Fat and Cardiometabolic Risk Burden

Dyah Purnamasari

Department of Internal Medicine, Faculty of Medicine Universitas Indonesia - Cipto Mangunkusumo Hospital, Jakarta, Indonesia.

Corresponding Author:
Dyah Purnamasari, MD., PhD. Division of Endocrinology and Metabolism, Department of Internal Medicine, Faculty of Medicine Universitas Indonesia - Cipto Mangunkusumo Hospital. Jl. Diponegoro 71, Jakarta 10430, Indonesia. email: dyah_p_irawan@yahoo.com.

In many Asian population, metabolic disorders rise relatively easily even in non-obese subjects (BMI<25 kg/m^2). However the clear mechanism of metabolic disorders in non-obese subjects has not been fully explained. In Indonesia, as many as 19.7% of men and 32.9% of women are obese, and 26.6% of adult population have central obesity.[1] Riskesdas' study also demonstrated that Indonesian people tend to have high carbohydrate diet, high fat diet, and low fiber diet. Approximately 50% of Indonesian people take unhealthy food (sweet and fatty) and more than 90% take low fiber diet. Furthermore, around a quarter of Indonesian people have sedentary activity >6 hour per day and it worsen along with age (especially >50 years old).[1] Excessive energy intake and low physical activity will induce obesity and other metabolic derangement. Obesity stays as the main cause of insulin resistance, type 2 diabetes and cardiovascular disease. However, as many as 30% of obese people do not have hypertension, dyslipidemia, or glucose intolerance. On the contrary, those metabolic disorders can happen among 20-30% of non-obese people. Both diet and physical activity have been considered to regulate intracellular lipid accumulation and associated with insulin sensitivity in muscle and liver independent of body weight.[2]

Ectopic fat accumulation due to adipose tissue dysfunction is not clearly understood. Several factors such as genetic, environmental and behavioral components are included in energy metabolism as well as physiologic versus pathologic fat accumulation.[3] There are 2 kinds of body fat distribution, visceral fat and subcutaneous fat distribution, which can be determined using CT-scan at umbilicus level. Visceral fat obesity has significant positive correlation with metabolic profile such as blood glucose, lipid profile and blood pressure. Beside fat's volume, fat's quality, determined by multiple detector computed tomography (MDCT), is associated with adverse cardiovascular risk.[4]

Physiologically, adipose tissue can store large amount of triglyceride. If the adipose tissue secretes adipokines with proinflammatory properties, it will stimulate ectopic fat accumulation in other tissues. Normally, tissues other than adipose tissue such as liver, skeletal muscle, heart, and pancreas, contain small amount of fat. Ectopic fat accumulation will disturb cellular function and thus disturb organ function, and is connected with insulin resistance.[3,5]

Insulin resistance is defined as an insufficient response to the biologic effects of insulin in tissues, such as skeletal muscle, liver, and adipose tissue. Clinically, there is difference between muscle insulin resistance and hepatic insulin resistance. Subjects with muscle insulin resistance will develop impaired fasting glucose while subjects with hepatic insulin resistance will demonstrate impaired fasting glucose. Fat accumulation in the liver lead to hepatic steatosis and insulin resistance.[5,6]

Ectopic fat accumulation in the liver without history of excessive alcohol intake is

indicated to as nonalcoholic fatty liver disease (NAFLD). Liver abnormalities in NAFLD ranges from hepatic steatosis with or without increases in serum transaminases to nonalcoholic steatohepatitis (NASH) with or without fibrosis, cirrhosis, and hepatocellular carcinoma. The prevalence of NAFLD is about 20% in general population, in varying degree across countries.[3,7] In Indonesia, there are only few studies about NAFLD. In 2015, Lesmana reported that the prevalence of NAFLD among healthy subject who underwent medical check up at private hospital was 51% (538 of 1054). There were 6 factors which are related to NAFLD: male sex, age >35 years, obese, hypertriglyceridemia, low HDL cholesterol, and high serum alanine aminotransferase (ALT).[8] In the previous study, Lesmana compared the clinical picture, insulin resistance status, and adipocytokines profiles of subject with NASH in Jakarta, Indonesia. They reported that subject with NASH had worse insulin resistance profile, which is known by greater HOMA-IR value, than that of subject without NASH. Besides, the level of proinfammatory cytokines such as tumor necrosis factor alpha (TNF-alpha) among subject with NASH was higher than that of control.[7] TNF alpha is known as potent proinflamamtory cytokines which play a role in the progression of atherosclerotic lesion. Further study is needed to investigate the progression of NAFLD and the following risk of cardiovascular endpoint among Indonesian people.

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