



REVIEW ARTICLE: HISTOLOGICAL DESCRIPTION OF HEPARS THAT EXPERIENCE FATTY LIVER

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ABSTRACT

The liver is one of the most vital organs and the largest gland, weighing approximately 1500 grams or 2.5% of the total adult body weight. One of the liver's functions is to metabolize nutrients such as fat, protein, and carbohydrates. Fats are synthesized from carbohydrates and proteins, mainly in the liver. Fat function as a source of energy provides essential fatty acids, and plays an important role in dissolving vitamins. A high-fat diet (HFD) is a diet that involves consuming fatty and high-cholesterol foods which can have the risk of causing an increase in lipid levels in the blood, known as hyperlipidemia. Excessive accumulation of fat in liver cells is called fatty liver. Histologically, Non-alcoholic Fatty Liver Disease (NAFLD) is categorized into two types, namely Non-alcoholic Fatty Liver (NAFL) which shows fatty liver without evidence of inflammation in the form of swelling of hepatocyte cells, and Non-alcoholic Steatohepatitis (NASH), namely the presence of fatty liver accompanied by inflammation in the form of swelling of hepatocyte cells, with or without fibrosis.

Keywords: fatty liver; high-fat diet; histology of fatty liver; liver

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INTRODUCTION

With a weight of over 1500 g, the liver is the biggest gland in the body and one of the most important organs. The diaphragm and thoracic cage conceal and shield the liver, which is situated in the upper right quadrant of the belly. The normal liver is situated between the right side's 7–11 ribs and the left nipple, across the midline. The liver is attached to the diaphragm via the falciform ligament. (Ozougwu, 2017). One of the liver's functions is to metabolizes nutrients such as fat, protein, and carbohydrates. Fats are synthesized from carbohydrates and proteins, mainly in the liver. Fat function as a source of energy provides essential fatty acids, and plays an important role in dissolving vitamins. Consumption of unsaturated fatty acids, or polyunsaturated fatty acids (PUFA), and saturated fatty acids, or saturated fatty acid (SFA), on the other hand, can be harmful to human health. When a person's body weight is much above normal due to an accumulation of excess body fat, they are considered obese. This condition arises when the amount of body fat tissue relative to total body weight is higher than usual. Obesity can occur because there is an imbalance between the energy from food that comes in which is greater than the energy used by the body (Sandjaja and Sudikno, 2014).

Overweight is an issue in many parts of the world, where it is becoming more and more common in both industrialized and developing nations. The global rise in obesity has a significant effect on health issues and a lower standard of living. Obesity has an important contribution to the incidence of cardiovascular disease, type 2 diabetes mellitus, cancer, osteoarthritis and sleep apnea throughout the world (Seidell and Halberstadt, 2015). Every year, about 2.8 million individuals die from obesity and overweight globally. Over 1.9 billion persons globally, or over 39% of those over the age of 18, were overweight in 2014, and roughly 671 million adults, or roughly 13%, were obese. Obesity and overweight cause higher mortality than underweight in most populations in the world (WHO, 2016). Metabolic diseases resulting from obesity impact blood pressure, insulin resistance, cholesterol, and triglycerides. A higher BMI is associated with a higher risk of ischemic stroke, type 2 diabetes mellitus, and coronary heart disease.

More than 50% of the 671 million obesity sufferers worldwide are found in the following 10 countries, including United States, China, India, Russia, Brazil, Mexico, Egypt, Germany, Pakistan, and Indonesia which ranks 10th (Murray, 2014). The obesity rate of the Indonesian population continues to increase from year to year. The Litbangkes Agency reported that the prevalence of overweight and obesity in Indonesia was 28.9% in 2013, which was higher than the agency's 2010 report of 21.7%. Data from the Research and Development Agency for 2007 shows that the prevalence of obesity and overnutrition in the population aged 15 years and over nationally is around 19.1%. (Badan Litbangkes, 2013).

METHOD

In preparing this review, the technique used was a library study technique by searching for sources or literature in the form of primary data in the form of national journals under 2000. Apart from that, in making this review, data was also searched using online media, such as: Google and journal sites (NCBI, PubMed, etc.).

RESULTS

Non-alcoholic fatty liver disease (NAFLD) causes many health problems in both children and adults who are obese. This disease is closely related to the lifestyle of today's society which tends to eat foods are high in carbohydrates and fat but low in protein and vitamins. This is closely related to the increasing incidence of NAFLD along with the increasing incidence of metabolic syndrome which includes obesity, increased blood pressure, diabetes (Diabetes Mellitus=DM), peripheral insulin resistance, hypertriglyceridemia and hyperinsulinemia (Sherif, et al., 2016). Non-alcoholic fatty liver disease, also called non-alcoholic fatty liver disease (NAFLD) is a range of conditions characterized histologically by the presence of macrovesicular steatosis (fatty) in the liver and occurs in individuals who do not consume large amounts of alcohol. This disease is divided into two main subtypes, namely non-alcoholic fatty liver (NAFL, called simple steatosis), which is a form of non-progressive NAFLD that rarely progresses to cirrhosis; and non-alcoholic steatohepatitis (NASH) which can cause cirrhosis, hepatocellular carcinoma, and liver disease-related death.

DISCUSSION

NAFLD is now becoming widely recognized as a major cause of liver disease with an increasing incidence throughout the world. In a population in western countries, it is reported that the prevalence of NAFLD can reach 15-30%. This prevalence rate can increase to 58% in someone who is overweight. In someone with non-diabetic obesity, the prevalence can increase to 90%. The incidence of NAFLD is more common in men than in women. NAFLD often occurs in middle to old age, and its prevalence increases with increasing age. NAFLD is

now the main cause of chronic liver diseases in developing countries. One-third of the general population has steatosis, which is confirmed by imaging evidence that the majority have simple steatosis at 70-90%. The stage at which NAFLD progresses is closely related to the presence of metabolic syndrome. About 90% of NAFLD sufferers meet 1 of the metabolic syndrome criteria, and about 33% of NAFLD sufferers meet 3 or more of the metabolic syndrome criteria. The metabolic syndrome component is thought to be involved in the pathogenesis of NAFLD, namely the Two-Hit theory.

From many studies, it has been proven that liver function test abnormalities due to fatty liver or NASH are disorders that are very often found in the community. Reported figures vary widely due to different survey methodologies. The prevalence of nonalcoholic fatty liver ranges from 15-20% in adult populations in the United States, Japan, and Italy. It is estimated that 20-30% of them are in the more severe phase (NASH). A study of obese populations in developed countries found 60% simple fatty liver, 20-25% NASH, and 2-3% cirrhosis. In the same report it was also stated that 70% of patients with type 2 diabetes mellitus had fatty liver, while in patients with dyslipidemia, the figure was around 60%. In Indonesia, there is still not much research on non-alcoholic fatty liver. Lesmana reported 17 NASH patients with an average age of 42 years with 29% of liver histology showing steatohepatitis with fibrosis. A population study with a fairly large sample by Hasan and friends found a prevalence of nonalcoholic fatty liver of 30.6%. Important risk factors reported are obesity, diabetes mellitus, and hypertriglyceridemia.

It is reported that 60% of the obese population has fatty liver. This can occur as a result of the rapid development of science and technology which makes every activity easier and can ultimately have an impact on unhealthy lifestyles. A diet of junk food and lack of exercise results in an unhealthy weight and height ratio. The prevalence of overweight throughout the world has generally increased from 1981 to 2008. Excessive weight gain or obesity ($BMI > 25 \text{ kg/m}^2$) is one of the effects of lifestyle changes. The more obese a person is, the higher the risk of getting the disease. Amarapurkar et al in 2007, stated that the prevalence of NAFLD in Indonesia reached 30% and obesity was the most contributing risk factor. To suppress the effects caused by Saturated Fatty Acid (SFA) as a trigger for NAFLD, Unsaturated Fatty Acid (USFA) plays a role in inhibiting inflammatory cytokines and the insulin resistance process, thereby preventing an increase in free fatty acids in the liver and circulation. USFA also induces an increase in the CPT-1 enzyme which will increase beta-oxidation activity in the liver by converting free fatty acids into acetyl CoA, resulting in a decrease in the esterification process of fatty acids into triglycerides. The expected effect is that triglyceride levels in the liver return to normal and reduce the risk of fatty liver and oxidative stress.

Histological Features Fatty liver

Alcohol-induced liver damage cannot be distinguished from nonalcoholic fatty liver histopathologically. Steatosis, inflammatory cell infiltration, hepatocyte ballooning and necrosis, glycogen nuclei, Mallory's hyaline, and fibrosis are among the characteristics of a liver biopsy. When fibrosis is found in nonalcoholic fatty liver, it suggests that the liver damage is getting worse. From various studies of liver histology that have been carried out, it can be seen that fibrosis of various degrees is found in almost 66% of cases when the diagnosis is made, 25% of which have severe fibrosis (septal fibrosis or cirrhosis) and 14% have real cirrhosis.

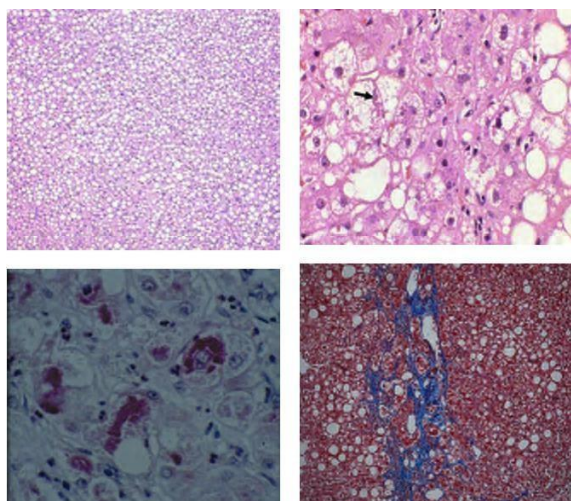


Figure 1. (**top left**) macrovesicular steatohepatitis (HE stain); (**top right**) ballooning with Mallory's hyaline in ballooning cells (arrow); (**lower left**) Mallory bodies stained with ubiquitin antibodies; (**lower right**) Masson trichrome staining shows pericellular fibrosis, especially in the centrilobular area

Nonalcoholic fatty liver is characterized histologically by the presence of fatty liver, either with or without inflammation. Fat is generally dominated by the appearance of macrovesicular cells that push the hepatocytic nuclei to the edge of the cells. In the early phase or mild steatosis, fat is found in zone 3 of hepatocytes. Inflammation is a basic component for stating the presence of nonalcoholic steatohepatitis. These inflammatory cells consist of neutrophils and mononuclear cells which are found in the liver lobules. If inflammatory cells are not found, it means the patient is still in the fatty liver stage. The presence of Mallory bodies and glycogen nuclei is a variation of the presentation of nonalcoholic steatohepatitis. Usually Mallory's bodies are smaller than those usually found in alcoholic steatohepatitis.

The knot

A group of illnesses collectively referred to as non-alcoholic fatty liver disease (NAFLD) are defined by the presence of steatosis (fatty) in the liver and the development of macrovesicular cells that push the hepatocytic nuclei to the periphery of the cells. The existence of fatty liver, with or without inflammation, is the histological feature of nonalcoholic fatty liver. Inflammation is a basic component for stating the presence of nonalcoholic steatohepatitis. If inflammatory cells are not found, it means the patient is still in the fatty liver stage.

CONCLUSION

Excessive accumulation of fat in liver cells is called fatty liver. Histologically, Non-alcoholic Fatty Liver Disease (NAFLD) is categorized into two types, namely Non-alcoholic Fatty Liver (NAFL) which shows fatty liver without evidence of inflammation in the form of swelling of hepatocyte cells, and Non-alcoholic Steatohepatitis (NASH), namely the presence of fatty liver accompanied by inflammation in the form of swelling of hepatocyte cells, with or without fibrosis.

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