

## Original Research Article

# INCIDENCE OF FATTY LIVER DISEASE IN PATIENTS REPORTING TO A PRIMARY CARE CENTRE IN NORTH INDIA

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## ABSTRACT

**Background:** Fatty liver is a disorder characterized typically by the excessive accumulation of fat in the liver. Globally, about 25.0%-50.0% people have a fatty liver depending upon various factors namely age, race, lifestyle, ethnicity, dietary habits, physical exercise, alcohol intake, genetic susceptibility, insulin resistance, etc. **Aim:** To study the incidence and pattern of fatty liver disease (FLD) in patients reporting to a primary care centre in North India.

**Materials and Methods:** A cross-sectional study conducted in a representative cohort of North India reporting in a primary care centre and the duration of the study was from January 2024 to December 2024. Patients above 18 years of age who visited OPD with any complaint and who have been subsequently diagnosed with fatty liver on USG abdomen (diffuse echogenicity relative to kidney, performed on Acuson S 2000 ultrasound device) were taken up for the study.

**Results:** Both alcoholic and non-alcoholic fatty liver disease are more prevalent in males as compared to females. Middle aged males and females are more predisposed to develop fatty liver although the disorder may be seen in all age groups. Risk factors associated with fatty liver include diabetes mellitus, hypertension, alcohol use, smoking, obesity, Hepatitis B and Hepatitis C. BMI is a strong predictor for the risk of development of fatty liver and significantly associated with USG grade of fatty liver ( $p < 0.05$ ).

**Conclusion:** In conclusion factors responsible for FLD include middle age, male gender, obesity, alcohol use, smoking, hypertension, and diabetes mellitus. Higher alcohol use, smoking, hypertension, and Diabetes Mellitus play an important role in increasing the severity and progression of the disease.

**Keywords:** Fatty Liver Disease, Alcoholic Fatty Liver Disease, Non-Alcoholic Fatty Liver Disease, Ultrasound Sonography

## INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) is a broad term which includes patients with simple steatosis as well as non-alcoholic steatohepatitis (NASH).<sup>[1]</sup> NASH is a recently recognized entity, which histologically simulates alcoholic hepatitis in the absence of alcohol ingestion or intake of <20g/day and has the propensity of progression to cirrhosis of the liver and hepatocellular carcinoma

(HCC).<sup>[2]</sup> Even though the pathogenesis of NAFLD is not fully understood, it may be considered a two-hit process. The first hit leads to deposition of fat in the liver parenchyma for which insulin resistance has been implicated as the major pathogenic mechanism.<sup>[3]</sup> The exact mechanisms promoting progressive liver injury are not well defined, although substrates derived from adipose tissue such as free fatty acid (FFA) leading to lipotoxicity,

tumour necrosis factor alpha, leptin and adiponectin have been implicated.<sup>[4]</sup>

Non-alcoholic fatty liver disease (NAFLD) is defined as the accumulation of fat >5% of liver weight. It is a spectrum of pathologic changes in the liver that ranges from simple steatosis to non-alcoholic steatohepatitis (NASH), early fibrosis, and cirrhosis and can progress to end stage hepatocellular carcinoma (HCC).<sup>[5]</sup>

In recent times it has emerged as the most common chronic liver disease in Western countries in patient with no alcohol intake history.<sup>[6]</sup> In India epidemiological studies suggest prevalence of NAFLD is around 9.0% to 32.0% with higher prevalence in overweight patient and those with diabetes or prediabetes.<sup>[7]</sup>

The prevalence of NAFLD increases with age, type 2 diabetes, obesity, and hypertriglyceridemia, hyperinsulinemia and systolic hypertension.<sup>[8]</sup> In recent times, certain surrogate markers of atherosclerosis have been devised which can help to assess the cardiovascular risk noninvasively. Assessment of carotid intima media thickness (CIMT)<sup>[9]</sup> and endothelial dysfunction,<sup>[10]</sup> is considered as a potential tool for predicting coronary atherosclerosis and future cardiovascular events. Hepatic steatosis being a common incidental finding in subjects undergoing abdominal ultrasonography for any other reason has been shown to be associated with carotid plaques and increased CIMT by several cross sectional studies.<sup>[11,12,13]</sup>

The pathogenesis is thought to involve the “two hits” hypothesis which was first proposed in 1998. The “first hit” is characterized by accumulation of Tri-Glycerides (TG) derived from the esterification of free fatty acid (FFA) and glycerol. The latter “second hit” arises from an imbalance of supply, formation, consumption and hepatic oxidation and disposal of TG. Fibrosis is the final stage or the “third hit” resulting from an imbalance between the rate of hepatocyte death and hepatocyte regeneration. This results in the activation of hepatic stellate cells thereby progressing to fibrosis.<sup>[14]</sup>

Fatty liver has been studied extensively in the west where gender differences have been noted, the disorder afflicting more women than men. Asian studies into this disorder have only picked up pace in the last one and a half decade. Indian and Asian studies have reported fatty liver to be more common amongst males as compared to females. This relationship held good for both alcohol-induced fatty liver disease as well as “non-alcoholic fatty liver disease”. Clinically, fatty liver has been found to be commonly asymptomatic though other features such as vague or non-specific right upper quadrant pain, nausea, and fatigue may also be common presenting features. Fatty liver is usually diagnosed incidentally on ultrasonography which is usually the accepted first line investigation for fatty liver screening. A good number of such patients may be obese, which usually indicates altered fat

metabolism and excess fat deposition. History of alcohol consumption [for alcoholic fatty liver] is of great importance. Although alcohol consumption is usually reported to be higher in Western nations, the changing cultural habits and increasing western influence has increased the prevalence of alcoholism in India.

Ultrasonography is a very efficient and widely available technique for the detection of fatty liver. The overall sensitivity and specificity of ultrasound in detection of moderate to severe fatty liver has been shown to be accurate and comparable to those of histology (gold standard). Other imaging modalities that have been tried include Liver Elastography [Fibroscan], Computed Tomography and Magnetic Resonance Imaging. The liver biopsy has several limitations such as risk of complications like bleeding, perforation, organ injury, infection. Therefore, liver biopsy is not a routinely performed investigation for evaluation of fatty liver.<sup>[15]</sup>

Despite the significant prevalence and burden, the overall awareness of these two entities remains limited in the general population. Our aim is to assess the prevalence and pattern of FLD in a representative cohort of North India reporting to our primary care centre.

## MATERIALS AND METHODS

A cross-sectional study conducted in a representative cohort of North India reporting to a primary care centre and the duration of the study was from January 2024 to December 2024. Written informed consent was obtained from each participant. Patients above 18 years of age who visited OPD with any complaint and who have been subsequently diagnosed with fatty liver on USG abdomen (diffuse echogenicity relative to kidney, performed on Aconson S 2000 ultrasound device) were taken up for the study. A general physical examination, anthropometry measurements (height, weight, BMI) were done for all patients. Laboratory investigations included complete hemogram, hepatitis B antigen, hepatitis C serology, liver function test, lipid profile, fasting blood sugar, glycosylated haemoglobin. Liver elastography was done for all patients.

Patients were interviewed and history regarding Fatty liver disease such as duration of the disease, dietary intake, medications, personal history and history pertaining to other comorbid conditions were obtained.

### Sample size calculation

The sample was calculated on the basis of prevalence using the formula.

$$n = \frac{Z^2 P (1 - P)}{d^2}$$

Z is the statistic corresponding to level of confidence,

P is expected prevalence

d is precision (corresponding to effect size).

### Sample size calculation

#### Assumptions

Precision = 5.0% (0.05)

Prevalence = 10.0% (0.10)

Population size = Infinite (0)

Z=1.96

Estimated sample size:

**n = 138**

95% Binomial Exact Confidence Interval

The final sample size for this study was 100 with prevalence of 10%. This is the reason the precision (d) decreases to  $\pm 5.9\%$ , which also implies that the end result may vary by  $\pm 5.9\%$ .

#### Statistical Analysis

Statistical analysis was done using the Statistical Package for the Social Sciences version 23.0 (SPSS Inc, Chicago, IL, USA). Normally distributed data was analysed using a general linear model analysis of variance [ANOVA]. The categorical data was analysed using the Chi square test. The level of significance usually denoted as  $\alpha$  has the following criterion as: if  $p < 0.05$  then hypothesis is said to be significant.

## RESULTS

The study noted that among 100 patients, Non-Alcoholic Fatty Liver Disease (NAFLD) was the most prevalent condition, affecting 46% of patients, followed by Alcoholic Fatty Liver Disease (AFLD) at 38%. Viral hepatitis infections were also present, with Hepatitis C affecting 8% and Hepatitis B affecting 5% of patients. A small proportion of patients had co-existing viral hepatitis and alcohol-related liver disease, with 2% having Hepatitis B and alcohol use and 1% having Hepatitis C and alcohol use. These findings suggest that NAFLD and AFLD are the dominant forms of fatty liver disease in this population [Table 1].

In this study we noted that the majority of patients (38%) were between 41-50 years old, with a mean age of  $48.61 \pm 12.3$  years. Males dominated the study population (72%), while females comprised 28%. In terms of BMI, most patients were either overweight (46%) or obese (32%), with only 22% having a healthy weight. The majority of patients (62%) followed a vegetarian diet, while 38% had a mixed diet. Regarding socio-economic status, the majority belonged to the middle class (52%), followed by low (30%) and high (18%) socio-economic groups [Table 2].

The most common risk factors for fatty liver were alcohol consumption (46%), diabetes mellitus (43%), and metabolic syndrome (42%). Hypertension was present in 38% of patients, while smoking was reported in 34% of patients. These findings suggest that lifestyle factors, such as alcohol consumption, and metabolic disorders, including diabetes and metabolic syndrome, are significant contributors to the development of fatty liver disease in this population [Table 3].

On the basis of symptoms, it was observed that majority 24 (24.0%) patients had generalized weakness and malaise symptoms followed by 22 (22.0%), 22 (22.0%), 16 (16.0%), 12 (12.0%) and 4 (4.0%) patients had burning sensation over epigastric region, right upper abdominal pain, nausea and vomiting, Increase in weight and gaseous distension symptoms respectively [Figure 1 & 2].

A significant association was found between BMI and the ultrasonographic grade of fatty liver disease ( $p=0.033$ ). As the grade of fatty liver disease increased, the proportion of patients with obesity also increased, with 66.7% of patients with Grade III fatty liver having obesity. Conversely, patients with healthy weight were more likely to have Grade I fatty liver (35.8%), and none had Grade III fatty liver. This suggests a strong correlation between increasing BMI and the severity of fatty liver disease [Table 4].

**Table 1: Prevalence and burden of various type of fatty liver disease**

Etiology	No. of patients (n=100)	Percentage
NAFLD	46	46.0%
AFLD	38	38.0%
Hepatitis B	5	5.0%
Hepatitis C	8	8.0%
Hepatitis B + Alcohol	2	2.0%
Hepatitis C + Alcohol	1	1.0%

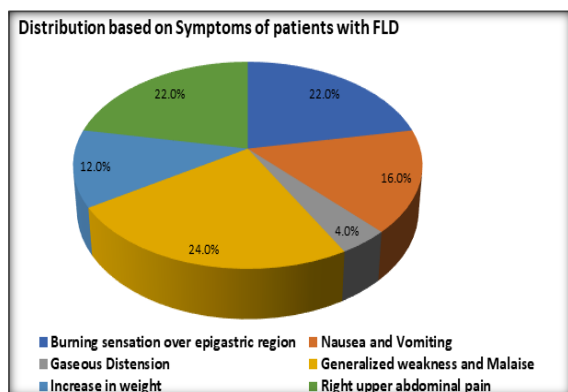
**Table 2: Distribution of studied patients based on sociodemographic status**

Characteristics		No. of patients (n=100)	Percentage
Age (Yasr)	<30 years	18	18.0%
	30-40 years	24	24.0%
	41-50 years	38	38.0%
	51-60 years	12	12.0%
	61-70 years	6	6.0%
	>71 years	2	2.0%
	Mean $\pm$ SD	48.61 $\pm$ 12.3	
Gender	Male	72	72.0%
	Female	28	28.0%

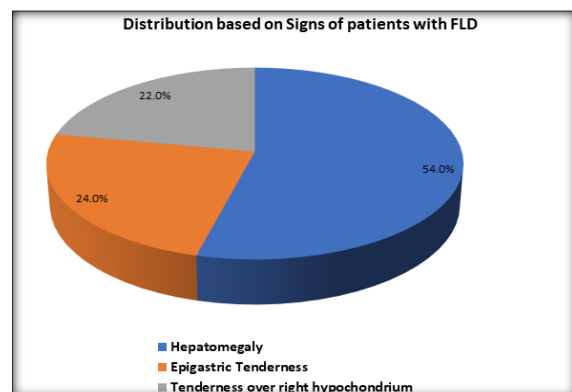
BMI (kg/m2)	Underweight (<18.5)	0	0.0%
	Healthy weight (18.5-24.9)	22	22.0%
	Overweight (25.0-29.9)	46	46.0%
	Obesity (Grade I) (30.0-34.9)	32	32.0%
	Obesity (Grade II) (35.0-39.9)	0	0.0%
	Extreme obesity (>40)	0	0.0%
Dietary Habits	Vegetarians	62	62.0%
	Mixed diet eaters	38	38.0%
Socio-economic status	High	18	18.0%
	Middle	52	52.0%
	Low	30	30.0%

**Table 3: Distribution of studied patients based on risk factors for fatty liver**

Etiology	No. of patients (n=100)	Percentage
Diabetes Mellitus	43	43.0%
Hypertension	38	38.0%
Metabolic Syndrome	42	42.0%
Alcohol	46	46.0%
Smoking	34	34.0%



**Figure 1: Distribution of studied patients based on Symptoms of patients with FLD**



**Figure 2: Distribution of studied patients based on Signs of patients with FLD**

**Table 4: Distribution of studied patients based on association of BMI with USG grade of fatty liver**

BMI	Ultrasonographic staging in FLD			p-value
	Grade I (n=67)	Grade II (n=24)	Grade III (n=9)	
Healthy weight (18.5-24.9)	24 (35.8%)	6 (25.0%)	0 (0.0%)	0.033
Overweight (25.0-29.9)	29 (43.3%)	9 (37.5%)	3 (33.3%)	
Obesity (30.0-34.9)	14 (20.9%)	9 (37.5%)	6 (66.7%)	

## DISCUSSION

Indian and Asian studies have reported fatty liver to be more common amongst males as compared to females. This relationship held good for both alcohols induced fatty liver disease as well as “non-alcoholic fatty liver disease”. Clinically, fatty liver has been found to be commonly asymptomatic though other features such as vague or non-specific right upper quadrant pain, nausea, fatigue may also be common presenting features. Fatty liver is usually diagnosed incidentally on ultrasonography which is usually the accepted first line investigation for fatty liver screening. A good number of such patients may be obese, which usually indicates altered fat metabolism and excess fat deposition. History of alcohol consumption [for alcoholic fatty liver] is of great importance. Although alcohol consumption is usually reported to be higher in Western nations, the changing cultural habits and increasing western influence has increased the prevalence of alcoholism in India.<sup>[18]</sup>

Fatty liver is now one of the most widely discussed topics in medicine all over the world. Reasons spark from the fact that it is a harbinger for chronic liver disease and at the same time amenable to intervention in most, if not all cases. The ability of the liver to revert back to its original state from a state of fatty liver speaks volumes about the resilience of this organ and the potential role its cells can play in further research on reversibility of cellular damage. Early identification of fatty liver serves the purpose of initiating timely intervention which subsequently reduces both morbidity and mortality.

We studied the distribution of the cases on the basis of their age and it was found that the majority of the studied patients were in the age category 41-50 years (38.0%) followed by 30-40 years (24.0%) with mean age  $48.61 \pm 12.3$  years and male predominance (72.0%). This statistic is consistent with a previous study that reported a 2 to 2.5 times higher prevalence in the 56–60-year-old age group compared with those aged less than 45 years.<sup>[19]</sup>



Also, in a study by Pegah Golabi et al,[20] the majority of patients were males (57.8%) while the mean age was 51.31 years which was comparable to our present study. Many other studies have indicated that FLD is more common in men.<sup>[21,22,23,24]</sup> Along with an earlier study by Pan JJ et al,<sup>[25]</sup> our study found that the prevalence of fatty liver disease was significantly higher in men than women.

In the present study the 46.0% of the patients were overweight and were having FLD with BMI between 25.0-29.9 kg/m<sup>2</sup> followed by those who are of obesity grade I 32.0% with BMI (30.0-34.9). Similar data was obtained by Brea A et al,<sup>[26]</sup> who reported BMI of NAFLD patients as 31.85.1 kg/m<sup>2</sup> also Uslusoy HS et al,<sup>[27]</sup> reported BMI of NAFLD as 30.6±5.24 kg/m<sup>2</sup>.

In our study the studied cases were distributed on the basis of etiology and it was found that the majority of the cases were having NAFLD (46.0%) followed by AFLD (38.0%), hepatitis C (8.0%), hepatitis B (5.0%), Hepatitis B + Alcohol (2.0%) and Hepatitis C + Alcohol (1.0%). 46.0% were alcoholics followed by 43.0% cases were having diabetes, metabolic syndrome (42.0%), hypertension (38.0%) and 34.0% were smokers. Our findings were in accordance with the findings of Shangari S et al,<sup>[28]</sup> who reported that maximum (45.83%) cases belonged to the NAFLD group followed by alcoholic liver disease (40.6%), (4.16%) had hepatitis B, (0.08%) had hepatitis B and alcohol use present, 9 (9.30%) had hepatitis C and (1.04%) had hepatitis C and alcohol use. (42.70%) had diabetes mellitus, (36.45%) had hypertension, (47.91%) had metabolic syndrome, (41.66%) had alcohol use, and (37.50%) had smoking history.

Sakitani K et al,<sup>[29]</sup> postulated in their study that diabetes, hypertension, obesity, metabolic syndrome, smoking and alcohol are strong risk factors for development of fatty liver. Hamaguchi M et al,<sup>[30]</sup> observed that metabolic syndrome patients have a 4 to 11 times higher risk for fatty liver. Paschos P et al,<sup>[31]</sup> concluded in their study that there was a strong correlation between NAFLD and diabetes mellitus, hypertension, dyslipidemia, obesity and metabolic syndrome. Cortez H et al,<sup>[32]</sup> reported from their study that about 33% of patients of NAFLD have diabetes mellitus. Kortonen A et al,<sup>[33]</sup> reported from their study on NAFLD that about 90.0% subjects diagnosed with NAFLD possess at least one risk factor of metabolic syndrome, and 33.0% possess all the features of metabolic syndrome. Shangari S et al,<sup>[29]</sup> also found that most of the patients had only mild [less than 4 times the upper limit of normal] elevation of liver function tests. In our study group, the triglyceride levels were raised but the levels of total cholesterol, LDL, HDL and VLDL were within normal limits for majority of the patients. Although the underlying process of development of fatty liver is one which involves abnormal liver function, altered fat metabolism is not the sole mechanism responsible for the pathogenesis of fatty liver disease.<sup>[34]</sup>

In our study nausea and vomiting, generalized weakness and malaise, increase in weight, burning sensation over epigastric region were the major symptoms whereas hepatomegaly, epigastric tenderness and tenderness over right hypochondrium were the major signs of fatty liver disease. Shangari S et al,<sup>[29]</sup> reported that 60.4% cases were asymptomatic followed by fatigue (23.9%), abdominal pain (22.9%) and nausea (6.25%). Worldwide, the most common presentation of fatty liver across all the various etiologies is "asymptomatic". Few patients may report fatigue, abdominal pain and nausea. The asymptomatic nature of the illness masks the disease and delays the presentation of the patient to the health care system. Most cases are therefore identified incidentally while performing routine tests. The altered liver function explains the occasional symptoms of fatigue, abdominal pain and nausea. Amarapukar D et al,<sup>[36]</sup> studied 1168 subjects of fatty liver and reported asymptomatic presentation to be the commonest. He also reported hepatomegaly in only 5.0% of the patients. Fatty liver is usually an obscure disorder, incidentally detected on ultrasonography. The importance of uncovering this disorder lies in the fact that it has multiple associations like diabetes mellitus, hypertension, dyslipidemia and metabolic syndrome. A finding of fatty liver in a patient population should be investigated to rule out these associations which can in due course of time develop multiple preventable complications.

In the present study the distribution of the cases was performed on the basis of severity of disease via ultrasonography and it was found that the majority of the cases were having mild disease (67.0%) followed by moderate (24.0%) and severe (9.0%). Our findings were consistent with the findings of Ganesh K et al, who reported that patients can be broadly classified into three different profiles based on radiological examination. With highest 71.0% belonging to mild fatty liver, 20.0% to moderate fatty liver and lowest 9.0% to severe fatty liver (USG) category. Singh SP et al,<sup>[37]</sup> in their study reported that mild fatty liver was present in 77.7% followed by moderate fatty liver (21.4%) and severe in 0.9%.

In our study the association of BMI with USG grade of fatty liver was recorded and it was found that as the BMI increases grade of fatty liver disease also increases significantly i.e., in obese cases 66.7% were of grade III. Our findings were comparable to the findings of Abangah G et al,<sup>[38]</sup> who conducted a similar study on 213 subjects of fatty liver and reported that increasing BMI was associated with an increased risk of higher grading on ultrasound (96). These findings were also confirmed by another study conducted by Cuenza LR et al,<sup>[39]</sup> who performed a study on 100 patients in Phillipines and observed similar results. Our study also shows a reasonable percentage of patients in the normal BMI

group, which is due to the fact that the incidence of fatty liver is also on the rise in lean individuals.

The symptoms and signs of FLD are non-specific and occur later in the course of the disease hence the physician should have a high index of suspicion in order to detect FLD early in the course of the disease. Higher prevalence of all the components of metabolic syndrome in cases of FLD was observed. Liver biopsy is considered the gold standard for diagnosing FLD but is not practical and most patients are not willing to undergo the test. Thus, patients must be evaluated for the presence of FLD by abdominal Ultrasonography. Early detection would help in modifying the disease course and delaying its complications.

#### Limitations of the study

- Relatively smaller sample size
- This study was conducted in such a way that there were no controls involved in this study
- Liver biopsy is the gold standard for grading of fatty liver but was not done due to risk of complications like infection, life threatening bleeding and organ perforation.

### CONCLUSION

In conclusion our study revealed that there is a positive correlation between middle age, male gender, obesity, alcohol use, smoking, hypertension, and diabetes mellitus and FLD. Higher alcohol use, smoking, hypertension, and diabetes mellitus play an important role in increasing the severity and progression of the disease. Early detection would help not only in modifying the disease course but also delaying its further complications. Our study recommended that all patients of fatty liver should be thoroughly investigated for underlying etiology as fatty liver represents the reversible stage in the pathogenesis of chronic liver disease. Grading of fatty liver should be preferably done with elastography.

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