relation to incidence of Metabolic Syndrome of patients studied

variables	Metabolic Syndrome		Total	P value
	NAFLD without metabolic syndrome	NAFLD with metabolic syndrome		
Waist Circumference	92.85±12.13	99.91±12.79	96.59±12.92	0.006**

In our study we observed that 99.91±12.79 was the mean waist circumferance which is higher in cases of NAFLD with metabolic syndrome when compared to 92.85±12.13 without metabolic syndrome.

We also noted that higher value of waist circumference in cases of NAFLD with metabolic syndrome is statistically significant with a p value of <0.006.

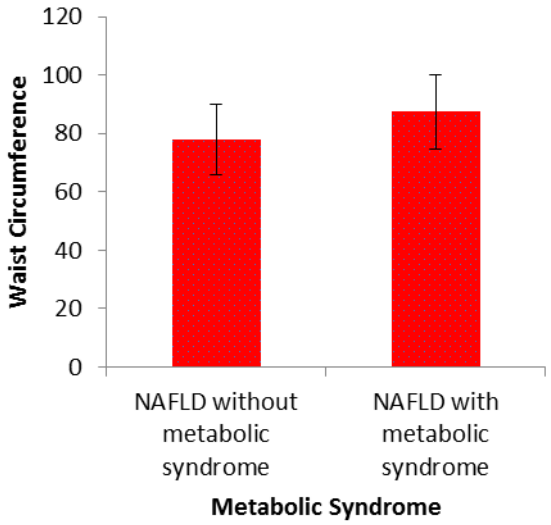
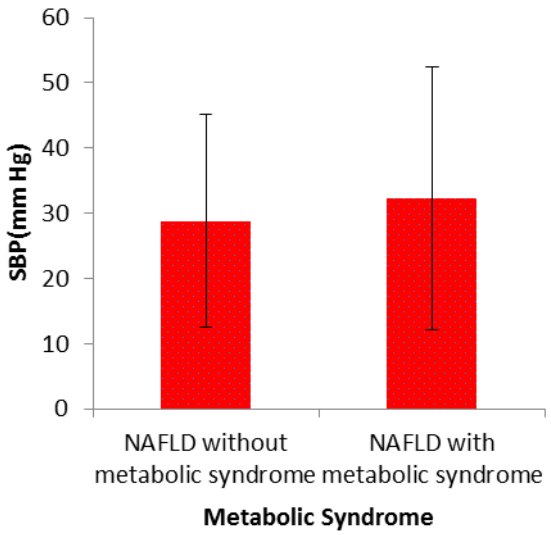


Table 14: Comparison of SBP in relation to incidence of metabolic syndrome of patients studied

variables	Metabolic Syndrome		Total	P value
	NAFLD without metabolic syndrome	NAFLD with metabolic syndrome		
SBP (mm Hg)	124.38±16.29	140.09±20.16	132.71±19.97	<0.001**



In our study we observed that 140.09±20.16 was the mean SBP in cases of NAFLD with metabolic syndrome when compared to 124.38±16.29 without metabolic syndrome. We also noted that higher value of SBP in cases of NAFLD with metabolic syndrome is statistically significant with a p value of <0.001.

Table 15: Comparison of DBP in relation to incidence of metabolic syndrome of patients studied

variables	Metabolic Syndrome		Total	P value
	NAFLD without metabolic syndrome	NAFLD with metabolic syndrome		
DBP (mm Hg)	77.87±8.83	87.36±11.03	82.90±11.08	<0.001**

In our study we observed that 87.36±11.03 was the mean DBP in cases of NAFLD with metabolic syndrome when compared to 77.87±8.83 without metabolic syndrome. We also noted that higher value of DBP in cases of NAFLD with metabolic syndrome is statistically significant with a p value of <0.001

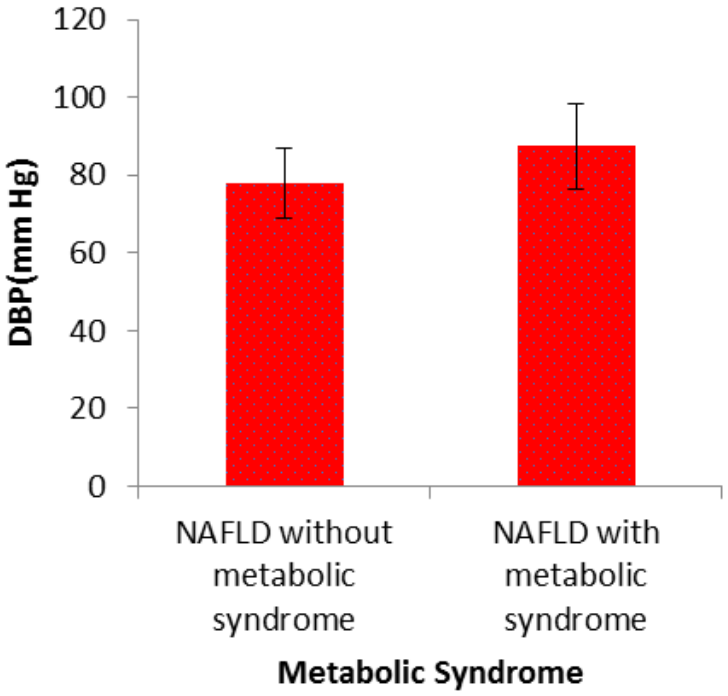


Table 16: Comparison of FBS in relation to incidence of metabolic syndrome of patients studied

variables	Metabolic Syndrome		Total	P value
	NAFLD without metabolic syndrome	NAFLD with metabolic syndrome		
FBS (mg/dl)	97.13±24.98	155.87±66.87	128.26±59.22	<0.001**

In our study we observed that the mean FBS was high (155.87±66.87) in cases of NAFLD with metabolic syndrome when compared to NAFLD without metabolic syndrome where mean fbs was 97.13±24.98.

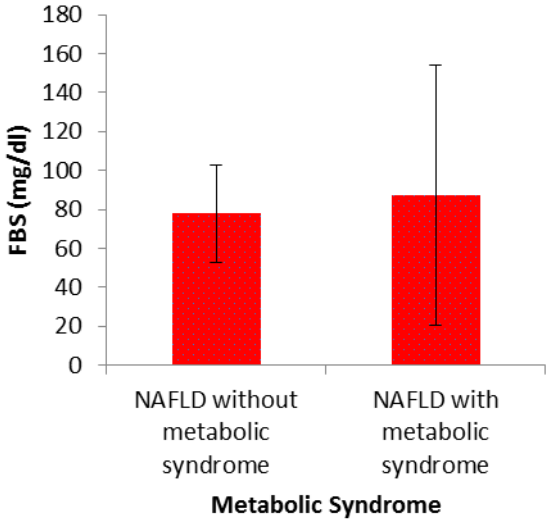


Table 17: Comparison of AST and ALT in relation to incidence of Metabolic Syndrome of patients studied

variables	Metabolic Syndrome		Total	P value
	NAFLD without metabolic syndrome	NAFLD with metabolic syndrome		
AST (IU/L)	28.68±18.78	25.08±11.12	26.77±15.23	0.239
ALT (IU/L)	36.38±34.61	29.19±15.21	32.57±26.29	0.173

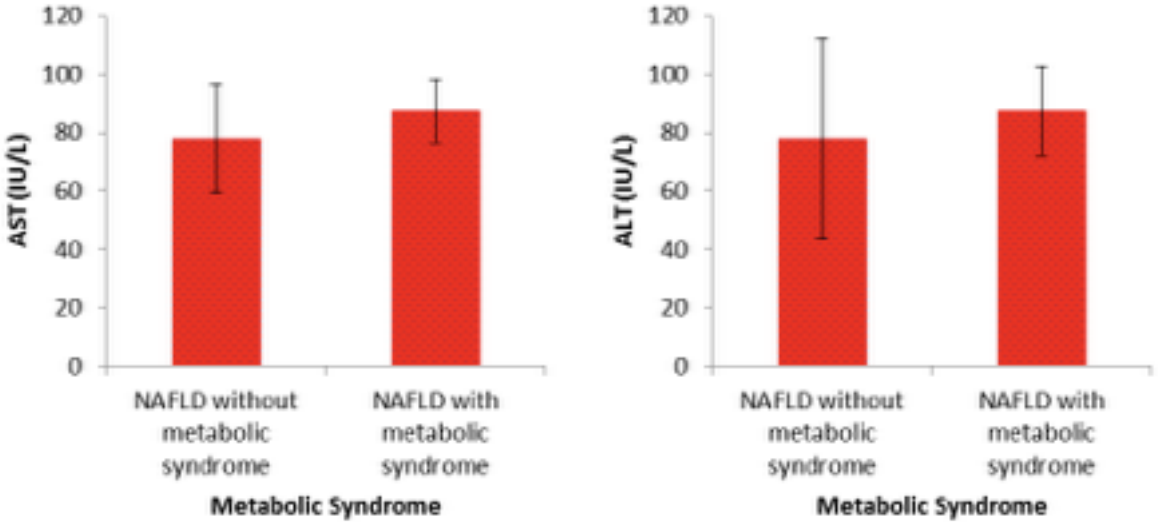
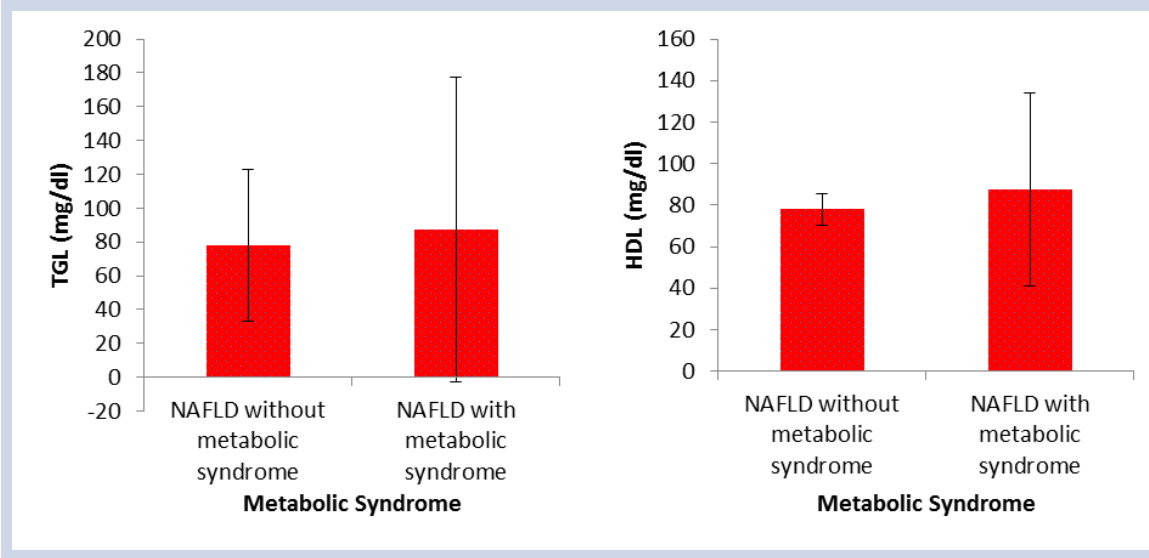


Table 18: Comparison of TGL and HDL in relation to incidence of metabolic syndrome of patients studied

variables	Metabolic Syndrome		Total	P value
	NAFLD without metabolic syndrome	NAFLD with metabolic syndrome		
TGL (mg/dl)	131.38±44.88	209.15±90.13	172.60±82.00	<0.001**
HDL (mg/dl)	42.51±7.69	42.77±46.62	42.65±34.19	0.970



In our study we observed that mean TGL was high (209.15±90.13) in cases with metabolic syndrome when compared to 131.38±44.88 in cases without metabolic syndrome and mean HDL was 42.77±46.62 in cases with metabolic syndrome when compared to 42.51±7.69 in cases without metabolic syndrome. We also noted that higher value of TGL in cases of NAFLD with metabolic syndrome is statistically significant with a p value of <0.001.

In our study, on statistical analysis there was a positive correlation with waist

circumference, FBS, triglycerides and NAFLD with metabolic syndrome had positive correlation with waist circumference, FBS, triglycerides and systolic blood pressure.

DISCUSSION

6.DISCUSSION

We conducted this study on 100 cases of NAFLD diagnosed by ultrasound.

NAFLD is known to be associated with various metabolic abnormalities including central obesity, type 2 diabetes mellitus, dyslipidaemia and hypertension which are all well established cardio vascular risk factors. Liver ultrasonography is frequently used to assess fatty infiltration of the liver, but there is little information on the association between the metabolic disease and the severity of fatty liver (as detected by ultrasound).

Table 19: Comparison of our study with other studies with respect to prevalence of metabolic syndrome in NAFLD cases

STUDIES	% OF NAFLD CASES WITH METABOLIC SYNDROME
Our study	53%
Rakesh Gaharwar et al	51.4%
Ajay Duseja et al	50%
Deepa Uchil et al	47.1%
Radu et al	61.09%

100 NAFLD cases were studied, out of which 53(53%) of NAFLD cases had metabolic syndrome according to the NCEP ATP III modified criteria using Asian Indian standards for waist circumference.Similar such studies showed results as follows: Rakesh Gaharwar et al (51.4%), Ajay Duseja et al (50%), Deepa Uchil et al (47.1%) and Radu et al (61.09 %).[96,97,100,101]

Table 20: Comparison of our study with other studies with respect to mean age.

STUDIES	MEAN AGE OF METABOLIC SYNDROME
Our study	42.01±12.48
Bajaj et al	40.11 ± 1.1
Rakesh et al	49.67±9.30

The mean age group of those having metabolic syndrome was 42.01±12.48 which is similar to that studies done by Bajaj et al (40.11 ± 1.1) and Rakesh Gaharwar et al (49.67±9.30).[98,100]

We have observed NAFLD with metabolic syndrome was more prevalent in the age group of 30-40 years which was little younger age group as compared to US population. This implicates that Asian Indian population develops NAFLD at a earlier age.[102]

STUDIES	MALES	FEMALES
Our study	43.39%	56.60%
Ajay et al	33%	67%
Rakesh et al	38.9%	61.1%

Table 21: Comparison of our study with other studies with respect to gender

In our study out of the 53 patients, 30 (56.60%) were females and 23 (43.39%) were males. 67% were females in a study conducted by Ajay Duseja et al and 61.1% were females and 38.9% males in a study conducted by Rakesh et al which shows females have a higher prevalence for metabolic syndrome.[96,100]

STUDIES	ASYMPTOMATIC	SYMPTOMATIC	ABDOMINAL PAIN	FATIGUE
OUR STUDY	35%	65%	55%	52%
RAKESH ET AL	34.28%	65.72%	55.71%	52.85%

Table 22: Comparison of our study with other studies with respect to symptoms

In our study we noticed that 35 out of 100 patients were asymptomatic while 65 were symptomatic. Abdominal pain and fatigue was present in 55% and 52% respectively. Almost similar results were obtained in a study done by Rakesh et al where they noticed 24 out of 70 patients were asymptomatic while 46 were symptomatic. Abdominal pain and fatigue was present in 55.71% and 52.85% respectively.[100]

Table 23: Comparison of our study with other studies with respect to waist circumference

STUDIES	NAFLD with increased waist circumference
Our study	94.33%
Bajaj et al	58.7%
Ajay Duseja et al	47.1%
Rakesh Gaharwar et al	77.77%

Out of 53 patients with NAFLD with metabolic syndrome, 50 (94.33%) patients had increased waist circumference (male > 90 cms, female > 80 cms) with a mean of 99.91±12.79 cms and this observation was statistically significant. 58.7%, 47.1% and 77.77% of cases had increased waist circumference as reported by Bajaj et al, Ajay Duseja et al and Rakesh Gaharwar et al respectively.[98,96,100.]

Increased waist circumference and adiposity is strongly linked with metabolic syndrome.

An increase of 1 cm of waist circumference increases the risk of metabolic syndrome by around 7.4%. [103]

Table 24: Comparison of our study with other studies with respect to BP

STUDIES	BLOOD PRESSURE PREVALENCE
Our study	56.60%
Bajaj et al	48.72%
Rakesh Gaharwar et al	47.2%

In our study we observed that 30 (56.60%) patients had blood pressure ≥ 130/85 mm Hg with a mean of 140.09±20.16/87.36±11.03 Hg which is higher compared to that reported by Bajaj et al (48.72%) and Rakesh et al (47.2%) .[98,100]

Table 25: Comparison of our study with other studies with respect to FBS

Studies	Impaired fasting glucose
Our study	77.35%
Ajay Duseja et al	72.4%
Rakesh Gaharwar et al	63.8%

In our study mean fasting plasma glucose of patients with NAFLD and metabolic syndrome was 155.87±66.87 mg/dl. 41(77.35%) cases had impaired fasting glucose (>100 mg/dl) and was found

to be statistically significant when compared to NAFLD without metabolic syndrome. 72.4% and 63.8% patients had impaired fasting glucose as reported by Ajay et al and Rakesh et al respectively.[96,100] Both peripheral and hepatic insulin resistance is present with patients with NAFLD, irrespective of the coexistence of impaired glucose tolerance and obesity. Insulin resistance and increased non esterified fatty acids are associated with increased intra hepatic production of free fatty acids from glucose which is not taken by peripheral adipocytes and myocytes. Excess fatty acids are not oxidized and are converted to diacyl and triacyl glycerols, and are stored in the hepatocyte cytoplasm leading to steatosis. Reduced insulin sensitivity is shown in many studies of patients with NAFLD. There is also direct correlation with degree of insulin resistance with severity of liver disease from mild NAFLD to severe NASH and cirrhosis.[104]

In our study we observed that AST and ALT in NAFLD patients with and without metabolic syndrome were in the normal mean range for most of the patients as similar to the study done by Ajay et al and Uchil et al, however in the study done by Rakesh et al deranged AST and ALT was observed in greater percentages in patients of NAFLD with metabolic syndrome than those without metabolic syndrome.[96,97,100]

Table 26: Comparison of our study with other studies with respect to triglyceridaemia

STUDIES	HYPERTRIGLYCERIDEMIA PREVELANCE
Our study	84.90%
Rakesh Gaharwar et al	86.1%
Deepa Uchil et al	43.6%

In patients of NAFLD with metabolic syndrome 45 (84.90%) had hypertriglyceridaemia (>150

mg/dl) with a mean of 209.15±90.13 which is similar to the study done by Rakesh Gaharwar et al (86.1%) and is significantly higher than those reported by Deepa Uchil et al (43.6%).[100,97]

Table 27: Comparison of our study with other studies with respect to HDL

STUDIES	HDL
Our study	84.90%
Bajaj et al	66.7%
Rakesh Gaharwar et al	94.4%

45 (84.90%) patients had low HDL levels (< 40 mg/dl in males and < 50 mg/dl in females) with a mean of 42.77±46.62 mg/dl as compared to 66.7% described by Bajaj et al and 94.4% described by Rakesh Gaharwar et al.[98,100] Dyslipidaemia between the two groups i.e., NAFLD with and without metabolic syndrome was significant both for prevalence as well as the respective means.

CONCLUSION

7. CONCLUSION

Despite the limitations, this is an attempt to characterize and define the profile of NAFLD patients who are commonly encountered in day to day practice. Our findings have important clinical and public health implications.

Our study reveals that there is high prevalence of all the components of metabolic syndrome in cases of NAFLD. Therefore whenever these parameters are encountered in the clinical setting, patients must be evaluated for the presence of NAFLD by abdominal ultrasonography.

The incidence of impairment of various parameters in cases of NAFLD with metabolic syndrome is higher when compared with those without metabolic syndrome . Therefore a conclusion can be drawn that there is a greater association of metabolic syndrome with increasing severity of fatty liver disease.

Early detection would help in modifying the disease course through simple interventions like lifestyle changes, and hence delaying its complications to reduced morbidity and mortality. It would also play a major role in preventive cardiology as its association with metabolic syndrome is frequent and its components are well documented cardiovascular risk factors.

A diagnosis of fatty liver on ultrasound in an asymptomatic person should alert clinician about metabolic syndrome and its progression to cardiovascular disease. NAFLD may be considered as the hepatic component of metabolic syndrome. Diagnostic importance of NAFLD as a criteria for the presence as well as for the risk of future development of metabolic syndrome needs to be emphasized, From the therapeutic point of view interventions aimed at reversing NAFLD are likely to be a rational approach in the prevention and treatment of hepatic insulin resistance, metabolic syndrome and its related complications

SUMMARY

7.SUMMARY

A observational and analytical study of 100 patients diagnosed as NAFLD, attending OPD and indoor patients of the Department of Medicine, Jawaharlal Nehrui medical college. All patients diagnosed as NAFLD were investigated for metabolic syndrome according to the NCEP ATP 3 Criteria and a relationship between NAFLD and metabolic syndrome studied.

Out of 100 patients diagnosed to have NAFLD, 50 patients were male and 50 were female belonging to the age group of 18 to 80 years, 53 patients with NAFLD were found to have metabolic syndrome, maximum number of patients were in the age group of 30 to 50 years, very few patients were found to be in the age group of 60 to 80 years. 65 out of 100 patients were found to be symptomatic, presence of symptoms such as fatigue and abdominal pain noted in our study. Most of the patients were found to be have prehypertension, impaired glucose tolerance, hypertriglyceridemia and increased waist circumference. However 31% had low HDL with less than 35mg/dl compared to 67% with HDL ranging from 35 to 60 mg/dl. There was a statistically positive correlation with FBS, SBP, waist circumference and TGL. In our study we observed transaminases were within normal range.

We compared our study with other similar studies done by Rakesh et al, Bajaj et al, Ajay et al, Deepa et al and Radu et al respectively. Prevalence of metabolic syndrome in NAFLD patients were ranging from 50 to 60%. Mean age of our patients was 42 years which was comparatively younger when compared to US population. Higher female prevalence of metabolic syndrome in NAFLD patients were noted in all studies. However our study showed increase in prevalence of metabolic syndrome in patients with increased waist circumference. Impaired glucose tolerance was found in patients of NAFLD with metabolic syndrome in all studies. Mean systolic and diastolic BP was found to be slightly higher when compared to other studies. A significant prevalence of triglyceridemia was found in our study when compared to other studies.

BIBLIOGRAPHY

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ANNEXURE

ANNEXURE

Jawaharlal Nehru Medical College, Belagavi

Department of General Medicine

RESEARCH INFORMED CONSENT FORM

Study Title: **—STUDY OF CLINICAL PROFILE OF PATIENTS OF NON ALCOHOLIC FATTY LIVER DISEASE AND ITS ASSOCIATION WITH METABOLIC SYNDROME .**

Principal investigator : Dr. Harish V Balllur

Co-Guide: None

Name of the subject:

Age:

Sex:

1. I have been informed that this study requires determination of _____and will not cause any harm to me.
2. I understand that my participation in the study may not have a direct benefit to me.
3. I understand that medical information produced by this study will become part of institutional record & will be kept confidential by the said institute.
4. I understand that my participation i s voluntary & I may refuse to participate or may withdraw my consent & discontinue participation at any time without prejudice to my present or future care at this institution.
5. I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose (s) I confirm that Dr. HARISH V BALLUR (Chief researcher) has explained to me the purpose of research & the study procedure that I will undergo and the possible risks & discomforts as well as benefits that I may experience, in my own language. Therefore, I agree to give consent to participate as a subject in this research project.

Participant‘s signature_____ Date:

I have explained to _____ (Subject) the purpose of the research, the possible risks and benefits to the best of my ability.

Investigator/ P.G (Guide) signature

Date:

PROFORMA

FOR DATA COLLECTION

NAME:

OP NO:

AGE: IP NO:

SEX: DATE:

ADDRESS: OCCUPATION:

DETAILED HISTORY: Detail history of right hypochondriac abdomen pain, fatigue, history of diabetes mellitus, hypertension, alcoholism history and drug history.

ANTHROPOMETRIC MEASUREMENT:

1. Height :
2. Weight :
3. Weist Circumferance :
4. Body mass index :

GENERAL EXAMINATION:

1. PULSE :
2. BLOOD PRESSURE :
3. PALLOR :
4. ICTERUS :
5. CYANOSIS :
6. CLUBBING :
7. OEDEMA :
8. LYPHADENOPATHY:

SYSTEMIC EXAMINATION:

1. CARDIOVASCULAR EXAMINATION :
2. RESPIRATORY EXAMINATION :
3. PER ABDOMEN EXAMINATION :
4. CENTRAL NERVOUS SYSTEM :

INVESTIGATIONS SUCH AS –

1. Fasting blood sugar (FBS)
2. Fasting serum lipid profile
3. Liver function test
4. HBsAg.
5. Ultrasonography of Abdomen

KEY TO MASTER CHART

FBS-	Fasting Blood Sugar
HDL-	High Density Lipoprotein
MS-	Metabolic Syndrome
Y-	Yes
N-	No
TG	Triglycerides
AB	Abdominal pain

MASTERCHART

SL.NO	NAME	AGE	SEX	AP	FATIGUE	WC	BP	FBS	AST	ALT	TG	HDL	MS
1	K.D SHIVANNA	40	M	P	P	97	150/90	145	17	15	265	33	Y
2	R.ANUPAMA	36	F	A	A	93	140/90	156	12	21	179	35	Y
3	SUSHMA B.M	46	F	P	P	86	116/80	84	20	16	171	35	N
4	GANGANNA	42	M	P	P	94	140/90	143	16	17	165	32	Y
5	SADASHIV REDDY	36	M	P	P	94	126/76	69	14	13	212	43	N
6	SARASWATHI	30	F	P	P	85	122/78	82	17	20	88	44	N
7	SUDHA RAMESH	27	F	A	A	87	132/80	96	17	16	88	36	N
8	SAVITHA.G	26	F	A	A	98	112/76	67	20	15	96	38	N
9	SAKAMMA	54	F	P	P	93	140/90	178	21	11	183	43	Y
10	UMADEVI	34	F	P	P	87	116/78	154	17	12	89	35	Y
11	PREMA. R SHETTY	27	F	A	A	104	146/84	140	17	15	212	35	Y
12	APARNA LOKESH	35	F	P	P	93	124-68	95	16	14	165	34	N
13	RAVISHANKAR	25	M	A	A	85	114/64	138	16	17	104	36	N
14	LOKESH CHANDRA	20	M	A	A	77	110/76	75	25	13	110	42	N
15	ARVIND A SHETTY	24	M	A	A	88	146/84	89	14	15	167	38	N
16	LOKANNA	37	M	P	P	85	124/82	91	20	16	110	40	N
17	SABINA TAJ	35	F	P	P	95	112/68	87	20	15	34	45	N
18	K.B.ANNE GOWDA	36	M	P	A	89	156/90	136	21	17	199	32	Y
19	ANIL KUMAR	46	M	P	P	87	126/82	164	13	20	98	42	N
20	ASHWINI	35	F	P	P	87	180/90	167	18	18	191	42	Y
21	SHIVAKUMAR	23	M	A	A	80	120/82	92	15	15	91	39	N
22	TAYAMMA	38	F	P	P	86	132/86	84	18	16	224	43	N
23	VIYAL N V	22	M	P	A	85	136/88	98	22	17	265	39	Y
24	ANANDAPPA	38	M	P	P	92	140/90	134	18	12	198	38	Y
25	RUKMINI BHI	49	F	P	P	94	110/78	184	17	16	204	39	Y
26	SREEVALLI	29	F	A	A	92	120/80	157	13	20	164	32	Y
27	ASMA BANU	32	F	A	A	94	150/100	76	15	17	110	42	N
28	LOKESH REDDY	48	M	P	A	97	140/90	148	17	16	187	32	Y
29	K.M.GOWDA	33	M	P	A	88	120/78	85	18	14	87	47	N
30	NAIKA ABDUL	26	M	A	A	92	132/84	178	14	13	168	34	Y
31	KENCHAMMA	33	F	P	P	88	110/80	76	15	22	88	34	N
32	VEDA SREE	45	F	P	A	91	116/90	92	15	17	200	34	Y
33	PADMAVATHI P	36	F	P	P	71	110/64	108	18	18	101	33	N
34	MOHAMMED ALI	35	M	P	A	81	142/90	87	23	15	121	34	N
35	SUNITHA RAJESH	37	F	A	P	88	171/90	88	17	13	224	38	Y
36	PADMAVATHY	38	F	P	P	85	160/100	88	17	21	187	32	Y
37	VENU GOPAL	42	M	P	P	94	124/78	81	30	15	190	39	N
38	SHARTH KUMAR	40	M	P	P	88	130/64	163	15	17	88	42	N
39	BHAGYAMMA	36	F	A	A	104	132/78	98	17	18	110	42	N
40	SWAMY	45	M	P	P	111	160/100	295	22	53	298	51	Y
41	VEERANNA	38	M	A	A	96	110/70	84	37	45	198	31	N
42	RADHA	58	F	P	P	95	150/90	200	26	37	90	42	Y
43	SAVITHRAMMA	40	F	P	P	93	130/80	193	15	28	238	36	Y
44	SYED RIAZ	60	M	A	P	95	138/86	203	16	27	166	33	Y

45	LAKSHMAMMA	55	F	P	A	96	170/100	106	72	63	235	34	Y
46	GULNAZ BEGUM	49	F	P	A	103	130/80	223	40	42	504	4	Y
47	CHINAMMA	50	F	A	P	77	148/94	238	16	25	159	37	Y
48	GOVIDAIAH	65	F	P	P	132	160/90	165	20	18	195	52	Y
49	CHANDRAPPA	55	M	A	A	120	100/70	89	37	55	132	42	N
50	PANDURANGAPPA	73	M	P	P	118	130/70	102	22	20	105	43	N
51	PARVATHAMMA	60	F	P	P	118	126/76	109	20	18	290	50	Y
52	MANJULA	50	F	P	P	117	140/78	110	20	25	95	38	Y
53	SUCHITHRA	63	F	A	P	117	120/80	129	28	30	204	45	Y
54	KRISHNAPPA	30	M	A	A	116	160/90	83	39	70	165	42	Y
55	BHIMAPPA	48	M	A	A	115	130/90	102	54	74	136	57	Y
56	BIDDAMMA	50	F	P	P	115	180/120	94	27	31	135	35	Y
57	SHARADAMMA	52	F	A	P	113	156/76	298	26	34	183	30	Y
58	JAHANTULLA	62	M	P	P	113	144/76	219	28	37	183	38	Y
59	PRADEEPA	39	M	A	A	112	130/80	95	29	53	218	35	Y
60	BINDU SAGAR	38	M	A	A	112	166/66	88	31	45	173	35	Y
61	KISHORE CHANDRA	35	M	A	A	112	120/80	120	30	36	600	33	Y
62	LOKANATH	41	M	P	P	111	106/92	138	30	36	278	32	Y
63	HANUMANTARAYA	50	M	P	P	111	180/110	285	20	26	415	56	Y
64	DEEPENDRA	30	M	A	A	111	110/70	90	26	46	160	47	N
65	BASANTHMMA	45	F	A	P	111	122/86	99	30	36	240	50	N
66	SYED AHMAD	60	M	P	P	111	136/76	95	29	28	144	30	Y
67	ASHOK	31	M	A	A	110	126/76	84	35	57	88	43	N
68	NIZAM ALI	49	M	P	P	110	166/76	88	38	68	150	54	N
69	RITA NAYAK	46	F	P	P	110	180/80	88	24	20	188	49	N
70	S N RAMESH	55	M	P	P	110	116/76	179	24	34	137	41	Y
71	PRABHU	42	M	A	A	110	122/76	88	23	55	180	40	N
72	UMAIZ BEGHUM	50	F	P	P	110	116/90	97	31	40	145	60	N
73	SUBRAMANYA	53	M	A	P	110	130/80	141	60	106	104	48	N
74	SANTHOSH V	29	M	A	A	110	166/92	108	26	38	199	34	Y
75	THIMMARAYAPPA	22	M	A	A	110	120/110	91	35	47	182	30	Y
76	NILEESH	31	M	A	A	109	106/70	85	67	150	140	58	N
77	MANJUNATH L	60	M	P	P	85	140/90	108	29	43	125	33	N
78	PRASHURAM	56	M	A	P	85	150/90	85	32	36	101	42	N
79	KARIYAPPA	31	M	A	A	85	110/70	126	34	38	150	37	Y
80	SUMITHRA	37	F	P	P	84	110/70	89	27	36	110	46	N
81	PUTTATHAYAMMA	40	F	P	P	84	90/60	79	64	96	101	54	N
82	GOWRAMMA	60	F	P	A	84	110/90	138	44	46	200	40	Y
83	PUTTALAKSHMAMMA	69	F	P	A	84	140/80	138	20	21	95	58	N
84	BIMAL KUMAR	28	M	A	A	84	120/70	97	121	180	190	36	N
85	DHIRENDRA	40	M	A	P	84	120/80	106	25	38	197	49	N
86	PRAVEEN	29	M	A	A	84	126/82	99	33	50	180	45	N
87	GANESH HOSMANE	36	M	A	A	84	130/90	90	32	50	145	54	N
88	PRADEEP K	40	M	A	A	84	130/98	110	28	20	105	43	N
89	PONAPPA	58	M	P	A	84	110/70	84	20	18	98	50	N
90	MAQBUL BEE	65	F	P	P	80	110/70	360	18	22	256	62	Y

91	JAYAMMA	60	F	P	A	82	130/80	120	15	18	247	28	Y
92	GANGAMMA	75	F	P	P	107	160/90	228	25	19	168	29	Y
93	ARPITHA	19	F	A	A	79	110/70	74	47	36	146	28	N
94	SHAHINA TAJ	39	F	A	P	92	136/86	34	30	35	136	369	Y
95	SHANTHAMMA	42	F	P	A	84	140/90	264	40	45	230	33	Y
96	SABINA BANU	25	F	A	A	118	120/70	103	25	18	110	42	Y
97	BANU BI	42	F	A	P	90	160/100	88	16	9	166	32	Y
98	SABEERA	50	F	P	A	88	120/90	260	36	35	278	13	Y
99	GEETHA	38	F	A	A	100	118/82	184	52	51	99	27	N
100	RATHNAMMA	42	F	P	A	100	154/114	188	32	34	242	27	Y