

Non-alcoholic Fatty Liver Disease:

An Overview

Key Points

- ※ Non-alcoholic fatty liver disease (NAFLD) refers to a spectrum of liver disorders ranging from accumulation of too much fat inside liver cells to fibrosis, cirrhosis, liver failure or liver cancer that is not due to alcohol consumption or other secondary causes.
- ※ NAFLD is pervasive in Hong Kong, with a prevalence of 27.3% and annual incidence of 3.4% among Chinese adults.
- ※ In the vast majority of cases, NAFLD arises in association with metabolic syndrome. With the rising prevalence of obesity and type 2 diabetes, particularly in the younger population, NAFLD will remain a major public health concern.

Prevention Tips

Adopting a healthy lifestyle is essential for a healthy liver and reducing the risk of NAFLD

- ※ Maintain an optimal weight and waistline
- ※ Eat a balanced diet
- ※ Be physically active
- ※ Avoid alcohol consumption
- ※ Do not smoke
- ※ Keep blood sugar, blood lipids and blood pressure at optimal levels

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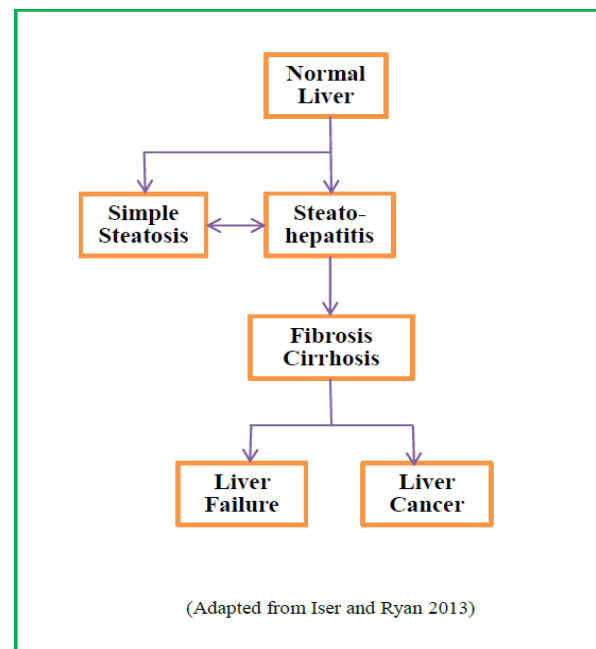
Liver is the second largest organ in our body. Its main functions include detoxifying or filtering harmful substances from blood (such as alcohol and chemicals), production of bile to help the breakdown of fats, converting glucose into glycogen, storage of important nutrients (including glycogen, vitamins and minerals) and regulating cholesterol and synthesis of plasma proteins. In fact, we cannot survive without a functional liver. For NAFLD, it is a common cause of abnormal liver function tests (i.e. blood test that detects inflammation and damage to the liver) as well as chronic liver disease in both adults and children in Western countries, affecting about one billion individuals worldwide.¹⁻³

Definition and Clinical Course

NAFLD refers to a spectrum of liver disorders associated with accumulation of too much fat inside liver cells (exceeding 5% of liver volume) that is not due to excessive alcohol consumption or secondary causes (such as medications or inborn errors in metabolism).^{3, 4} While the clinical course of NAFLD is still unclear and debatable^{5, 6}, studies indicated that its spectrum could range from simple steatosis (i.e. fat accumulation) with a relatively benign prognosis, to steatohepatitis with inflammation and scarring, liver fibrosis and eventual cirrhosis. Over time, it may lead to liver failure or liver cancer (Figure 1).^{7, 8}

Most people with NAFLD are asymptomatic. NAFLD is typically suspected based on the abnormal results of liver function tests as part of routine testing or an incidental finding during abdominal ultrasound.³ Depending on the tissue stage of disease at presentation, studies show that 5% to 20% of patients with fatty liver will develop non-alcoholic steatohepatitis (NASH) over the clinical course; in some 10% to 20% this develops into significant fibrosis; in less than 5% this progress to full-blown cirrhosis.⁹ A systematic review of cohorts with cirrhotic NASH reported a cumulative incidence of liver cancer between 2.4% over 7-years and 12.8% over 3-years.¹⁰

Figure 1: Clinical course of non-alcoholic fatty liver disease



Major Risk Factors and Associations

NAFLD is a multifactorial disease that its development is likely to depend on a complex interplay among genetic predisposition, lifestyle-related and environmental risk factors (such as level of physical activity and type of diet). Male sex and Hispanic origin are known to have higher prevalence of NAFLD. In the vast majority of cases, NAFLD arises in association with one or more risk factors of the metabolic syndrome, namely obesity, impaired fasting glucose, dyslipidaemia and hypertension.^{11, 12} Sharing the same metabolic risk factors, NAFLD is also closely associated with cardiovascular disease, chronic kidney disease, obstructive sleep apnoea and polycystic ovary syndrome (in female).¹³⁻¹⁷ Several studies showed that people with NAFLD had higher overall mortality. This increase in overall mortality stems from the metabolic syndrome that is often comorbid with NAFLD.¹⁸ A study in the U.S. showed that cardiovascular disease was the major cause of death among people with NAFLD, followed by malignancy and liver disease.¹⁹

Incidence and Prevalence

NAFLD is seen in both genders, all age groups, all ethnic groups, and all regions of the world.¹⁷ Owing to the lack of prospective studies, incidence of NAFLD is not well defined. In Japan, a study using elevated aminotransferases (liver enzymes) as a surrogate for NAFLD estimated an incidence of NAFLD to be 31 per 1 000 person-years in non-alcoholics.²⁰ Another study based on new patients attending the outpatient hepatology clinic in England showed an annual incidence of 29.5 per 100 000 population for NAFLD (including 9 per 100 000 population for NASH).²¹

Depending on the definitions of NAFLD, population studied and diagnostic tools used, NAFLD prevalence in general adult population widely ranged from 2% (in Iran) to 35% (in the U.S.).^{12, 22} For NASH, the estimated prevalence was lower. In the general U.S. population, estimates of NASH prevalence ranged from 3% to 5%.¹² Among adult Japanese population, 9% to 30% of them demonstrated evidence of NAFLD by ultrasound and the prevalence of NASH was estimated to be 1% to 3%.²³ While NAFLD could occur in young children, its prevalence was estimated to be 3% to 10% in the general paediatric population and it was more common among adolescents.^{1, 24} In Australia, a population-based cohort study showed a NAFLD prevalence of 12.8% among adolescents with a mean age of 17 years.²⁵

In high risk populations, prevalence of NAFLD was extremely high. For example, the prevalence of NAFLD in individuals with dyslipidaemia attending lipid clinics was estimated to be 50%. Patients with type 2 diabetes mellitus showed a NAFLD prevalence of 69% by ultrasound.^{12, 26} Among obese patients undergoing bariatric surgery, as many as 96% had NAFLD and up to 25% had NASH.¹⁸ In obese children, NAFLD prevalence

could also reach 70% to 80%.^{1, 24} With the rising prevalence of obesity and type 2 diabetes, particularly in the younger population, NAFLD will remain a major public health concern.^{2, 12, 13}

Hong Kong Situation

NAFLD is also pervasive in Hong Kong. Using proton-magnetic resonance spectroscopy and transient elastography as the assessment tools, an epidemiological study of 922 randomly selected community-dwelling Hong Kong Chinese adults aged 19 to 72 (with a mean of 48 years) between May 2008 and September 2010 reported a NAFLD prevalence of 27.3% — 36.8% in men and 22.7% in women. The prevalence increased with age, from 14% among people aged less than 30 years to 67% among people aged over 70 years (Table 1).²⁷

Table 1: Prevalence of NAFLD among Chinese adults in Hong Kong by sex and age group

| Age group (years) | Male | Female | Overall |
|-------------------|------|--------|---------|
| <30 | 15% | 12% | 14% |
| 30-39 | 30% | 16% | 21% |
| 40-49 | 41% | 16% | 26% |
| 50-59 | 38% | 28% | 32% |
| 60-69 | 42% | 39% | 41% |
| >70 | 50% | 75% | 67% |

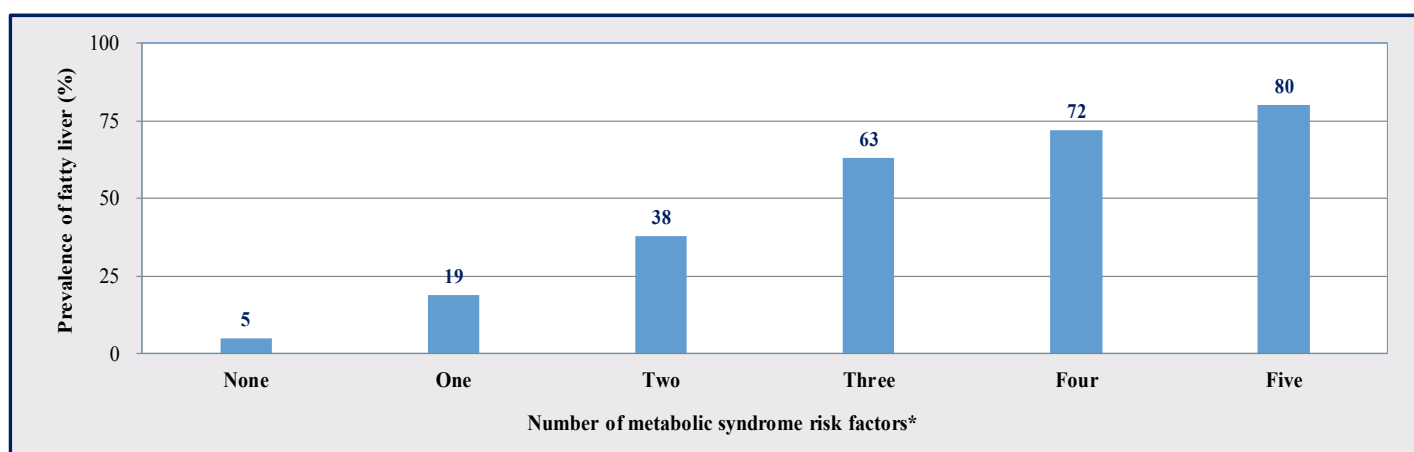
Source: Wong et al 2012.

Further analyses also showed that metabolic syndrome had a strong association with NAFLD. Subjects with central obesity (waist circumference >90 cm in men and >80 cm in women), suboptimal levels of triglycerides (>1.7 mmol/l), reduced high-density lipoprotein cholesterol (<1.03 mmol/l in men and <1.29 mmol/l in women), impaired fasting glucose (>5.6 mmol/l) or diabetes, and hypertension (blood pressure >130/85 mmHg) were about 4.3, 2.9, 2.5, 2.2 and 1.5 times respectively as likely to have NAFLD as the subjects without corresponding risk factors. Moreover, NAFLD prevalence increased with the number of metabolic syndrome risk factors, from 4.5% in subjects without any risk factor to 80% in those with all five risk factors (Figure 2). Overall, 3.7% of subjects with NAFLD had advanced fibrosis.²⁷

The subsequent study followed-up of 565 subjects without NAFLD at baseline from October 2012 to October 2013 (with a median follow-up interval of 47 months) and found that 76 of them developed fatty liver, giving a population incidence of NAFLD 13.5% at 3 to 5 years (or 3.4% per year). Again, metabolic syndrome was the most important risk factor associated with incident NAFLD.²⁸

By liver ultrasound scan and transient elastography of the liver, the Hong Kong Liver Health Census Study revealed a higher prevalence of NAFLD. Such cross-sectional study recruited 2 493 subjects aged 17 to 80 (with a median of 44 years) from the Red Cross Transfusion Centre in Hong Kong between August 2010 and March 2012. All subjects reported no significant alcohol intake and were screened negative for hepatitis B and C infection. Results showed that 42.3% of subjects had NAFLD. Of these, 17.7% had mild steatosis, 19.5% had moderate steatosis, and 5.1% had severe steatosis. Overall, 1.2% and 0.002% with NAFLD had advanced liver fibrosis and cirrhosis respectively. Male was about three times as likely to have NAFLD as female. Similar to the previous finding from a local study, risk of NAFLD increased with age and metabolic risk factors.²⁹

Figure 2: Prevalence of NAFLD in subjects by the number of metabolic syndrome risk factors



Note: * Metabolic syndrome risk factors include: central obesity (waist circumference >90 cm in men and >80 cm in women); triglycerides >1.7 mmol/l; reduced high-density lipoprotein cholesterol (<1.03 mmol/l in men and <1.29 mmol/l in women); blood pressure >130/85 mmHg; and fasting plasma glucose >5.6 mmol/l.

Source: Wong et al 2012.

Prevention and Management

To date, there are no established treatment guidelines and no single approved pharmacological agents for NAFLD treatment.^{6, 17} However, NAFLD is largely preventable and reversible if caught early in its development. Living a healthy lifestyle can play a big role in preventing and controlling the disease. According to a systematic review of 23 studies, lifestyle modifications leading to weight reduction and increased physical activity consistently reduced liver fat and improved glucose control.³⁰

Maintain an optimal weight and waistline.

For Chinese adults in Hong Kong, aim for a body mass index between 18.5 to 22.9 kg/m². Irrespective of their BMI, men should keep their waist circumference below 90cm (~ 36 inches) and women should keep theirs below 80cm (~ 32 inches). For people who are overweight and obese, weight loss can help lessen build-up of fat in the liver. A systematic review also showed that weight reductions of 4% to 14% resulted in decreasing liver fat.³⁰

Eat a balanced diet, including at least 5 servings a day of fruits and vegetables that are rich in anti-oxidants and moderate amounts of fish that are rich in omega-3 fatty acids. Avoid foods that are high in oil, sugar and salt. Studies also found a positive association between sucrose- or fructose-rich diets and NAFLD.³¹ Thus, people should avoid soft drinks and other sugar-sweetened beverages that contain lots of sucrose or fructose.

Be physically active. Regular physical activity reduces metabolic risks and liver fat, thereby reducing the risk of NAFLD and slowing the disease progression in people with NAFLD.^{31, 32} Adults should do at least 150 minutes of moderate-intensity physical activity (such as brisk walking, swimming slowly or cycling leisurely) or 75 minutes of vigorous-intensity physical activity (such as

jogging, fast swimming or vigorous cycling), or equivalent amounts throughout the week. Children and adolescents should accumulate at least 60 minutes of moderate- to vigorous-intensity physical activity daily.

Avoid alcohol consumption. As the chief organ responsible for the breakdown of alcohol, the liver is particularly vulnerable to the effects of alcohol metabolism. By definition, people with NAFLD do not have significant alcohol consumption. Excessive drinking, however, can make the liver getting fat and more than 90% people who drink heavily develop alcoholic fatty liver disease.³³

Do not smoke. Smoking may enhance progression of NAFLD partly through its effects on insulin resistance.³⁴ Smoking together with overweight and obesity can have a synergetic effect on NAFLD development.³⁵

Keep blood sugar, blood lipids and blood pressure at optimal levels. Healthy adults are generally advised to maintain a systolic blood pressure of less than 120 mmHg and a diastolic blood pressure of less than 80 mmHg; a fasting blood glucose of less than 5.6 mmol/l; and a total blood cholesterol of less than 5.2 mmol/l.

Of note, people with NAFLD generally have no symptom. When symptoms appear, they are usually vague with increased tiredness or a sense of pressure in the right upper abdomen.^{3, 7} For people who are concerned about the disease, they should never try over-the-counter medications for self-treatment, but have to consult their family doctor. For more information about healthy living, please visit the Central Health Education Unit website at <http://www.cheu.gov.hk>, or call the 24-hour Health Education Hotline at 2833 0111 of the Department of Health.

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Data Brief

Liver cancer is a common cancer in Hong Kong. In 2012, there were 1 790 new cases of liver cancer with a male to female ratio of 3.2 to 1. Liver cancer is one of the major causes of cancer death mortality in Hong Kong as well. In 2013, there were 1 524 people who died from liver cancer which accounted for 11.2% of all cancer deaths in that year.

Important risk factors of liver cancer include chronic hepatitis infection, liver cirrhosis, alcohol consumption, obesity, type 2 diabetes, consumption of aflatoxin contaminated food, smoking and exposure to certain chemicals (e.g. vinyl chloride and arsenic). Therefore, avoiding these risk factors through being vaccinated against hepatitis B and leading a healthy lifestyle help prevent liver cancer.

| | Liver cancer incidence, 2012 | | | Liver cancer mortality, 2013 | | |
|---|---------------------------------|--------|---------|---------------------------------|--------|---------|
| | Male | Female | Overall | Male | Female | Overall |
| Number of cases registered | 1 364 | 426 | 1 790 | 1 123 | 401 | 1 524 |
| Rank | 4 | 10 | 4 | 2 | 4 | 3 |
| Proportion of all cancers (%) | 9.6 | 3.1 | 6.4 | 14.2 | 7.1 | 11.2 |
| Median age (years) | 63 | 73 | 65 | 68 | 76 | 70 |
| Crude rate (per 100 000 population of respective sex) | 41.0 | 11.1 | 25.0 | 33.7 | 10.4 | 21.2 |
| Age-standardised rate (per 100 000 standard population) | 25.1 | 6.5 | 15.5 | 19.4 | 5.6 | 12.1 |

Sources: Hospital Authority, Department of Health and Census and Statistics Department.

Non-Communicable Diseases (NCD) WATCH is dedicated to promote public's awareness of and disseminate health information about non-communicable diseases and related issues, and the importance of their prevention and control. It is also an indication of our commitments in responsive risk communication and to address the growing non-communicable disease threats to the health of our community. The Editorial Board welcomes your views and comments. Please send all comments and/or questions to so_dp3@dh.gov.hk.

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