

## **ABSTRACT – TAN SRI DATO’ SERI DR. HAJI MD. ISMAIL MERICAN**

### Fatty Liver – Approach and Expectations

NAFLD (Non-alcoholic fatty liver disease) is fast becoming the most common cause of liver disease globally, affecting 20-30 % of people worldwide, with an anticipated increase in liver-related complications and mortality.

The most important risk factor is metabolic syndrome (MS) and components of MS including hypertension, hypertriglyceridemia, diabetes, and insulin resistance. NAFLD is suspected if individuals at risk have either a ‘bright’ liver on abdominal ultrasound (at least 5% of hepatocytes are infiltrated with fat) or raised liver enzymes in those who consume little or no alcohol, and without any other cause for liver disease or hepatic steatosis. It can be confirmed by a liver biopsy although now we have non-invasive screening tools in NAFLD which are more acceptable and convenient for patients.

Cardiovascular disease is the leading cause of mortality in NAFLD patients. It is important from the outset, to establish if the patient has NAFL (just fatty liver) or NASH (Non-alcoholic steatohepatitis) as the prognosis for both are different. NASH is the more severe form of NAFLD that is defined histologically, by the presence of significant hepatic steatosis, lobular inflammation, and hepatocyte ballooning. Most patients with NASH will develop progressive liver disease and once bridging fibrosis is present, 20% of such patients will develop cirrhosis over the next 2-3 years, with the risk of developing liver-related mortality and morbidity and hepatocellular carcinoma.

Non-invasive tests for liver fibrosis, can be divided into blood or imaging-based tests. Blood tests include the fibrosis-4 (FIB-4) score which uses age, aspartate aminotransferase, alanine aminotransferase, and platelet count. Others include APRI (AST to Platelet Ratio Index) and the NAFLD Fibrosis Score. There are some proprietary blood-based tests for diagnosis of liver fibrosis, but these are more costly and not widely available.

The imaging-based tests, include transient elastography (TE) and magnetic resonance elastography. Although magnetic resonance elastography has higher success rates and higher accuracy compared with TE, its application is limited by cost and availability. Sequential testing, using two different non-invasive tests is preferred. FIB-4 followed by TE has been shown to have high diagnostic accuracy, avoiding unnecessary referral to a specialist.

Liver biopsy is considered the gold standard for the assessment of NAFLD, but is limited by sampling variability, intra-observer and inter-observer variability, risk of serious complications and is only done if necessary.

Treatment is lifestyle modification, and management of metabolic risk factors to reduce cardiovascular disease risk. These include a healthy lifestyle, smoking cessation, losing weight for those who are overweight or obese, good control of diabetes, hypertension and hypertriglyceridemia. Weight loss, through lifestyle intervention (diet and exercise) has been found to improve histology, including a greater reduction in inflammation and fibrosis. While clinical benefits can be seen with any amount of weight loss, greater weight loss is associated with a greater disease improvement.

No drug has been approved for use in NAFLD by regulatory bodies. Pioglitazone has been found to reduce progression of fibrosis, and Vitamin E may be considered in adults without diabetes, albeit with some concerns. Another drug that is often quoted is obeticholic acid. Several drugs are under investigation to reduce NASH activity, without worsening of fibrosis or improving fibrosis. Anti-inflammatory, anti-fibrotic agents and metabolism modulators, have been tested in Phase III or IIb randomised controlled trials with minor positive results. Bariatric surgery may be considered, as a treatment of NAFLD in patients with body mass index  $\geq 35$  kg/m<sup>2</sup>, who have failed lifestyle intervention.

Screening for hepatocellular carcinoma, as with all patients with cirrhosis is advisable.

Increasing the awareness and knowledge, of the various stakeholders on NAFLD are vital, and healthcare professionals in primary care and family medicine, should be roped in to manage patients with non-communicable diseases (NCDs).

Only patients with severe NAFLD need to be referred to a hepatologist or gastroenterologist.