

## ASSESSMENT AND MANAGEMENT OF NON-ALCOHOLIC FATTY LIVER DISEASE

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**ABSTRACT**

**Non-alcoholic fatty liver disease (NAFLD) has become the commonest chronic liver disease in the world. Overall improvement in public health, active screening of blood products, and universal vaccination of hepatitis B have led to a drop in incidence of hepatitis B and C worldwide. NAFLD is strongly associated with metabolic syndrome. With the rise in overweight status and obesity worldwide, it is not surprising that NAFLD is on the rise. Diagnosis of NAFLD requires confirmation of fatty infiltration in liver, as well as liver damage such as elevated liver enzymes and presence of fibrosis. Currently, the best treatment for NAFLD is weight loss, and the proven method would be dieting with regular exercises. Vitamin E and pioglitazoles are promising medications for treating NAFLD, but each medication has their shortcomings. Until more studies are conducted, lifestyle modification remains the only reliable way to treat NAFLD. Family physicians ought to look out for cardiovascular diseases, as well as being vigilant in cancer screening, as NAFLD is associated with higher risks of ischemic heart disease and cancer.**

**Keywords: Obesity; Fatty Liver, metabolic syndrome, diabetes mellitus, cirrhosis**

**What is Non-alcoholic fatty liver disease (NAFLD)?**

There must be evidence of fat in liver of  $\geq 5$  percent, usually confirmed by imaging studies,<sup>1</sup> with no secondary causes such as significant alcohol consumption, medications, or genetic disorders.<sup>2</sup>

NAFLD comprises of a spectrum of diseases, depending on the degree of inflammation, and extent of liver fibrosis.

Non-alcoholic fatty liver (NAFL) refers to presence of fat in liver without significant inflammation or fibrosis. Risk of progression to cirrhosis or liver failure is minimum.<sup>2</sup>

Non-alcoholic steatohepatitis (NASH) refers to presence of fat with inflammation. NASH can progress to cirrhosis.<sup>2,3</sup>

NASH cirrhosis refers to cirrhosis with current or previous histological of steatosis or steatohepatitis.<sup>2</sup>

**How prevalent is NAFLD?**

No population study has been done in Singapore. However, based on data from some cohort studies, NAFLD is common locally. One local study showed that NAFLD is present in 56 percent of patients undergoing cholecystectomy. Another showed that

among attendees to a public health forum, 40 percent had ultrasonic evidence of NAFLD.

Population studies in Asia showed NAFLD to be present in about 25-40 percent of the general population. Fortunately, less than 5 percent of NAFLD patients have significant fibrosis.

NAFLD is particularly common in patients with metabolic syndrome. NAFLD is present in more than 95 percent of obese patients undergoing bariatric surgery, two-thirds of diabetics have NAFLD, and half the patients with dyslipidemia have NAFLD.

**What is the natural history of NAFLD?**

Generally speaking, patients with NAFL alone have very low risk of progression to liver cirrhosis. However, patients with steatohepatitis, especially those with fibrosis, may progress to cirrhosis or even liver cancer.

Interestingly, cancer and cardiovascular diseases are the top 2 causes of death in patients with NAFLD.<sup>2</sup> Possible explanations include overweight status and metabolic syndrome as risk factors for certain cancers, such as pancreatic, breast, and colon cancer. Moreover, patients having NAFLD would have concurrent metabolic syndrome, which in itself is a risk factor for cardiovascular disease.

**How do I confirm the diagnosis of NAFLD?**

Firstly, there must be documentation of fat in liver, which is usually diagnosed on ultrasound scan. Most patients with NAFLD have their disease diagnosed via routine screening. Rarely, fatty liver is diagnosed on CT or even laparoscopy when patients undergo abdominal or pelvic surgeries.

Next, there may be liver inflammation so their liver profile may show elevated GGT or ALT.

Also, alternative causes of liver injuries, such as viral hepatitis B or alcohol, should be excluded. Safe limit of alcohol has been of much debate. The consensus is that the safe limit of alcohol consumption for a man is 21 units a week, and 14 units for a woman.<sup>2</sup> One unit of alcohol is approximately one can of beer, one glass of wine, or one shot of hard liquor.

Lastly, NAFLD is commonly associated with metabolic syndrome so clinicians ought to look out for overweight status, hypertension, dyslipidemia, diabetes or pre-diabetes.

## How can I stage the severity of NAFLD?

NAFLD progresses into the following stages: pure fat, steatohepatitis, fibrosis, then cirrhosis.

The ideal method to stage the disease is through percutaneous liver biopsy<sup>2,3</sup>, which could tell the degree of inflammation and stage of fibrosis. But as biopsy is associated with small risk of complications such as hemoperitoneum, patients rarely agree to it.

While transaminases such as ALT and GGT may reflect the degree of liver inflammation, they do not correlate accurately with inflammation in liver histology<sup>3</sup>.

Several non-invasive methods of assessment for NAFLD are available commercially.

Hepatic steatosis can be quantified by MR imaging accurately<sup>3</sup>. Besides, MR Elastography can also stage the amount of liver fibrosis, as well as identifying any focal liver lesions. But its limited availability and high cost make it difficult for general use in primary care.

Several panels utilize laboratory and clinical markers, such as platelets, albumin, BMI, age, ALT, etc. to insert into a particular formula to estimate risk of liver fibrosis. Some are available for use in Singapore.

Fibroscan®, which measures liver stiffness,<sup>2,3</sup> is also available locally to estimate the amount of liver fibrosis. Notably, 10-25 percent of fibroscan studies may fail to obtain reliable readings, as an appropriate probe size is needed for different patient sizes.

## How should I manage at a primary care clinic?

Establishing the diagnosis, i.e., confirming presence of fat in liver, with exclusion of alternative liver diseases is the first line of management. One also ought to look for other components of metabolic syndrome as they are almost always present in patients with NAFLD. Next step is to establish severity of liver damage by noninvasive methods. Those with advanced fibrosis or cirrhosis should be referred for specialist care.

The most proven management of NAFLD is weight loss.<sup>4</sup> Weight loss of 3-5 percent from baseline often leads to improvement in

hepatic steatosis. Further weight loss of 7-10 percent would lead to improvement of inflammation and fibrosis histologically.<sup>1,4</sup>

Exercises alone may not be sufficient in improving stage of NAFLD so it should be combined with dieting.<sup>1</sup>

Metformin has been discarded as a treatment of choice as meta-analysis showed no improvement in liver histology.<sup>4</sup>

Pioglitazone, vitamin E at 800 IU/day have been showed to improve liver histology in NASH patients.<sup>1</sup> However, the use of Pioglitazone is associated with weight gain, increased bone loss, as well as small risk of bladder cancer.<sup>2</sup> Also, Vitamin E at a dose of 400 IU/day has been associated with an increased risk of prostate cancer and all-cause mortality in some studies.<sup>1,2</sup> Therefore, their benefits and risks ought to be discussed with patients before starting it.

Bariatric surgeries, which lead to significant weight loss, can lead to improvement in liver histology.<sup>2</sup> Careful patient selection, as well as long-term post-operative support, are important in ensuring maintenance in weight loss.

## Pointers to achieve weight loss

A few points can be written on losing weight.

Firstly, there must be a calorie deficit whereby a patient's calorie intake is less than his requirement. The type of diet, be it low-carbohydrate diet, ketogenic diet, Mediterranean diet, Subway diet etc., is not important. The most important part of dieting is its sustainability, as many studies showed only a quarter to one-third of participants can complete a 1-year program to lose weight.

Next, the patient must have sufficient insight into the problem to improve self-motivation. Emotional support from family members is essential for success.

Certain food like desserts, soft drinks, snacks should be minimized.<sup>1</sup>

Also, a low-calorie diet leads to reduced metabolic rate and muscle loss. Therefore, any form of dieting should be accompanied with moderate amount of exercises to avoid loss of lean mass and maintenance of metabolic rate.

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## LEARNING POINTS

- **NAFLD is now the commonest cause of liver disease in Singapore, as well as the rest of the world. It will emerge as the leading cause of cirrhosis, liver cancer, and liver-related mortality in time to come.**
  - **NAFLD is associated with metabolic syndrome and the family doctor ought to look out for and treat different components of metabolic syndrome.**
  - **There is currently no magic way to lose weight. Much efforts in taking low calorie diet and doing daily exercises must be preached to all patients constantly.**
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