Nonalcoholic fatty liver disease

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Non-alcoholic fatty liver disease affects about 15 to 20% of the population and is linked to obesity. Its prevalence in the community is increasing with the rising prevalence of people who are overweight or obese.

Remember

- Nonalcoholic fatty liver disease (NAFLD) is the most common cause of abnormal liver enzymes in the Australian community. Current estimates are that 15 to 20% of the adult population have NAFLD.[1]
- NAFLD is caused by the accumulation of triglyceride in hepatocytes. It coalesces into lipid droplets that displace cellular organelles to the periphery of the hepatocytes (Figure). This histological feature is called hepatic steatosis. The spectrum of NAFLD runs from bland steatosis to steatosis with hepatocyte injury, inflammation and fibrosis.
- The more severe form of NAFLD is known as nonalcoholic steatohepatitis (NASH). The prevalence of NASH is estimated to be 2 to 3% of the adult population. Patients with NASH are at risk of progressive liver disease, and about one-third of these patients will develop significant hepatic fibrosis or cirrhosis. Once patients have cirrhosis they can develop life-threatening complications such as liver failure and hepatocellular carcinoma.
- The pathogenesis of NAFLD is linked to obesity, particularly central obesity. The prevalence of NAFLD is increasing with the prevalence of people who are overweight or obese. Genetic factors also play a role, with the prevalence of NAFLD varying in different ethnic groups and with a given degree of overweight or obesity.
- NAFLD appears to be the hepatic manifestation of the metabolic syndrome. This syndrome comprises central obesity, dyslipidaemia (including low levels of high-density lipoprotein and hypertriglyceridaemia), hypertension and impaired glucose metabolism.
- Patients with NAFLD, particularly those with NASH, are at increased risk of early death from cardiovascular and liver diseases and other obesity-related conditions including some malignancies.[2]
- Management of NAFLD is aimed at addressing the underlying pathogenic factors and preventing associated complications.

Assessment

- Patients with abnormal liver enzymes and obesity are likely to have NAFLD. However, obesity-related hepatic steatosis may coexist and contribute to disease severity with other liver diseases. Patients with suspected NAFLD should have bilirubin and liver enzyme tests, fasting lipids and glucose measured (to check for metabolic impairment), and a hepatic ultrasound.

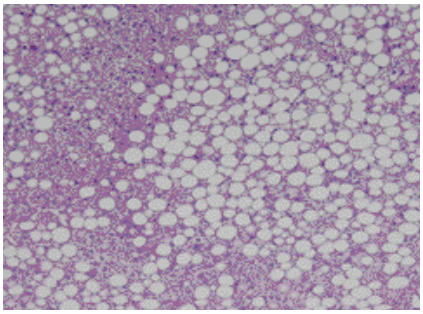

Figure. Hepatic steatosis. Note the large lipid droplets in hepatocytes displacing cytoplasm and organelles. This can be seen in patients with NAFLD, who have an excessive alcohol consumption, who take some medications (particularly tamoxifen), who have chronic hepatitis C infection or a combination of these. The diagnosis depends on the appropriate clinical scenario and laboratory investigations.

- Hepatic steatosis is a feature of some other liver diseases, including hepatitis C infection. It also occurs with intake of some medications, particularly tamoxifen and amiodarone.
- In patients with NAFLD, other liver diseases need to be excluded, including chronic viral hepatitis B and C infections in at-risk populations (test for presence of hepatitis B surface antigen and hepatitis C antibody). Ferritin levels are frequently elevated in patients with NAFLD, probably secondary to hepatic inflammation.
- Patients with NAFLD may be heterozygous for mutations of the haemochromatosis gene *HFE*. In distinction to haemochromatosis, transferrin saturation, particularly fasting values, is usually less than 45% in these patients, and hepatic iron stores are usually normal or only slightly increased.
- Patients can be considered to have NAFLD if alcohol consumption is less than National Health and Medical Research Council guidelines[3] (no more than two standard drinks per day for both men and women, with a standard

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drink being 10 g of alcohol), but obesity-related hepatic steatosis may coexist with alcoholic liver disease.
- In patients with NAFLD, levels of alanine transaminase (ALT) are typically higher than those of aspartate aminotransferase (AST). If AST levels are higher than ALT then other diagnoses, such as excessive alcohol intake, should be considered. In addition, AST may be higher than ALT in patients with cirrhosis from any cause.
- The key ultrasound feature of hepatic steatosis is increased liver echogenicity. This is usually only detected in moderate or severe steatosis, when more than 33% of hepatocytes are steatotic. Increased hepatic echogenicity also occurs with hepatic fibrosis. However, in the Australian community patients with hyperechoic or bright livers on ultrasound are more likely to have hepatic fat accumulation, particularly if they are overweight or obese.
- The disease at the most severe end of the spectrum of NAFLD is NASH, which at present can only be diagnosed by liver biopsy. This is relevant because only patients with NASH appear at increased risk of early death. Criteria for deciding which patients with NAFLD to biopsy for NASH have not yet been definitively established.
- Patients with NAFLD should be screened for other features of the metabolic syndrome including hypertension, dyslipidaemia and impaired glucose metabolism. Other correlates of the metabolic syndrome include obstructive sleep apnoea, polycystic ovary syndrome and renal impairment.

Management

- Management strategies focus on addressing the aetiological factors of overweight and obesity. This includes situations where obesity-related steatosis is a cofactor in liver injury in other liver diseases. However, there is a paucity of data on the efficacy of dietary and exercise measures. Pilot studies suggest they are beneficial, and there is preliminary evidence that modifying dietary fats and sugars may ameliorate NAFLD. The issue is most relevant for patients with NASH because they have the greatest increased risk of death. Laparoscopic gastric banding surgery has been shown to be beneficial in patients with NASH.
- Various pharmacological interventions have been examined in small pilot studies. The most promising of these are the glitazones, particularly pioglitazone,[4] the insulin-sensitising agent metformin and vitamin E. These agents need to be studied in larger populations and optimal dosing regimens determined. At present there is insufficient evidence to recommend their use in patients with NAFLD.
- Attention should be paid to comorbid conditions because patients with NAFLD appear more likely to die of cardiovascular disease than liver failure or hepatocellular carcinoma. MT

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COMPETING INTERESTS: None