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MODIFIABLE AND NON-MODIFIABLE RISK FACTORS ASSOCIATED WITH NON-ALCOHOLIC FATTY LIVER DISEASE

Ayesha Saeed[1], Hassnain Ijaz[*2], Hasan Ijaz[3], Ayyaz Ahmad[4], Umm e Summaya[5], Shafia Tayyab[6], Huma Ishaq[7], Rubab Arshad[8], Fajar Khalid[9], Ramisha Shahbaz[10]

[1,7,8,9]Department of Medical Imaging Technology, Aziz Fatima Medical and Dental College, Faisalabad, Pakistan
*[*2]Department of Radiological Science and Medical Imaging, The Superior University, Faisalabad, Pakistan*
[3]Faculty of Allied Health Sciences, Department of Pathology , Faisalabad Medical University, Faisalabad, Pakistan
[4]Department of Radiology Social Security Hospital, Faisalabad, Pakistan
[5]Department of Medical Imaging Technology, Riphah International University, Faisalabad Campus, Pakistan
[6]Fazle Omer Hospital, Zubaida Bani Wing (Gynecology & Obstetrics Ultrasound Department), Chenab Nagar, Chiniot, Pakistan
[10]Department of Medical Imaging Technology, Riphah International University, Faisalabad Campus, Pakistan

[*2]hassnain.ijaz.95@gmail.com, [3]hasanijaz17@gmail.com

Corresponding Author: *
Hassnain Ijaz
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ABSTRACT

Background: *Various modifiable and non-modifiable risk factors are associated with NAFLD. The most important aspect for coping with non-alcoholic fatty liver disease is lifestyle modification.*

Objective: We aim to determine the association of each modifiable and non-modifiable risk factor with NAFLD frequency wise.

Methodology: *The study conducted at Aziz Fatima Hospital focused on assessing risk factors for Non- Alcoholic Fatty Liver Disease (NAFLD) in a population of 213 patients aged 30 to 70. Using a cross- sectional design, we collected data on modifiable factors (such as diabetes, hypertension, obesity, etc.) and non-modifiable factors (age, gender) through a self-structured questionnaire validated via a pilot study. Participants were diagnosed with NAFLD based on ultrasound findings and excluded if pregnant, consuming alcohol, or had certain viral infections or liver diseases. Convenience sampling was used, and statistical analysis was performed using SPSS 20 software. Ultrasounds were conducted by a Sonologist using a GE LOGIQ P7 Ultrasound machine. This comprehensive approach aimed to provide insights into NAFLD risk factors within the specified population.*

Results: *The study investigated modifiable and non-modifiable risk factors associated with non- alcoholic fatty liver disease (NAFLD). Among modifiable factors, hypertension demonstrated the highest prevalence (66.7%), followed by diabetes (63.4%), high cholesterol (50.2%), and heart disease (38.0%). Additionally, dietary habits such as regular consumption of oily (70.0%) and junk foods (65.7%) were prevalent among participants. Sedentary lifestyle was common, with a significant proportion reporting barriers to exercise (42.7%). Most participants were overweight (38.5%) or obese (33.3%), and insufficient sleep duration (66.2%) was prevalent.*

Demographic findings revealed a higher incidence of NAFLD among women (63.8%) and individuals from rural areas (50.7%). These findings shed light on the multifaceted nature of NAFLD risk factors, emphasizing the need for comprehensive prevention and management strategies.

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Conclusion: *Age and gender remain immutable factors, lifestyle modifications targeting diabetes, hypertension, and unhealthy dietary habits offer avenues for prevention. Obesity, sedentary behavior, and inadequate sleep emerge as significant modifiable risk factors contributing to NAFLD prevalence, particularly among women. Dietary changes and regular physical activity hold promise in reducing NAFLD incidence and mitigating its progression to advanced liver diseases.*

Key words: *NAFLD, BMI, Ultrasound, Modifiable, Non-modifiable, Risk Factors.*

INTRODUCTION

1.1 Anatomy of Liver:

The liver, which is slightly heavier in males than in females, is the largest and heaviest glandular organ in the body. It weighs 1.5 kg on average for adults (or roughly 2% of body weight). The liver has a smooth surface, a soft-to-firm consistency, and a deep burgundy color that reflects its rich vascularity in healthy individuals. The right hypochondrial region is mostly occupied by the liver, which is located high up in the abdominal cavity. It also reaches the area of the stomach. (1)

1.1.1 Lobes of Liver:

The right and left lobes are distinguished from one another somewhat unevenly on the diaphragmatic surface by the attachment of the falciform ligament to the anterior and superior aspects of the diaphragmatic surface. The latter is only approximately 25% or 1/5 of the size of the right lobe. If the inferior surface of the liver is inspected, two more lobes - the quadrate lobe and the caudate lobe, are also visible. (1)

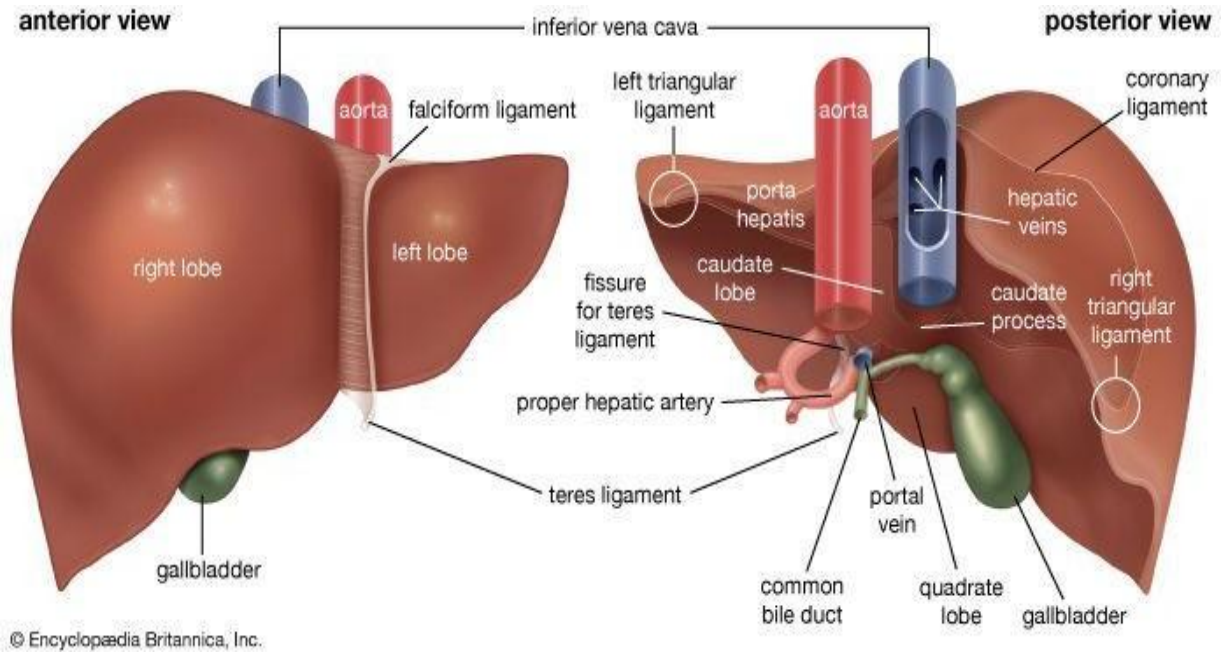


Fig 1.1 shows the lobes of Liver & its anatomy.

1.1.2 Surface marking of liver:

An irregular triangle with moderately convex edges can be used to approximate the surface depiction of the liver. The top border of the liver stretches from a point 7–8 cm lateral to the midline on the 5th left intercostal gap, across to a position inferolateral to the right nipple and overlaying the right 5th rib. This line is located at the xiphisternal junction level. (1)

1.1.3 Peritoneal Attachments:

The liver lies entirely within the peritoneum, with the exception of a tiny exposed spot on the posterosuperior portion of the right lobe. The lines of attachment of the right triangular ligament and the top and lower layers of the coronary ligament enclose the bare area. The anterior abdominal wall's posterior surface forms the falciform ligament, which extends to the liver. The ligamentum teres is the term for the cord-like bottom edge, or free border, of the falciform ligament. (1)

1.1.4 Segmental Anatomy:

The liver can be segmented using a variety of methods. The Couinaud system, which divides the liver into eight segments based on three portal scissura (the right, middle, and left hepatic veins), is the most widely used and recognized standard. Every segment function as a separate functional unit with its own purpose, blood inflow and outflow, and lymphatic and biliary drainage. The right and left hemi-liver make up the first-order division. Therefore, segments V through VIII make up the right hemi-liver, and segments II through IV make up the left hemi- liver. The division of two hemi-livers into the following sections is the second-order division: the right hemi-liver is divided into anterior (segments V and VIII) and posterior (segments VI and VII) sections, while the left hemi-liver is divided into medial (segments IVa and IVb) and lateral (segments II and III) sections. The right hemi liver is divided into anterior and posterior sections by the right hepatic vein. Segment V is the anterior segment of the right hemi liver located below the bifurcation of the portal vein and anterior to the right hepatic vein. Segment VIII is the portion of the right hemi liver located anteriorly, above the portal vein bifurcation and prior to the right hepatic vein. Segment VII is the posterior segment posterior to the right hepatic vein and above the portal vein bifurcation; segment VI is the posterior segment below the portal vein bifurcation. The fissure for the ligamentum teres and the middle hepatic vein are separated by the left medial section. The segments IVa and IVb are located above and below the bifurcation plane of the portal vein, respectively. Segment II is located above and segment III is located below the portal vein bifurcation plane in the left lateral section, which is situated medial to the ligamentum teres fissure. (2)

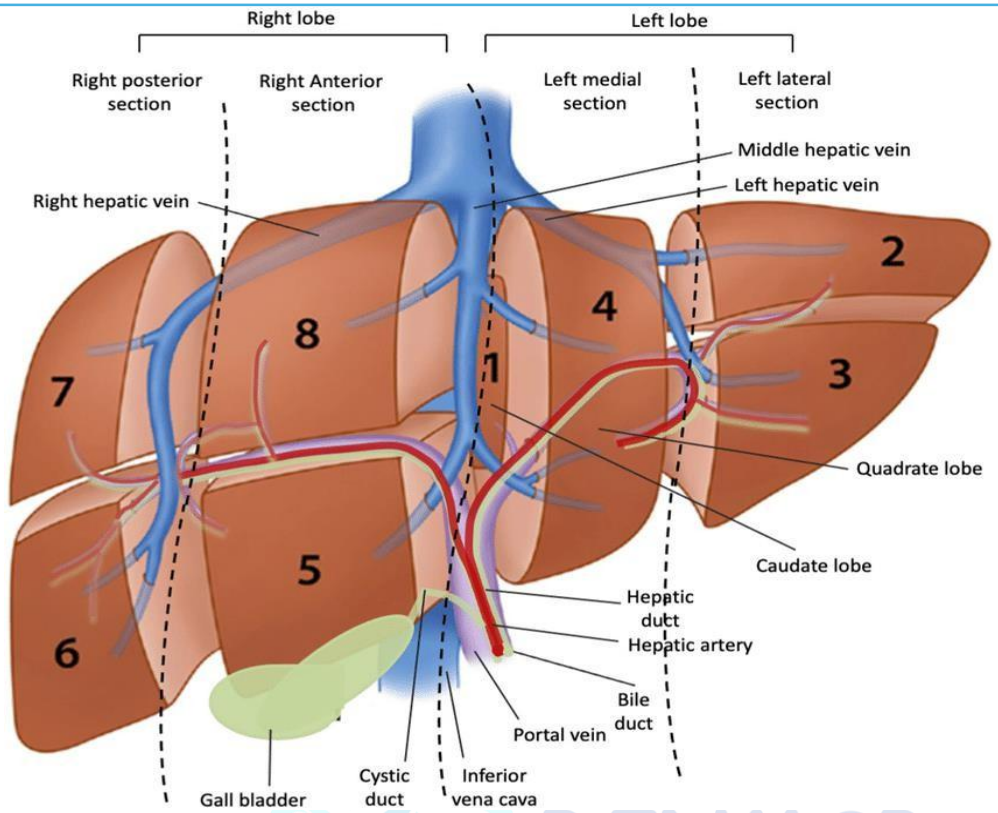


Fig 1.2 illustrates the Segmental anatomy of Liver.

1.1.5 Vascular Anatomy of Liver:

The portal vein, hepatic artery, common hepatic duct (CHD), nerves, and lymphatics all enter the liver through the porta hepatis, which is the liver's hilum. (2)

1.1.6 Blood Supply:

Among the solid viscera, the liver is unique in that it receives blood from the hepatic artery and the portal vein, respectively, two venous and arterial sources. The hepatic artery supplies the remaining 25–30% of the inflow, with the portal vein providing the remaining 70–75%. (1) The common liver artery (CHA) supplies about 20-25% of the liver's blood supply. It's often referred to as a "celiac trunk". The celiac trunk originates from the D12-L1 vertebrae. After a few inches, it usually tifuracs into the common liver artery, the left gastric, and the splenic arteries. The common liver artery continues as the proper liver artery (HA), which is usually located anterior to portal veins and medial to bile ducts. It divides into a right and left branch, supplying the appropriate lobes of your liver. In some cases, the middle liver artery may supply segment IV of your liver. This variation occurs in about 20% of cases. (2)

1.1.7 Venous Drainage

The hepatic veins carry venous blood from the liver back to the inferior vena cava. The right hepatic vein, the middle (or central) hepatic vein, and the left hepatic vein are the three main hepatic veins. (1) The left portal vein is located in segment II and III and drains segments IV. The middle portal vein is situated in segment IV and drains segments IV most of the time. The middle vein also receives branches from segment V and segment VIII. The right portal vein is the biggest in segment V to VIII and most of the time drains segments V-V8. Single or multiple separate vein channels drain the Caudate lobe directly into the IVC. In 60-95% of cases, the middle and left liver veins join together to form a trunk. (2)

1.1.8 Lymphatic Drainage of Liver:

The superficial lymph node, located inside Glisson's capsule, and the deep network of lymph nodes are the two lymph node networks into which the hepatic lymph node first empties. The majority of the posterior liver's superficial lymph nodes are grouped in the open area, from whence they travel through the inferior vena cava

to the posterior mediastinal lymph nodes. The thoracic duct is the last outflow for these nodes. (1)

1.2 Non-Alcoholic Fatty Liver:

In 1980, a similar disease to alcoholic fatty liver disease that developed in patients without a history of excessive alcohol consumption was named non-alcoholic fatty liver disease (NAFLD)
(3). As the hepatic manifestation of metabolic syndrome, non-alcoholic fatty liver disease (NAFLD) is linked to progressive hepatocellular lipid accumulation, primarily of triglycerides, up to more than 10% of liver weight. This condition includes a broad spectrum of liver diseases, ranging from non-alcoholic steatohepatitis (NASH) to simple non-alcoholic fatty liver (NAFL). If left untreated, these diseases can have life-threatening side effects, including cirrhosis and hepatocellular carcinoma. Although one-third of NAFLD patients eventually progress to NASH, which is characterized by inflammation and hepatocellular injury, NAFLD is generally thought to be a benign and reversible condition. Although the causes of NAFLD have been extensively studied, the primary factors influencing the development of NAFLD into NASH are still largely unknown and are the subject of ongoing research. Numerous experimental findings revealed that oxidative stress, proinflammatory mediators, and lipotoxicity might play a major part in this process, which can happen with or without consuming a lot of fat in the diet. In addition, the development and progression of non-alcoholic fatty liver disease (NAFLD) are linked to the consumption of unbalanced diets (such as high fat and sugar intake) and altered gut flora. In instance, meals heavy in fat and sugar may alter the composition of the microbiome and the integrity of the gut barrier, which may facilitate bacterial translocation and inflammation in addition to encouraging the accumulation of fat in the liver. Additionally, it has been demonstrated that oxidative stress and inflammation are important factors in a variety of extrahepatic diseases, including disorders of the central nervous system (CNS), such Alzheimer's disease (AD). (4) The existence of ≥5% hepatic steatosis without hepatocyte injury is referred to as NAFLD. The exclusion of secondary causes of hepatic fat accumulation, such as the use of steatogenic medications (e.g., corticosteroids, amiodarone, methotrexate), hereditary disorders (e.g., Wilson's disease, alpha-1 antitrypsin deficiency), or viral infections (e.g., hepatitis C infection), is necessary for the diagnosis of non-alcoholic fatty liver disease (NAFLD). Furthermore, the daily limit for alcohol consumption for males and women is 20 g and 30 g, respectively. These criteria for alcohol consumption are not absolute though, as guidelines from the Asian-Pacific region and Germany have recommended lower limits of 10 g/day and 20 g/day, respectively. (5)

1.3 Range of the evolution of NAFLD:

Simple steatosis (or NAFL), NASH, liver cirrhosis, and ultimately HCC are the four phases of NAFLD development. Simple steatosis is caused by various factors such as obesity, T2DM (especially the accompanying IR), Western HFHSDs, and other metabolic illnesses. NASH is a result of a number of factors, including hepatocyte death and inflammation. A transitory phase of NASH known as hepatic fibrosis leads to the development of liver cirrhosis. The degree of liver fibrosis in patients with nonalcoholic steatohepatitis (NASH) and cirrhosis is used to categorize the disease into four phases. (6)

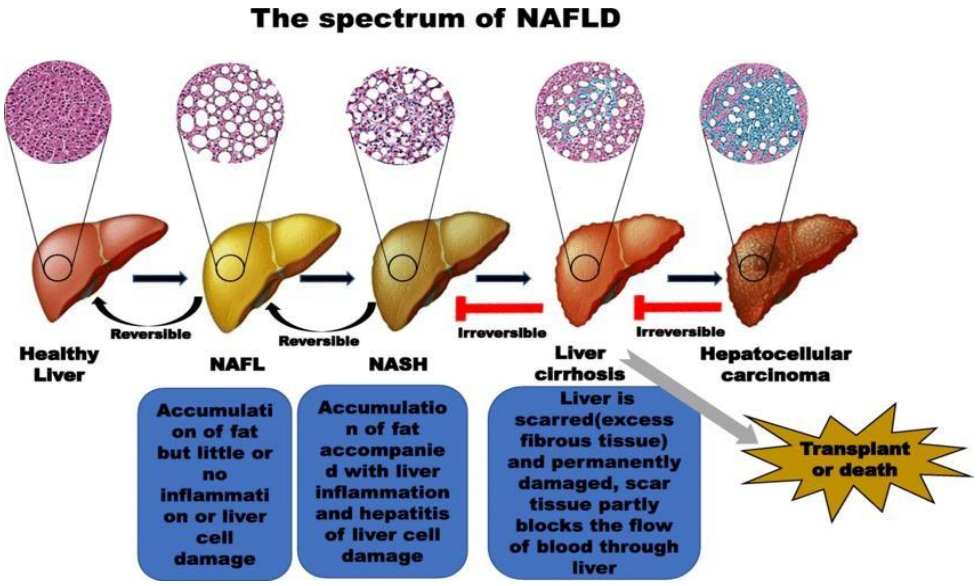


Fig 1.3 demonstrates the spectrum of NAFLD.

1.4 Prevalence:

The prevalence of NAFLD has increased to 25.2% worldwide, and by 2030, it is predicted to reach 33.5%. (7) Urban populations, where obesity and metabolic syndrome are more common, have the highest prevalence of NAFLD (27%). About 24% of people in Europe are estimated to have NAFLD. Depending on whether the patients were from rural or urban areas in India, the prevalence of NAFLD varied from 8.7% to 32.6%. NAFLD is more common as people get older. Hispanics had the highest prevalence of NAFLD, followed by non-Hispanic white people, and African Americans had the lowest prevalence (10%). (8)

1.4 Risk Factors:

Type 2 diabetes mellitus (T2DM), obesity, insulin resistance, HTN, hyperlipidemia, and metabolic syndrome (MS) are all linked to nonalcoholic fatty liver disease (NAFLD). The risk of NAFLD is increased by obesity. A body mass index (BMI) of 30 or higher is considered obese. The global aging population and rising rates of obesity and type 2 diabetes in adults and children are contributing to the rise in the incidence of non-alcoholic fatty liver disease (NAFLD).

Additionally, the incidence of HCC linked to NAFLD is rising. (8) There is an inverse relationship between physical activity (PA) and nonalcoholic fatty liver disease (NAFLD). One independent predictor of NAFLD has been identified as sedentary behavior. Women had a lower probability to meet the PA Guidelines, although PA exhibited a 10% greater connection with risk reduction of NAFLD in women. Regardless of NAFLD condition, trends in overall sitting duration increased dramatically. (9) Increased intake of tea, coffee, and soft drinks is linked to NAFLD as well. (10) A shorter sleep duration is linked, on its own, to a higher chance of incident non-alcoholic fatty liver disease. (11) Women with PCOS had an increased risk of NAFLD. (12) In young, premenopausal women, longer or irregular menstrual cycles were linked to a higher risk of incident and prevalent NAFLD. (13) There is also a correlation between an increased risk of NAFLD, increasing age and female gender. (8)

1.5 Classification of Risk Factors:

They are classified as modifiable and non-modifiable risk factors.

Early detection of modifiable risk factors is crucial for preventing non-alcoholic fatty liver disease (NAFLD). They include:

- Obesity

- Type 2 diabetes mellitus
- Hypertension
- Hyperlipidemia
- Physical inactivity
- Shorter sleep duration
- PCOS
- Increase consumption of coffee, tea and soft drinks.

Non modifiable risk factors are those that cannot be changed and their identification does not prevent NAFLD. These include:

- Increasing age
- Gender
- Menopause
- Genetics/ Family history (14)

1.6 Mortality Rate

Compared to the general population, NAFLD patients have a significantly higher death rate. In patients with early-stage NAFLD, the most prevalent consequences are cardiovascular events and non-hepatic cancers, whereas those with severe fibrosis or cirrhosis (≥fibrosis stage F3) have the highest risk of liver-related death. (5)

1.7 Clinical Manifestation and Symptoms:

The complex interactions between the primary drivers of non-alcoholic fatty liver disease (NAFLD), which include poor dietary and lifestyle choices, a dysfunctional microbiota, genetic predisposition, and environmental stimuli that cause metabolic dysfunction and liver disease, ultimately determine the clinical manifestations of the disease. (3) The diagnosis of NAFLD in patients exhibiting nonspecific symptoms is on the rise. Patients with NAFLD may have symptoms like

- Exhaustion
- Anxiety
- Depression
- Loss of self-worth
- Cognitive Impairment (15)

1.8 Effect on Quality of life:

Quality of life related to health is impacted by NAFLD. NAFLD patients report a greater impairment of their physical health than their mental health. Patients with NAFLD stated that their health was either fair or poor. HRQOL is impacted by NAFLD. (15)

1.8 Role of Ultrasound:

Transabdominal ultrasound is the primary imaging method in patients with suspected NAFLD. Using B-Mode ultrasound imaging to calculate the hepatorenal index (HRI) may improve the diagnostic precision of hepatic steatosis identification and grading. The ratio of the liver parenchyma and renal cortex echo intensities is known as the hepatorenal index (HRI).
(16)

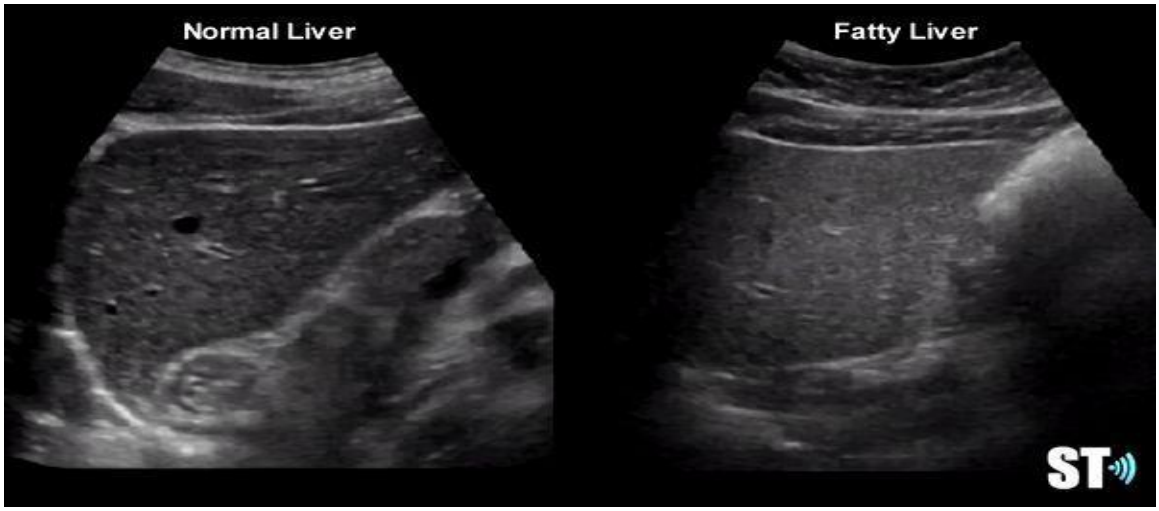


Fig 1.4 shows Normal vs Fatty Liver on the Ultrasound.

1.8.1 Significance:

There are no negative effects. It is widely accessible and reasonably priced. The primary indicator of steatosis is the liver parenchyma's higher echogenicity when compared to the right kidney's cortex due to intracellular fat vacuole accumulation reflecting the ultrasound beam. The sensitivity and specificity of B-mode ultrasound in detecting hepatic steatosis range from 53 to 76% and 76 to 93%, respectively. When there is impaired diaphragm visualization, there is a 100% chance that hepatic steatosis will occur. When steatosis is only slightly severe (less than 20–30%), B-mode sonography's sensitivity is low. (16)

1.8.2 Grading on Ultrasound:

The classification of hepatic steatosis is usually graded as follows:

Grade 0:
The right liver's echogenicity is normal when compared to the right kidney's cortex.

Grade 1:
Normal visualization of the diaphragm and intrahepatic vessel borders with a slight, diffuse increase in fine echoes in the liver parenchyma.

Grade 2:
Mildly impaired visualization of the diaphragm and intrahepatic vessels with a moderate, diffuse increase in fine echoes.

Grade 3:
A significant increase in fine echoes accompanied by poor or absent visualization of the diaphragm, posterior right lobe of the liver, and the borders of the intrahepatic vessels. (16)

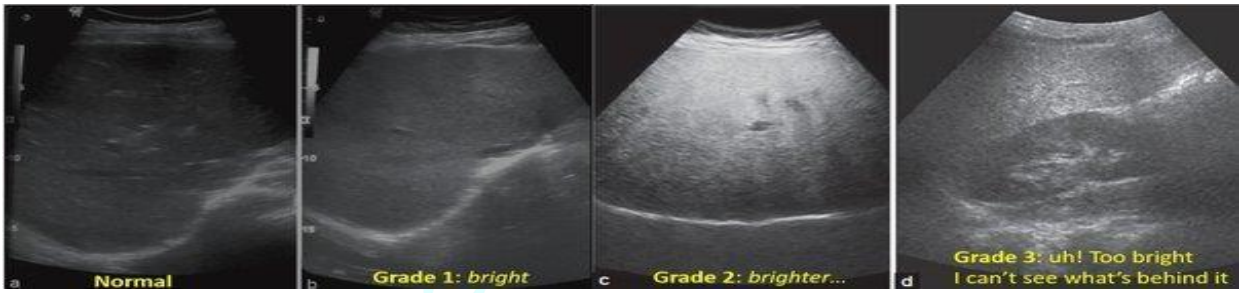


Fig 1.5 exhibits the grades of Fatty Liver on Ultrasound.

1.9 Management:

As of right now, there is no approved medication to treat non-alcoholic fatty liver disease (NAFLD). Instead, risk factors are mitigated by avoiding foods high in trans fats, high- fructose corn syrup, red meat, low in fiber, and high in energy density. However, the main goals of treatment - which are frequently achieved through a multimodality approach - remain weight loss and improved insulin resistance. (17) The cornerstone of managing non-alcoholic fatty liver disease (NAFLD) is lifestyle change. (10)

3.1: OBJECTIVE:

The objective of the study is to evaluate the frequency of various modifiable and non-modifiable risk factors associated with Non-alcoholic fatty liver disease (NAFLD).

3.2: SIGNIFICANCE OF STUDY:

Due to high prevalence of NAFLD, the proportion of liver related complications resulting from NAFLD such as Cirrhosis, hepatocellular carcinoma, liver transplantation and mortality is expected to be higher. By controlling the risk factors, prevalence of NAFLD can be reduced.

MATERIAL AND METHODS

4.1 : Study Design: Cross Sectional Study.

4.2 : Settings: Aziz Fatimah Hospital

4.3 : Study Duration: Study was conducted for the period of 5 months from October 2023 to February 2024

4.4 : Sample Size: 213

The sample size is calculated by open epi through the following formula

$$n = deff \times \frac{Np\hat{q}}{\frac{d^2}{196^2}-1+p\hat{q}} \quad (34)$$

n = sample size

deff = design effect = 1

N = population size = unlimited

pˆ = the prevalence of NAFLD based on the ultrasound above 20 years of age is 0.189. (18)
qˆ = 1 - pˆ = 0.811

d = desired absolute precision or absolute level of precision= 5%

4.5 : Study subjects: NAFLD

4.6 : Sampling Technique: Convenience sampling

4.7 : Sample Selection:

4.7.1 : Inclusion Criteria: Fatty liver patients diagnosed on Ultrasound

4.7.2 : Exclusion Criteria: Alcohol intake

Pregnant women
Positive serology for hepatitis B and C virus History of another known liver disease,
Liver Biopsy Patients taking Chemotherapy drugs, Anti-TB drugs, steroids.

4.8 : Equipment(s): Ultrasound with curvilinear transducer having frequency of 2-5 MHz
Modifiable and non-modifiable risk factors were evaluated by the self-structured questionnaire.

4.9 : Study Variables:

Independent: Non-modifiable: Age, Gender, Menopause Modifiable: Diabetes, HTN, CVD, Obesity, Sleep
Dependent: Fatty Liver.

4.9 : Hypothesis:

Null hypothesis: There is no association between risk factors and fatty liver.

Alternate hypothesis: There is an association between risk factors and fatty liver. receive good quality sleep.
Diabetes: A chronic condition brought on by insufficient insulin production by pancreas or Insufficient utilization by body. HbA1c results = or >6.5% indicates diabetes. Fasting Plasma glucose level greater than or equal to 126mg/dl indicates diabetes.

Hypertension: It is a medical condition in which the blood pressure in the arteries is persistently elevated. The SBP will be more than or equal to 140mm Hg and DBP will be more than or equal to 90mm Hg.

Cardiovascular Diseases: It is defined as the diseases related to the heart and blood vessels.

4.10 DATA COLLECTION PROCEDURE

The Cross-sectional study was conducted on a total 213 patients including both male and female of age between 30 to 70 to assess the risk factors related to NAFLD. NAFLD patients were enrolled on the basis of Ultrasound findings. Modifiable risk factors DM, HTN, CVD, Obesity, sleep and non-modifiable risk factors like age and gender were gathered on a self-structured questionnaire formed by reviewing different literature which was validated by pilot study. Fatty liver patients diagnosed on ultrasound will be included in this study. Pregnant women, people with alcohol consumption, positive serology for hepatitis B and C virus and patients with chronic liver disease or history of any known liver disease were excluded in this study. A convenience sampling technique was used and statistical analysis was done on SPSS 20 software. All the Ultrasounds were done by a Sonologist by using GE LOGIQ P7 Ultrasound machine with a convex probe having frequency of 2-5MHz at Aziz Fatimah Hospital after approval from the Ethical Research Committee of Aziz Fatimah Medical and Dental College Faisalabad.

4.11 DATA ANALYSIS PROCEDURE

- Statistical analysis was conducted on SPSS 20 Software by using
- Means ± SD for continuous variables (Age)
- Frequency and percentages for categorical variables (gender etc.)
- Chi square for comparison of categorical data (percentages)
- The level of significance will be taken as $p < 0.05$

RESULTS

The study was conducted between October 2023 to February 2024 on 213 patients who were diagnosed NAFLD on the basis of Diagnostic Ultrasound. Out of which 136(63.8%) were female and males were 77 (36.2%). The study shows that females were more likely to affected by NAFLD than male.

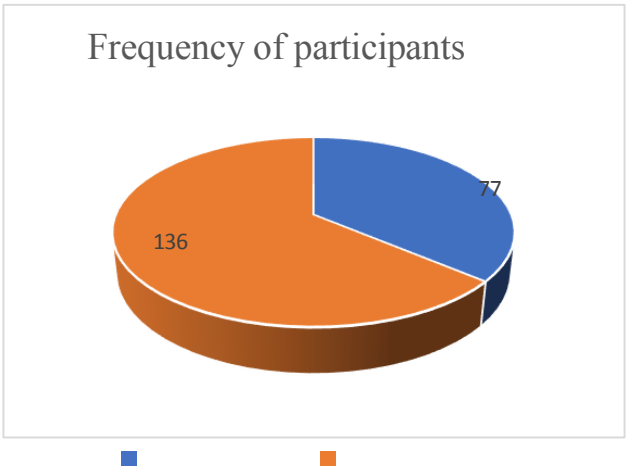


Fig 5.1 shows the gender distribution of patients.

(Fig 5.1) The mean age of patients was 49.1690, with an upper bound of 51.0234 and a 95% confidence interval of 47.3146 for the mean lower bound. (Fig 5.2)

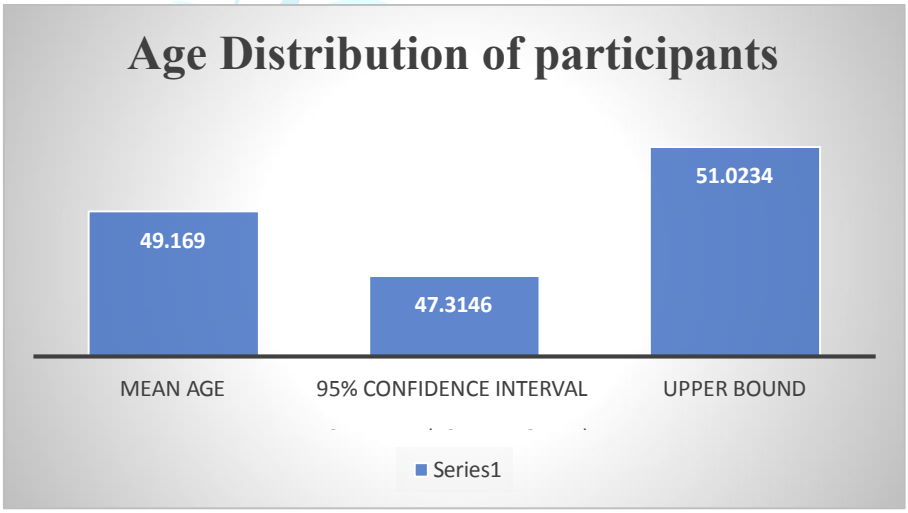


Fig 5.2 shows that mean age of the patients included in our study

This study shows the frequency of modifiable and non-modifiable risk factors linked with non-alcoholic fatty liver disease (NAFLD) and determines how frequently each risk factor contributes to the disease. The modifiable risk factors for non-alcoholic fatty liver disease (NAFLD) include diabetes, hypertension, heart disease, and excessive cholesterol. HTN had the highest frequency of connection with NAFLD among these four, at 142 (66.7%). Among the NAFLD patients, the prevalence of diabetes, heart disease, and high cholesterol was 135 (63.4%), 81 (38.0%), and 107 (50.2%),
respectively. (fig 5.3)

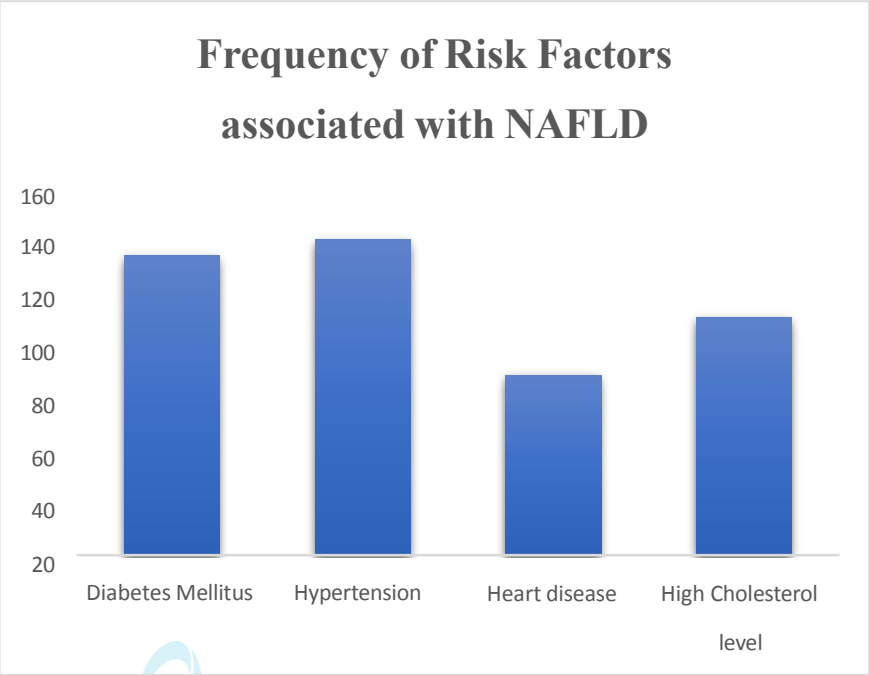


Fig 5.3 shows frequency of modifiable risk factors (DM, HTN, CVD & High Cholesterol)

After a review of the participants' eating habits, it was found that 149 (70.0%) of the participants regularly consumed oily foods, while 64 (30.0%) of the participants did not. Nonetheless, 72 (33.8%) patients did not consume junk food, compared to 140 (65.7%) patients who did. 112(52.6%) preferred eating meat as compared to 101 (47.4%) patients eating vegetable. (Fig 5.4)

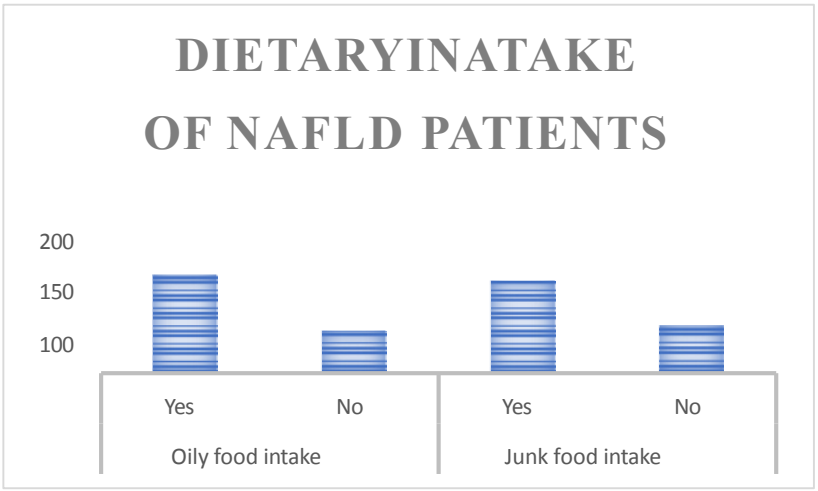


Fig 5.4 illustrates frequency of participants regularly consumed oily foods and junk foods.

Inactive or sedentary lifestyle is another modifiable risk factor of NAFLD. Results of the study revealed that 81 (42.7%) patients never did any exercise. Only 54 (25.4%) patients were doing exercise twice a week. 60 (28.2%) patients were doing exercise once a month and 8 (3.8%) patients were doing exercise once a week. The factors that

restrict patients from doing exercise are following: Fatigue (30.5%), Lack of time (25.4%) Lack of energy (27.2%) and Body pain (16.9%). (Fig 5.5) Our study shows that out of 213 participants, 149 patients had difficulty in maintaining their weight and 64 patients had no trouble in maintaining their weight. (Fig 5.6)

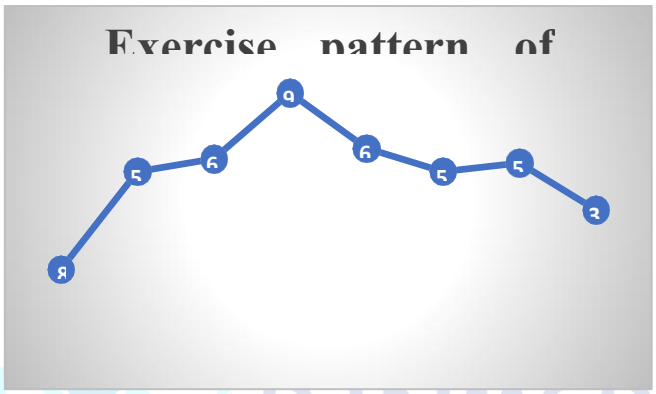
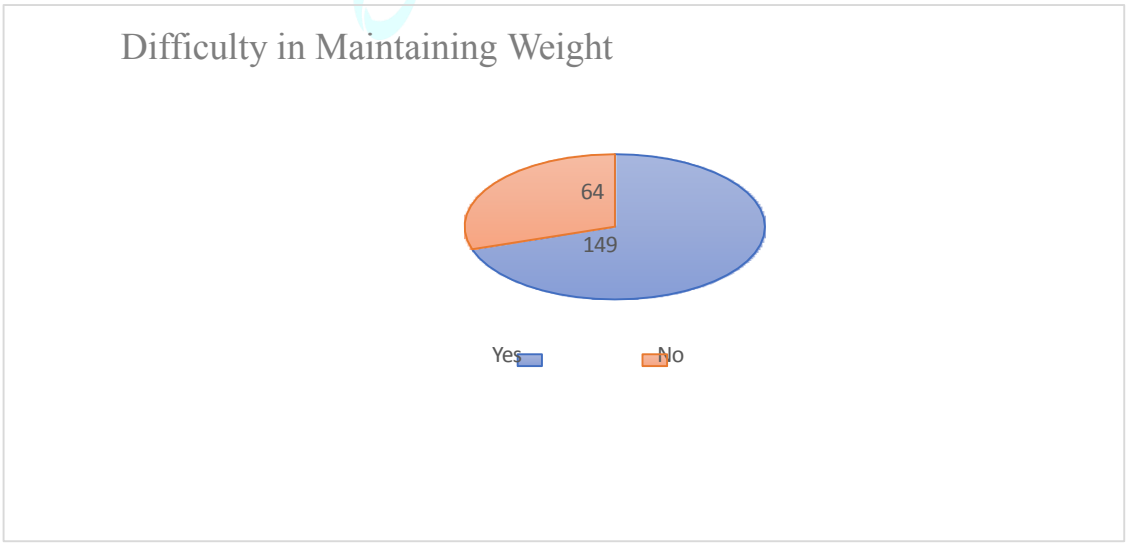


Fig 5.5 illustrates the exercise pattern

Fig 5.6 shows the ratio of patients having difficulty in maintaining weight



Insomnia or shorter sleep duration is another modifiable risk factor associated with NAFLD. According to our research, 72 (32.8%) patients slept for more than eight hours, while 141 (66.2%) of the 213 participants slept for less than eight hours. (Fig 5.7)

ONCE A WEEK TWICE A WEEK ONCE A MONTH NEVER	FATIGUE LACK OF PAIN TIME LACK OF ENERGY BODY
FREQUENCY OF DOING EXERCISE	FACTORS THAT RESTRICT DOING EXERCISE/WORKOUT

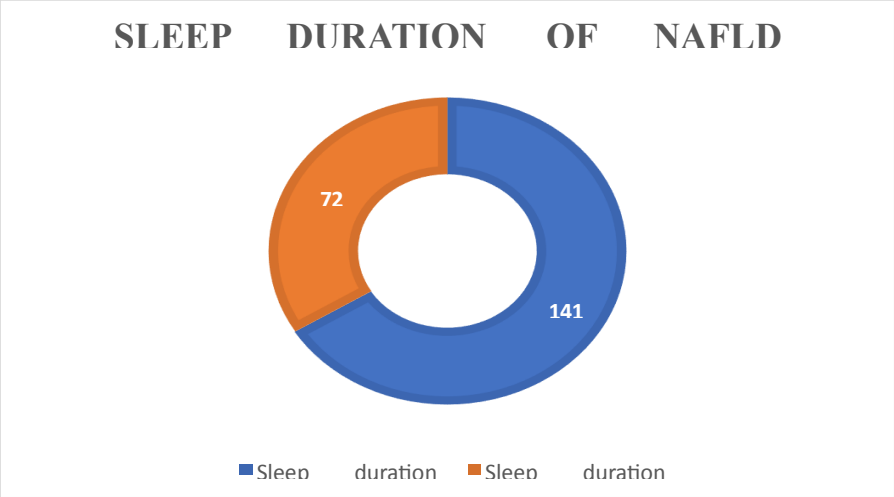


Fig 5.7 shows the sleep duration of NAFLD patients

Table 5.1 shows the demographic profile of the patents

Variables	Categories	Frequency	%
Marital status	Married	176	82.6
	Unmarried	37	17.4
Education status	Below Matric	98	46.0
	Intermediate	77	36.2
	Graduation	38	17.8
Occupation	Unemployed	73	34.3
	Job	120	56.3
	Business	20	9.4
	Rural	108	50.7

Residency	Urban	105	49.3

Table 5.1 shows the demographic profile of the participants. Out of 213 NAFLD patients, 37 patients were unmarried and 176 patients were married. 105 patients came from urban regions while 108 were from rural areas. The analysis of the education profiles showed that only 38 patients had graduated, whilst 77 had completed intermediate education and 98 had less than matriculation education. An examination of the patients' occupations shows that 20 patients had their own businesses, 120 patients were employed, and 73 patients were jobless.

Out of 213, 53 patients had a healthy weight, 71 patients had Obesity, 82 patients were Overweight, and just seven patients were Under weight. According to this study, most of the NAFLD patients were Over Weight. 119 patients were checking their weight regularly and 94 were not checking their weight. 107 patients tried to lose weight and 106 patients had not tried. (table 5.2)

Table 5.2 illustrate the BMI and weight related profile of patients.

Variables	Categories	Frequency	%
BMI	Under weight	7	3.3
	Healthy weight	53	24.9
	Overweight	82	38.5
	Obesity	71	33.3
Checking Weight Regularly	Yes	119	55.9
	No	94	44.1
Try to lose weight	Yes	107	50.2
	No	106	49.8

DISCUSSION

Globally, one of the most frequent causes of chronic liver disease is non-alcoholic fatty liver disease (NAFLD). When no other factors, such as excessive alcohol intake, are shown to be the cause of secondary hepatic fat buildup, hepatic steatosis is the hallmark of nonalcoholic fatty liver disease (NAFLD). NAFLD spans from non-alcoholic fatty liver (NAFL), a more benign illness, to non-alcoholic steatohepatitis (NASH), a more serious disorder. NAFLD may develop into cirrhosis and fibrosis over time. Hepatic steatosis is seen in NAFLD but not in NASH; in NASH, hepatic steatosis is linked to lobular inflammation and apoptosis, which may result in cirrhosis and fibrosis. (27)

NAFLD patients frequently have one or more metabolic syndrome (MS) characteristics, such as diabetes, dyslipidemia, insulin resistance, and systemic hypertension. An increasing body of research suggests that abdominal adiposity increases the risk of NAFLD. There are various levels of NAFLD treatment, with conservative and surgical therapies

being the most well-known forms of care. Patients with non-alcoholic fatty liver disease (NAFLD) are generally treated with a multimodal intervention that addresses many components of their condition, such as medication optimization, lifestyle adjustments, and weight loss. (27)

213 patients constitute the sample size for the current study which was conducted at Aziz Fatima Hospital. Every patient had their demographic information, including age, gender, height, weight, and residency status, documented using a standard questionnaire. Data on blood pressure, cholesterol, cardiovascular disease, way of life, and food habits were also noted to evaluate the modifiable and non-modifiable risk factors associated with NAFLD. A similar investigation was conducted by Alia Ali et al on 185 participants in total to find out how common NAFLD is among type 2 diabetic patients and what risk factors are connected with it. All type-2 diabetics, regardless of age, were separated into two groups and subjected to abdominal ultrasonography evaluations; the groups with and without fatty liver disease were further assessed by BMI, obesity, HbA1c, and lipid profile measurements. Age and HDL cholesterol did not significantly differ between the groups of cases with and without fatty liver disease, whereas instances with NAFLD had considerably higher levels of BMI, TGs and cholesterol levels, ALT, and AST. Among patients with Type-2 diabetes, BMI >24.5, HbA1c
>7.0, and ALT >40.0 can predict NAFLD with 96.8% accuracy. (20) In contrast, 135 out of 213 individuals in the current study had diabetes. 63.4% are diabetic while 36.6% are non-diabetic in the present study.

NAFLD and HTN have a bidirectional association that is unaffected by conventional cardiometabolic risk factors, according to another study by Gerui Li. Significantly, there is a 1.55-fold increased risk of incident HTN in the presence of NAFLD, and a 1.63-fold increased risk of incident NAFLD in the presence of HTN. It is crucial to acknowledge NAFLD as a risk factor for HTN and vice versa in order to enhance risk prediction, pinpoint main preventative measures, and investigate treatment plans for these two progressively common and debilitating illnesses. According to pooled data, having NAFLD was substantially linked to a higher chance of incident HTN (pooled HR 1.55; 95% CI: 1.29–1.87; n = 9 trials, 46,487 participants. There was evidence of possible heterogeneity amongst the individual studies (I2 = 80.5%, < 0.01). (28) However, the current study's results also shown a high correlation between HTN and NAFLD. Out of the 213 NAFLD patients in total, 142 had hypertension and 71 did not. In the current study, 33.3% of patients had NAFLD without hypertension, while 66.7% of patients had both.

As in the previous analysis, this new study found a stronger correlation between hypertension and NAFLD than between diabetes mellitus and the NAFLD.

According to this study, another risk factor for NAFLD is cardiovascular illness. According to the current study, 132 individuals had NAFLD without heart disease while 81 patients had both heart disease and NAFLD. 38.0% patients had both NAFLD and cardiovascular illness.

In contrast to the current study, a meta-analysis by Philipp Kasper et al. showed that there is a clear correlation between cardiac arrhythmias, coronary artery disease, and heart disease, and that individuals with NAFLD had a 64% higher chance of experiencing fatal or non-fatal cardiovascular events than patients without NAFLD. (5) According to the current study, heart disease and NAFLD have the least relationship among these three conditions (HTN. DM and CVD), although hypertension has a stronger relationship than the other two.

Another study by Amedeo Lonardo et al. revealed that patients with obesity are more likely to develop non-alcoholic fatty liver disease (NAFLD) than people who are normal weight and metabolically fit. (29). However, in the current study, 53 patients had a healthy weight, 71 patients had Obesity, 82 patients were Overweight, and just seven patients were Under weight. According to this study, most of the NAFLD patients were Over Weight.

In this study, 106 individuals had cholesterol levels less than 120 mg/dl, while 107 NAFLD patients had high cholesterol levels. It is not supported by enough data that a high cholesterol level increases the risk of NAFLD. A study by Jun-Hyuk Lee et al. used data from a large- sample prospective cohort study in Korea and discovered that individuals with NAFLD had inadequate management of LDL cholesterol. They discovered that compared to people without NAFLD, fewer patients with NAFLD met their LDL cholesterol goals. (30)

According to a meta-analysis by Kiarash Riazi et al., adopting a low-calorie diet over time is linked to a reduction in liver fat and an improvement in cardiovascular risk. A fatty liver was improved by reducing calorie intake by at least 30%, or by roughly

750 to 1000 kcal/day.

Nonetheless, there is little chance that such hypocaloric diets will last. Diets high in carbs (50– 65% of total calories) have been linked to obesity, increased insulin resistance, and a transition from benign fatty liver toward non-alcoholic steatohepatitis (NASH). (31) Seventy-two patients in the current study did not consume junk food, compared to 140 patients who did. Of the patients, 119 consumed junk food twice a week, while 29 only did it once. 64 patients did not frequently consume oily food, whereas 149 patients consumed it virtually every day. Sjaak Pouwels looked into how diet affected NAFLD risk and management. He discovered that long- term use of sugary drinks was positively correlated with the disease, and that many NAFLD sufferers had higher than average consumption levels of red meat and sugary drinks. (27) While in our study, 112 patients preferred eating meat as compared to vegetables.

Preetam Nath and colleagues conducted a study at the Biju Patnaik State Police Academy in Bhubaneswar, Odisha, India. The academy requires six months of physical training prior to hiring or promoting officers. Male middle-aged police recruits were the subjects; they were chosen for a six-month physical training program. A total of 37 subjects—out of 62 police recruits—were determined to have NAFLD; of these, 18 engaged in moderate- and 19-intense exercise regimens throughout a 6-month period. Results revealed that compared to low-intensity exercise, moderate-intensity physical activity for six months improves hepatic steatosis, serum transaminitis, glycemic and lipid profiles, as well as insulin resistance. For best results, all NAFLD patients should engage in moderately strenuous physical activity. (24) In the present study, 119 patients were not doing any exercise or workout while 94 are doing exercise. 91 patients never did an exercise, while 54 patients were exercising twice a week. According to a study by Oriol Juanola, compared to healthy adults, those with fatty livers had lower levels of physical activity and longer sitting times. (32) According to a study by Donghee Kim et al. those with NAFLD had lower PA Guidelines compliance than people without NAFLD. Though women's risk reduction of NAFLD was shown to be 10% stronger when PA was used, women also exhibited a lower inclination to meet the PA Guidelines. Regardless of NAFLD condition, trends in overall sitting duration increased dramatically. One independent predictor of NAFLD has been identified as sedentary behavior. In the cohort with NAFLD, there was a reduced overall compliance with the PA guidelines. (9)

According to another study by Yoo Jin Um, insufficient sleep quantity may contribute to the incidence and severity of non-alcoholic fatty liver disease (NAFLD) in young adults. Short sleep duration was independently linked to an increased risk of incident NAFLD with or without an intermediate/high fibrosis score. Research indicates that insulin sensitivity may be lowered by sleep disturbance and deprivation, which is a major pathogenic cause of non-alcoholic fatty liver disease. Second, lack of sleep results in proinflammatory activity (such as elevated IL-6 or tumor necrosis factor–alpha), which is another way that NAFLD causes inflammation. Low melatonin levels may also have an impact on liver disease. Additionally, melatonin is known to have potent antioxidant properties. (11) In the current study, 141 patients had short sleep duration of less than 8hrs while 72 patients had sleep duration greater than 8hrs. However, this is the limitation of our study that we had not evaluated the sleep quality in the NAFLD patients we collected information from the patient only regarding the sleep duration. All the risk factors correlated so far are the Modifiable risk factors associated with NAFLD.

Age, Gender, Race and genetics are non-modifiable risk factors associated with NAFLD. According to a study by Souveek Mitra et al. one of the most reliable epidemiological factors for NAFLD, NASH, and fibrosis is growing age, and there is a substantial correlation between NAFLD and aging. Not only is advanced age a risk factor for hepatic steatosis, but advanced age also increases the chance of death and the advancement of the disease to fibrosis and hepatocellular cancer. It's probable that the older NAFLD patients' longer disease duration explains the correlation between age and fibrosis advancement. The majority of epidemiological research found that NASH and fibrosis increased steadily with age, especially after the fifth decade. (33) The current study included the age from 30-70years, the mean age was 41.1690 with the 95% confidence interval for mean age the lower bound was 47.3146 and upper bound was 51.0234.

However, it is not as simple to determine how sex affects the occurrence and progression of NAFLD, according to another meta-analysis. The studies that are now available are uneven in terms of sex; some show a majority of males over females in the prevalence of NAFLD, while others show the opposite. (33) According to another study, when it came to the

NAFLD phenotype, men had a larger prevalence of the MS, thicker visceral adiposity, higher transaminase levels, higher fasting glucose, and higher systolic blood pressure than women did. However, women had a much higher prevalence of NAFLD than men had.(32) In the present study, 136 patients were females while 77 were males So there is female dominance in this study. The research conducted in the USA including multiethnic groups have shown the greatest racial disparities in the prevalence of NAFLD. (33)

The prevalence of MS-related clinical problems such as NAFLD and obesity is rising due to sedentary lifestyle adoption, inactivity, and increased engagement in knowledge-based economic employment. (33) In the current study 149 patients had difficulty in maintaining weight while 64 patients had no difficulty. According to a study by Sjaak Pouwels, weight loss is the main treatment for the majority of NAFLD patients. Patients with NAFLD may have improvements in their quality of life, serum insulin levels, liver histology, and liver biochemical testing after losing weight. After three months of combined exercise and dieting, aminotransferases,cholesterol, and fasting glucose dramatically improved in a study including twenty-five Japanese adults. (27)

Mostafa et al. conducted a similar study on 224 patients to find the prevalence and risk factors for depression, sleep problems, and fatigue in MAFLD patients. As compared to the control group, which had a prevalence of 21%, 16.4%, and 19.5%, the MAFLD group had a prevalence of 67.8%, 75%, and 62.5% of fatigue, depression, and sleeping difficulties, respectively. (23) While in the current study 56 NAFLD patients were not doing any exercise due to fatigue, 36 patients had body pain. Lack of energy and lack of time was the reason for not doing exercise in 54 and 58 patients respectively. In this study 141 patients had insomnia.

Due to diffuse fatty infiltration, US frequently shows a bright liver or a hyperechoic texture. When it comes to identifying increasing fibrosis and steatosis, US has a sensitivity and specificity of 89 and 93%, respectively. But the US is the least expensive approach and has historically been the most often employed modality in clinical practice. Patients that are obese have lower US sensitivity. Steatosis is suggested by the US if it reveals hyperechogenic liver tissue in comparison to the spleen or renal echogenicity. Nonetheless, in these cases, US sensitivity is only 60–94%. (27) The main imaging technique used to evaluate patients with confirmed or suspected NAFLD is ultrasound. The initial goal is to diagnose and identify NAFLD patients. While B-Mode ultrasound has a low sensitivity for mild steatosis, it is a good way to identify individuals with intermediate and severe steatosis. (16)

7.1 CONCLUSION:

According to our study, women were more likely to acquire NAFLD. The NAFLD patients had higher frequencies of the following risk factors than any other, including eating a lot of oily food and having trouble maintaining a healthy weight. Junk food consumption was also quite frequent; the majority of patients consumed junk food twice a week. Compared to the frequency of high cholesterol and heart disease, NAFLD patients also had higher rates of diabetes and hypertension. Most NAFLD patients slept for shorter periods of time. Few NAFLD patients had healthy weights and underweights, according to BMI classifications, whereas the majority of the patients were obese and overweight. The majority of the patients weren't exercising. Few patients exercised twice a week, while the majority of patients never did. Fatigue was the primary excuse given by NAFLD patients for not exercising, with additional factors being lack of time, lack of energy, and body pain. In the current study, married people had a greater frequency of NAFLD. The majority of patients had education levels below graduation.

7.2 RECOMMENDATIONS:

By changing the lifestyle, dietary habits, doing exercise and having an adequate sleep, NAFLD can be reduced and its progression to NASH, Cirrhosis and HCC can be prevented. Our research recommendations are to evaluate other non-modifiable risk factors linked with NAFLD such as race, family history or genetics which are not evaluated in our study. Some other modifiable risk factors like PCOS, depression, anxiety, smoking and cognitive impairment should also be evaluated.

7.3 LIMITATIONS:

Our study evaluated only two non-modifiable risk factors (age and gender). It lacks data on other non-modifiable risk factors like race, family history or genetics.

Our study did not evaluate other modifiable risk factors associated with NAFLD like PCOS, depression, anxiety smoking and cognitive impairment.

Ultrasound underestimates the prevalence of hepatic

steatosis when it is lower than 20%. Ultrasound has low sensitivity for detecting mild degrees of steatosis. Severe obesity may also limit the capability to reliably detect liver echogenicity due to thick layers of subcutaneous fat.

The current study was conducted to access various modifiable and non-modifiable risk factors associated with NAFLD in the patients between the age of 30 to 70 years. By overcoming the modifiable risk factors, NAFLD can be reduced and its progression to other chronic liver diseases can be reduced. Total sample size was 213 patients. The study was conducted at Aziz Fatima Hospital. Study design was Cross sectional study. The data was collected through convenient sampling and the data was collected on the basis of inclusion criteria i.e., 30-to-70- year individuals were included while individuals below 30 and above 70 were excluded.

Pregnant women, alcohol intake, positive serology for hepatitis B and C, intake of Anti TB drugs and steroids were also excluded. Before the data collection ethical approval was taken from the medical education department of Aziz Fatima Medical College. After the collection of data, it was analyzed through SPSS software.

In the current study, the frequency of females was higher than the frequency of males. The mean age of the participants was 49.1690. Age and gender were the non-modifiable risk factors. Our study lacks data on other non-modifiable risk factors like race and genetics.

Modifiable risk factors are those that can be controlled to reduce the severity of NAFLD and prevents the progression of disease to cirrhosis and HCC. HTN, diabetes, high cholesterol level, heart disease, sedentary lifestyle, shorter sleep duration, difficulty maintaining weight, lack of doing exercise, oily and junk food consumption are the major changeable risk factors related to NAFLD. Results of the study revealed that out of all modifiable risk factors, difficulty in maintain weight and oily food consumption had the highest frequency followed by HTN, Diabetes and shorter sleep duration. Other contributing factors are lack of exercise, high cholesterol level and heart disease. Most of the participants were married and belong to both rural and urban areas. Consumption of junk food was another risk factor associated with NAFLD most patients were consuming junk food twice a week. Fatigue was most common in NAFLD patients and it was the major excuse of the participants for not doing exercise while other excuses include Lack of time, Lack of energy and body pain. NAFLD patients should do exercise, reduce weight and should sleep for almost 8hrs at night to manage their disease. The prognosis can be considerably altered by identifying comorbidities like diabetes and cardiovascular disorders and treating them immediately. Since there are no approved drugs for NAFLD at this time, lifestyle modifications should be the mainstay of treatment. In order to determine the precise impact of each risk factor associated with NAFLD and to eliminate modifiable risk variables that are linked to the disease, more research is needed on this topic.

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