



NON-ALCOHOLIC FATTY LIVER DISEASE (NAFLD) IS AN ALARMING SIGN OF CHRONIC LIVER DISEASE IN RECENT AGE. A REVIEW ARTICLE

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ABSTRACT

Non-alcoholic fatty liver disease (NAFLD) occurs when there's excess fat accumulates in liver cells in people who consume little or no alcohol. NAFLD is associated with various metabolic risk factors, such as obesity and diabetes typeII, triglycerides, Polycystic ovary syndrome, Sleep apnea, hypopituitarism, hypothyroidism. Nonalcoholic fatty liver disease occurs in every age group but especially in those people who are in their 40s and 50s and are at high risk of heart disease because of such risk factors like as obesity and type II diabetes. Early-stage NAFLD doesn't usually cause any harm to our body, but it can lead to serious liver damage, including cirrhosis, if it gets worse. In this review we will only discuss the NAFLD epidemiology mostly, regarding risk factors, complications and diagnosis and then draw a conclusion.

Keywords: Non- Alcoholic fatty liver disease (NAFLD), Metabolic Syndrome (MS), PREVALENCE

INTRODUCTION

Fatty liver disease in middle age Americans is very common, with the incidence increasing with the obesity epidemic. It is also the most common form of chronic liver disease in United States, affecting an estimated 80 to 100 million people. Up to 80% of obese people have the disease and up to 20% normal-weight people might develop it. NASH and NAFLD are the leading cause of chronic liver disease as documented in 2017.¹

Nonalcoholic fatty liver disease (NAFLD) is recognized as an important public health problem now a days. NAFLD develops through 4 main stages as follows;

- ❖ **Simple fatty liver (Steatosis):** a largely harmless buildup of extra fat (more than 5 -10 percent) in hepatocytes.^{2/3}
- ❖ **Non-Alcoholic Steatohepatitis (NASH):** A bit more serious form of NAFLD. Here hepatocytes get inflamed, and this condition documented to affect about 5 percent of UK population.
- ❖ **Fibrosis:** Persistent inflammation causes scar tissue formation around the liver and nearby blood vessels, but liver is still functioning normal.
- ❖ **Cirrhosis:** Most severe stage of NAFLD, occurring after many years as a result of inflammation, where the liver get shrinks and becomes scarred and lumpy; now this damage is permanent and can lead to hepatic failure and eventually hepatocellular carcinoma (HCC).

Epidemiology:

The percentage of people with non-alcoholic fatty liver disease ranges from 9 to 36.9% in different areas of the world.^{4/5} However, studies based on elevated liver enzymes systematically underestimated the true prevalence worldwide, and ultrasonography and proton NMR spectroscopy studies suggest about 25% of the population seems to be affected by NAFLD or NASH. NAFLD is the most common chronic liver disease in West.⁶ It is reported that approximately 20% population of the United States have non-alcoholic fatty liver.⁶ While in another study About 12 to 25% of people in the United States have NAFLD.⁷ NASH affects between 2 and 12% of people in the United States.^{7/8/9} Boys are more likely to be diagnosed with NAFLD than girls as of a systemic review and Meta-Analysis.¹⁰ In children who were aged 1 to 19, prevalence was found to be approximately 8% in the general population, up to 34% data in studies was collected from child obesity clinics.¹⁰

Progression of NAFLD in US as follows:

STAGES	AGE (years)	RESULT
Toddlers	(3 – 5)	very rare
Children	(6 – 13)	rare
Teenagers	(14 -18)	common
Young Adults	(19 – 40)	common
Adults	(41 – 60)	very common
Seniors	(60+)	very common

20% of world population occupied by South Asia, which made its geographically most densely and populated area in world. Therefore, this territory has most of MS and NAFLD cases. Whereas the risk factors and course of NAFLD do not make any difference with South Asia and other ethnic population around the world. In South Asia now a day's obesity more epidemically growing than the rest of world. Although the disease is commonly associated with obesity, up to 80 percent of obese people have the disease, but a significant proportion of cases are normal weight or lean. Lean NAFLD affects between 10–20% of Americans and Europeans, although some countries have a higher incidence (e.g., India has a very high proportion of lean NAFLD and almost no obese NAFLD). According to an international cohort study lean NAFLD people are at the same or higher risks, with a poorer median survival rate (free of liver transplantation) than for obese NAFLD people. In lean people a genetic predisposition such as, PNPLA3 polymorphism appears to be more important in the development of NAFLD. Thus, regardless of obesity people suffering from NAFLD should be considered as a potential population for treatment.^{1/11/12} The relationship between central obesity and insulin resistance (IR) both are at high prevalence of Diabetes as well as Metabolic Syndrome (MS) and Cardiovascular risk among South Asians.¹³

NAFLD prevalence can also be found in Europe and Asia-Pacific countries similar to as of US prevalence (20% mentioned above) although less data is available there.¹ While hepatocellular carcinoma (HCC) and end-stage liver disease (ESLD) secondary to NAFLD remain uncommon, a rising trend has emerged. Around 8-19% of Asians with body mass indexes (BMI) less than 25kg/m² are also found to have NAFLD, a condition often described as "lean" or "non-obese" NAFLD. It is also increasing alarmingly in South Asia, where it has reached by an epidemic proportion of 30 percent and the main reasons behind of it were epidemic of obesity and Metabolic Syndrome (MS) in younger south Asians since last 2 decades.

In type 2 DM prevalence of fatty liver was 60.8 % which was almost similar with one of Indian study (NAFLD prevalence in Diabetes was 49 percent).¹⁴ High BMI was found to be an independent predictor in this study. In diabetics NAFLD was 51 percent and majority (92.15 percent) of patients with NAFLD had hypertriglyceridemia and heaviness in upper right abdomen was most common (64.7%). There's no wonder NAFLD/NASH prevalence is expected to increase to the point of becoming the leading cause of liver transplantation by 2020.¹⁵

Risk Factors:

NAFLD itself a risk factor for fibrosis, hypertension, myocardial infarction, chronic kidney disease, atrial fibrillation, ischemic stroke and death from cardiovascular causes based on very low to low quality evidence from observational studies.^{16/17/18}

1. Omega-6 fatty acids lipids and fructose sugar, in diet composition and quantity play an important role in disease progression from NAFL to NASH and fibrosis.^{19/20} Choline deficiency leading to the development of NAFLD.²¹ Diet enrich in carbohydrates & sugars for instance can be a contributing factor for metabolic diseases including NAFLD.^{22/23}

2. NAFLD in particular, have been documented in between dysbiosis of the gut microbiota and liver diseases. NASH patients can have increased levels of blood ethanol. More aggressive NAFLD patients were found to have a choline depletion which linked to an increased choline metabolism.^{24/25/26/27}
3. More than one family member having NAFLD in those families where history of diabetes type 2 is 66.67%. For those family members where someone was diagnosed with NASH, there's a higher risk of fibrosis.²⁸ Moreover, Hispanic people having higher prevalence of NAFLD rather than white individuals, while in black population lowest susceptibility is observed.
4. Insulin resistance (IR) and metabolic syndrome (MS) such as (High blood pressure, obesity, combined hyperlipidemia, diabetes mellitus (type II), as well as insulin resistance, persistent elevated transaminases, panhypopituitarism and hypoxia caused by obstructive sleep apnea, increasing age and BMI, all are associated with NAFLD and with some of them are much strong enough predictors of disease progression.^{29/30/31/32/33}

Complications:

NAFLD is the leading cause of chronic liver disease (CLD), which is strongly associated with the metabolic syndrome (MS). In the last decade, it has become apparent that the clinical burden of NAFLD is not restricted to liver related morbidity or mortality, and the majority of deaths in NAFLD patients are related to cardiovascular disease (CVD) and cancer. These findings stating that NAFLD may be a new, but added risk factor for extrahepatic diseases such as cardiovascular disease (CVD), chronic kidney disease (CKD), colorectal cancer, endocrinopathies (including typeII diabetes mellitus & thyroid dysfunction), and osteoporosis.³⁴ NAFLD is a clinicopathological entity that encompasses simple hepatic steatosis, necroinflammation with varying stages of fibrosis known as nonalcoholic steatohepatitis (NASH), and cirrhosis. It has strong association with the metabolic syndrome (MS) and may be the leading cause of chronic liver disease worldwide, and reaching epidemic proportions in many high income countries.^{35/36} Compared with the general population of similar age and gender, NAFLD increases the risk of end stage liver disease, hepatocellular carcinoma (HCC),³⁷ as well as liver related and all of these causes mortality.^{38/39} There is general consensus, however, that the majority of deaths among individuals with NAFLD are attributed to cardiovascular disease and malignancy.^{36/40} Unsurprisingly, these observations have filled concern that NAFLD, either independently or in combination with other metabolic risk factors, could pose an important risk factor or driver of extrahepatic diseases.

Diagnosis:

Biopsy only the gold standard test accepted widely and even can be used to assess the severity of the inflammation and resultant fibrosis. But mostly people affected by NAFLD approximately asymptomatic, that's why liver biopsy remains too risky for routine diagnosis, so there are others less risk containing and cost-effective methods available, such as liver ultrasonography (USG). Children & young adults still advised USG. For precise evaluation biopsy still the mainstay way. For NAFLD detection routine liver function blood tests (LFTs) aren't sensitive enough, and the biopsy only procedure that can reliably differentiate NAFL from NASH.¹³ Elevated LFTs and a liver USG showing steatosis are common findings.

CONCLUSION

NAFLD being most common in Europe, prevalence is increasing in Asians too, and with rising incidence of obesity and diabetes. Regardless of obese lean people too aren't in avoidance of NAFLD. NAFLD patients, particularly those with NASH and diabetes, are at risk of liver-related complications such as cirrhosis and hepatocellular carcinoma. Current, treatment is limited to weight loss, exercise and the control of metabolic risk factors. Effective pharmacotherapies are still awaited. Furthermore, studies should be conducted on it to find out more protective way to get rid of complications regarding NAFLD

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