

# Nonalcoholic fatty liver disease: truly a disease?



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Increasing high caloric food intake coupled with reduced energy expenditure is generating the highest rates of obesity and diabetes in Australia ever recorded. The liver related consequence of these metabolic conditions is nonalcoholic fatty liver disease (NAFLD), now the commonest liver condition in the world, affecting up to 30% of North Americans and probably a similar proportion of Australians. Although the association between obesity or diabetes and the accumulation of hepatic fat has been recognised for decades, it is only recently that NAFLD has been linked to significant hepatic, cardiovascular and metabolic sequelae.

## Associated morbidity

The risk of developing cirrhosis with associated complications of liver failure and hepatocellular carcinoma is dependent upon the histological subtype of the disease. Hepatic steatosis without inflammation or fibrosis has a relatively benign course with 2% dying from liver disease over a one to two decade period, whereas hepatic steatosis with evidence of liver injury, inflammation or fibrosis (known as nonalcoholic steatohepatitis or NASH) has a liver related death rate of up to 17.5% over a similar time period.<sup>(1)</sup> With up to 3% of the population having NASH, this will potentially translate to a significant health problem in the coming decade.

The liver is a metabolic organ involved in lipid and glucose homeostasis and the production of inflammatory atherogenic cytokines. Consequently, evidence has emerged that NAFLD is associated with an up to three-fold increased risk of developing diabetes as well as being an independent risk factor for the development of cardiovascular disease.<sup>(2)</sup> Therefore, management of patients with NAFLD should include exclusion of diabetes and assessment of cardiovascular risk factors. Statins are safe to use in this population and should not be withheld due to raised liver tests due to NAFLD.

## Diagnosis

The diagnosis of NAFLD requires confirmation of hepatic steatosis by imaging, determination of pathogenic risk factors such as insulin resistance, central obesity and glucose intolerance and exclusion of secondary causes (alcohol, glucocorticoids). Liver enzymes are often normal in subjects with NAFLD and do not correlate well with histological severity and thus are unreliable to diagnose or stage the severity of liver disease.

Patients with diabetes and obesity are more likely to have NASH and thus a worse prognosis, however there are currently no non-invasive methods that can accurately distinguish patients with NASH from those with steatosis without fibrosis or inflammation. Non-invasive diagnostic methods such as the serum based tests or ultrasound based technology such as Fibroscan™ may be useful in the future to identify those with histologically aggressive disease who would benefit most from specific treatment.

## Treatment

Treatment revolves around improving insulin resistance with weight loss and exercise. However, this is unfortunately often unsuccessful in the long term. There are currently no pharmacotherapeutic agents approved for use for NASH, although insulin sensitising agents such as metformin and pioglitazone have been used with varying success. There is currently a lack of long term studies demonstrating efficacy and safety of these agents. The Gastroenterology and Hepatology Departments at Sir Charles Gairdner Hospital and Fremantle Hospital are currently running clinical treatment trials for patients with NASH.

### References

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2. Targher G, Marra F, Marchesini G. Increased risk of cardiovascular disease in non-alcoholic fatty liver disease: causal effect or epiphenomenon? *Diabetologia* 2008;51:1947-53. ■