Association between apolipoprotein B and dietary fibers

Almira Devina Gunawan¹, Saptawati Bardosono³, Ninik Mudjihartini²

¹. Department of Nutrition, Faculty of Medicine, Universitas Indonesia-Dr. Cipto Mangunkusumo General Hospital, Jakarta, Indonesia
². Department of Biochemistry, Faculty of Medicine, Universitas Indonesia, Jakarta, Indonesia

Abstract

Introduction: Global awareness to the importance of natural fibers in vegetables and fruits are still generally very low. Indonesian people consume less fibers, which has been associated with the development of heart disease. Heart disease has been known as the leading cause of morbidity and mortality. Apolipoprotein B (ApoB) is a component of atherogenic particles that can be used as a marker for an increased risk of cardiovascular disease. Researches on apoB profile and its relationship with fiber intake has provided inconsistent results. This is an article review of the current literatures on the relationship between dietary fiber and serum apoB levels.

Methods: This is an article review of the current literatures on the relationship between dietary fiber and apoB. We searched PubMed and Google Scholar using keyword “dietary fibers” and “ApoB” to capture meta-analyses, observational and experimental studies. A total of 97 publication and abstracts were screened for this review. After careful screening, nine studies were finally included.

Results: Two studies did not find associations between dietary fiber and serum apoB, while other seven found the association. Dietary fiber has been reported to be involved in the metabolism of serum cholesterol and blood pressure; hence, the deficiency of dietary fiber intake is believed to contribute to the epidemic of cardiovascular diseases. Several factors including nutritional status, dietary diet pattern, age, gender, physical activity, and smoking habits might influence the relationship between dietary fiber and serum apoB.

Conclusion: More studies are required in the future for better understanding on the effect of dietary fiber on the apoB; hence, the risk of cardiovascular diseases.

Keywords: apolipoprotein B, fibers, cholesterol metabolism, heart disease, healthy promotion
Introduction

Fruits and vegetables are considered in dietary guidance because of their high concentrations of dietary fiber.\(^1\) According to the National Basic Health Research (Riskesdas) data in 2013, the national average proportion of low fruit and vegetable consumption prevalence for Indonesians aged 10 years and older was 93.5%. Similarly, the Riskesdas data showed the prevalence of 95.5% in 2018.\(^2\) These data suggesting that public awareness and knowledge regarding the consumption of dietary fiber from vegetables and fruit is considerably very low and tend to get worse. According to data from the Ministry of Health, the Indonesian population consumes fiber 10.5 g/day generally.\(^3\) This finding indicating that Indonesian met only half of the recommended daily fiber intake. Recommended fiber requirements based on the Nutrition Adequacy Rate (AKG) is 30–38 g/day. These values are also lower compared to the mean fiber intake in the UK and USA, which are 18 g/day and 16 g/day respectively.\(^4\) Additionally, the data from the World Health Organization (WHO) shows that Indonesians consume fruit and vegetables only 34.55 kg per year,\(^5\) which is less than half the Food Agriculture Organization (FAO) recommendation of 73 kg per capita per year.\(^6\)

Many evidences have directed to the role of dietary fibers to prevent the development of several chronic diseases such as cancer, type 2 diabetes, obesity and cardiovascular.\(^7,8\) In respect to the cardiovascular disease, dietary fiber has repeatedly been reported to be beneficial in reducing serum cholesterol and blood pressure; hence, the deficiency of dietary fiber intake is believed to contribute to the epidemic of cardiovascular disease.\(^9\) In support, the results of a study indicated that consuming fiber 15-29 grams per day is sufficient to reduce mortality and the incidence of heart attacks and higher intakes of dietary fiber could provide even greater protection.\(^10\)

Heart disease is a major health problem and cause approximately one-third of deaths globally.\(^11\) WHO data showed that seventeen million people in the world are estimated die from heart disease in 2015, 75 % of which occur in developing countries.\(^12\) Riskesdas data in 2018 shows that 1.5% Indonesians suffer from coronary heart disease.\(^13\) Over 200 risk factors for heart disease have been identified, abnormal lipids profile is regarded as the most important risk factor.\(^14\) Atherogenic dyslipidemia characterized by elevated levels of serum triglyceride (TG) levels and low-density lipoprotein cholesterol (LDL-C) with low levels of high-density lipoprotein cholesterol (HDL-C) plays a significant role in the development of heart disease.\(^15\) Study by Snideman et al.\(^16\) highlighted the age-dependent association between apoB and the risk of cardiovascular events. ApoB have been proposed as a marker to quantitate the atherogenic damage, due to the fact that it is the component constituent of the atherogenic particles; hence, plasma apoB levels reflect the total numbers of atherogenic particles.\(^16\) Study suggested that the apoB is a better candidate risk parameter than non-HDL cholesterol for identifying a subgroup of individuals with elevated cardiovascular risk.\(^17\)

There are several factors that affect the circulating apoB levels. These factors are divided into groups, namely the nutritional and non-nutritional factors. The nutritional factors including nutritional status, dietary fibers, fat, and carbohydrates, while the non-nutritional factors are age, gender, physical activity, and smoking habits.\(^18\) The dietary fiber can reduce levels of apoB through a distinct mechanism for each fiber source. Recently, study suggesting that the dietary fiber can reduce levels of apoB through gel formation which increases food transit time, delays gastric emptying, decreases nutrient absorption, and slows digestion.\(^19\) Additionally, study showed that animals fed with fibers exhibited increased LDL-ApoB turnover, leading to the upregulation of hepatic ApoB and trigger faster catabolism and clearance.\(^19\)

Decreasing apoB levels due to the dietary fibers can result in the reduced risk of cardiovascular disease. Research on the effect of soluble fiber on lipid profiles has been reported by several independent studies. One clinical trial by Ramos et al.,\(^20\) in 116 people with hypercholesterolemia showed that apoB levels in the group fed with fiber significantly lower after after 12 weeks. Another clinical trial in 28,984 Swedish individuals showed a significant correlation between dietary fiber intake and apolipoprotein B.\(^21\) Unfortunately, research on the profile of apolipoprotein B and its relationship

\(\text{World.Nutr.Journal} \mid 74\)
with fiber intake so far has provided inconsistent results. In this manuscript, we provide a systematic literature review on the highly variable research results on the association between Apolipoprotein B and fiber intake to gain a comprehensive insight.

Methods

This article is a literature review using any meta-analyses, observational and experimental studies that are relevant to this article. According to Creswell and Poth, literature reviews are written summaries of articles from journals, books, and other documents that describe theories and information both past and present; organizing literature into the topics and documents needed. The type of data used by the author in this study was searched from PubMed and Google Scholar using the explode function for subgroup terms with operators (“and,” “or”) for keyword “dietary fibers” and “Apolipoprotein B” to capture all meta-analyses, observational and experimental studies that included findings on the relation of dietary fibers and apoB. Hand-searching was used to identify further potential eligible studies. A total of 97 publication titles and abstracts were screened for this literature review. The inclusion criteria used in this study are categorized based on study design, specific interventions, participants, and outcome assessed. Study designs of evaluations included in the review was controlled trials with either a randomised crossover or parallel study design with an intervention period equal or greater than 14 days. The analysis was limited to primary sources of fibre for which there were more than 5 trials per type of fibre (i.e. for oat products, psyllium, pectin and guar gum). Specific interventions included in this review were water-soluble dietary fibers from a single source, including pectin, oat bran, guar gum, and psyllium. Participants included in this review were men or women who either healthy, hyperlipidemic, obese or diabetic. Outcomes assessed in this review were correlation between dietary fiber intake and apolipoprotein B. After careful screening, nine studies were finally included. The data obtained then analyzed by descriptive analysis method. The method of descriptive analysis is carried out by describing the facts which are then followed by analysis with sufficient understanding and explanation.

Results and Discussion

Dietary fibers

Definition and classification of fibers

Dietary fiber was originally defined as a non-digestable constituents of the cell wall of the plant. Later on, dietary fiber was determined as any component of plant that resistant to hydrolysis by human digestive enzymes. In 2000, American Association of Cereal Chemists (AACC) defined dietary fibre as the edible parts of plant or analogous carbohydrates that are resistant to digestion and absorption in the human small intestine with complete or partial fermentation in the large intestine. Dietary fiber includes cellulose, hemicellulose, lignin, pectins, gums, β-glucan, resistant starch, fructans, chitosan and chitin.

Fibers can be classified according to their type and solubility. Based on the type, fiber is divided into dietary fiber and functional fiber. Dietary fibers include cellulose, hemicellulose, pectin, lignin, gum, resistant starch, fructans, and psyllium. Fiber can also be classified based on its solubility into soluble fiber and insoluble fiber. Soluble fibers include hemicellulose, pectin, gum, β-glucan, and psyllium; while insoluble fibers include lignin, cellulose, fructans, and polyols.

Dietary fiber can be obtained from daily food ingredients such as vegetables, nuts, fruit, and cereals. The amount and composition of fibers vary between food. The fiber content of different food sources is listed in Table 1.

Recommended daily intake for dietary fibers

Current dietary guidance recommends that Americans consume 14 g of fiber per 1,000 kcal. Recommendations for fiber intake for adults and children are shown in Table 2. However, most Americans only consume about 15 g of fiber per day. Meanwhile, in Indonesia, recommended fiber requirements based on the Nutrition Adequacy Rate
(AKG) is 30–38 g/day depend on the age and gender of the individual. At 19-29 years of age, it is recommended that men consume 37 grams of fiber/per day while woman is 32 grams/day. At the age of 30-49, 36 grams per day are recommended for men while for woman is 30 grams per day. Regardless, the Indonesian population consumes fiber 10.5 g/day generally.33

Apolipoproteins

Structure of the apolipoproteins

The complete amino acid sequence of the ApoB100 consists of 4536 amino acids with a molecular weight of 550 kDa.26 The mature ApoB100 is the 27 amino acids N-terminal truncated version of the premature ApoB100 with the molecular mass of 513 kDa.27 ApoB100 has a globular amino terminal domain, which reacts with microsomal triglyceride transfer proteins. The apoB gene is located on the short arm of chromosome 2. Study have identified one hundred twenty-three genetic variants in the apoB gene. The apoB100-3,500Arg-Gln affects its receptor binding and causes a disorder known as familial defective apolipoprotein B-100 (FDB).28 ApoB100 is synthesized in hepatocytes and it could be degraded under certain conditions.29 ApoB is an atherogenic component found in VLDL, IDL, and Lpa. Therefore, apoB represents the circulating atherogenic lipoprotein particles.

ApoB48 consists of 2152 amino acids with a molecular mass of 264 kDa. ApoB100 and apoB48 are produced from a single gene. ApoB48 is generated by cell-specific RNA editing of a CAA codon to a premature UAA termination codon and is identical to the N-terminal 48% of apoB100.30 ApoB48 is synthesized by enterocytes, secreted in chylomicrons and stored in chylomicron remnant. Since one molecule of apoB48 is present in each chylomicron particle, it can be used as a marker for the chylomicrons.31 Particles smaller than 70–80 nm can penetrate blood vessel walls. Therefore, chylomicron remains, but not nascent chylomicrons, are considered to be atherogenic. Chylomicron waste is enriched with ester cholesterol by exchange with HDL.32

Lipoprotein classes

Insoluble lipids are transported in a complex with proteins as lipoproteins by circulatory system. Lipoproteins have a central hydrophobic core of non-polar lipids, consisting of cholesterol esters and triglycerides that is surrounded by a hydrophilic membrane consisting of phospholipids, free cholesterol, and apolipoproteins. Plasma lipoproteins are divided into five classes chylomicrons, Very Low Density Lipoprotein (VLDL), Low Density Lipoprotein (LDL), High Density Lipoprotein (HDL), and lipoprotein.33 Apolipoproteins regulate and control lipoprotein metabolism and lipid transport by acting as ligands for lipoprotein receptors, guiding the formation of lipoproteins, and serving as activators or inhibitors of enzymes involved in the metabolism of lipoproteins.34

Lipoprotein metabolism

Lipoproteins are lipid protein particles that carry hydrophobic substances in a hydrophilic environment of the blood. Lipoproteins are classified based on their hydrated density, in an ascending order, into chylomicrons, VLDL, IDL, LDL and HDL.35 Apolipoproteins or apoproteins are proteins that make up lipoproteins, which serve as receptor-binding and regulatory proteins. The cores of these particles contain hydrophobic molecules such as triglycerides (TG) and cholesteryl esters. The liver, intestines, spleen, brain and testes synthesize apolipoproteins and at their surface contain lipoproteins. There are 4 main types of lipoproteins, namely Apo A, B, C, and E. One or more apolipoproteins make up each lipoprotein covering the apoprotein including apo A is the main apolipoprotein constituent of High-density lipoprotein (HDL), while apo B100 is the main apolipoprotein in LDL and can also be found on VLDL. Lipoproteins have different sizes according to their lipid composition and apolipoprotein content. This characteristic changes as a result of the reaction of enzymes such as lipoprotein lipase (LPL), hepatic triglyceride lipase (HTGL), lecithin-cholesterol acyltransferase (LCAT) and cholesterol ester transfer protein (CETP).36 Apolipoprotein functions to activate and regulate enzymes in lipoprotein metabolism, maintain the integrity of the lipoprotein complex structure, and become ligands for specific cell surface receptors. The formation and metabolism of lipoproteins is influenced by both the apolipoprotein
content and its conformation. Hepatocytes produce apoB100 and the small intestine produces apoB48 which is a glycoprotein of the apo B group. Apolipoproteins control cellular intake of lipoproteins by binding with lipoprotein receptors. ApoB100 and apolipoprotein E (apoE) bind to the apoB/E (LDL) receptor. ApoE also binds to LDL receptor-related protein (LRP). Apolipoprotein A binds to the BI scavenger receptor.

The exogenous lipoprotein pathway starts with the absorption of the dietary cholesterol and fatty acids in the intestine, and incorporation into chylomicrons. Chylomicrons enter the circulation and travel to peripheral sites. Chylomicrons are triglyceride-rich and normally catabolized within minutes by the endothelium-associated lipoprotein lipase (LPL), releasing free fatty acids (FFA), which are taken up and metabolized by the liver, muscle, and adipose tissues; and chylomicron remnants are formed. Chylomicron remnants are then taken up by the liver. via the low-density lipoprotein (LDL) receptor and the LDL receptor–related protein (LRP).

The endogenous lipoprotein pathway begins in the liver with the assembly and secretion of triglyceride-rich VLDL particles, which transport triglycerides from the liver to peripheral tissues. The triglycerides carried in VLDL are hydrolysed by LPL in muscle and adipose to form intermediate-density lipoproteins (IDL) or VLDL remnants, which can be taken up by the liver or can be further hydrolyzed to LDL particles. LDL is converted to bile acids in the liver, then secreted into the intestines; while in non-hepatic tissues, LDL is used for the synthesis of hormones, cell membrane, or being stored. LDL is also taken up by macrophages.

LDL transports cholesterol to hepatocytes and other peripheral tissues with the help of ApoB100 for the recognition and uptake of LDL by the LDL receptor. Meanwhile, the oxidized LDL (ox-LDL) is taken up by macrophages and vascular smooth muscle cells. These can lead to excess accumulation and the formation of foam cells, which is a major step in the plaque formation and development of atherosclerosis. The small dense LDL cholesterol (sdLDL-c) is one of LDL subclass associated with raised TG and decreased HDL-c levels and more atherogenic than larger LDL particles.

HDL plays a crucial role in reverse cholesterol transport, acting as a vehicle for cholesterol shuttle from peripheral cells to the liver for excretion and catabolism which occurs in three phases: extravascular, intravascular, and intrahepatic. It also provides a reservoir of C apolipoproteins, which are required for the metabolism of chylomicrons and VLDL. Reverse cholesterol transport can be performed in three different routes: (1) HDL with multiple apoE is taken up by the liver mediated by LDL receptor, (2) accumulated cholesterol esters from HDL is taken up by the liver via the scavenger receptor B1, (3) cholesteryl esters are transferred by the cholesteryl ester transfer protein (CETP) from HDL to triglyceride-rich lipoproteins. Many experimental and epidemiologic studies have indicated the protective effect of HDL against atherogenesis indicates its function in reverse cholesterol transport. Disturbances in the metabolism of lipoproteins is a major contributor of the antiatherogenic properties of HDL; thus, determined as risk factor for coronary heart disease.

Factors affecting apolipoprotein B
There are several factors that cause an increase in apo B including nutritional factors (nutritional status, dietary fibers, fat, and carbohydrates) and non-nutritional factors (age, gender, physical activity, and smoking habits).

1. Nutritional status
Obesity is one of the risks of cardiovascular disease due to its relationship with high triglycerides, LDL cholesterol, low HDL cholesterol, increased blood glucose, insulin resistance and hypertension. New findings regarding metabolic risk factors associated with fat and obesity are the presence of a small dense LDL phenotype, postprandial hyperlipidemia with atherogenic accumulation and excessive lipoproteins production containing apolipoprotein B. These lipid disorders are characteristic of metabolic syndrome and is associated with an inflammation which partly due to the adipose tissue itself. An important relationship between obesity, metabolic syndrome and dyslipidemia, is insulin resistance in peripheral tissues that leads to increased liver fatty acids from food sources.
intravascular lipolysis and from adipose tissue resistance to the antilipolytic effect of insulin.\textsuperscript{44}

2. Diet pattern
Study in 28,984 Swedish individuals showed a significant correlation between dietary fiber intake and apolipoprotein B.\textsuperscript{21} Another clinical trial by Ramos \textit{et al.}\textsuperscript{20} in 116 people with hypercholesterolemia showed that apoB levels in the group fed with fiber significantly lower after 12 weeks. Additionally, study by Anggadiredja \textit{et al.}\textsuperscript{45} in 41 individuals with hypercholesterolemia showed that 4 weeks of fibers supplement treatment affects apolipoprotein B levels.

3. Age and gender
Research conducted by Anagnostis \textit{et al.}\textsuperscript{46} showed that advancing age is positively associated with increased levels of apolipoprotein B. Those study also explains that at the age of 50-55 years, men generally have a higher average apolipoprotein B than women.

4. Smoking habits
Smoking is one of the causes of heart attacks. Nicotine causes the secretion of catecholamines, cortisol, and growth hormone, which results in adenyl cyclase activation in the adipose tissue. Lipolysis will be initiated from triglycerides and fatty acids will be secreted into the plasma. Circulating fatty acids binds with albumin and results in increased synthesis of triglycerides and VLDL in the liver. Thus, results in increasing triglycerides and VLDL and decreasing HDL. Since apolipoprotein B is required to produce LDL and VLDL, high levels of LDL and VLDL is associated with high apolipoprotein B.\textsuperscript{47}

5. Physical activity
Study revealed that months of aerobic exercise decreased apoB concentration in hypercholesterolemic men.\textsuperscript{46} In contrast, another study by reported that aerobic exercise for 20 weeks did not affect the concentration of apoB. Others found no change in apoB concentrations during either long or short aerobic exercise. Some factors must result in these various outcomes such as age.\textsuperscript{49}

\textbf{Association between apolipoprotein B and dietary fibers}

Dietary fiber has been studied by various researchers to provide evidences of its beneficial effect in lowering cholesterol levels. The increased risk of cardiovascular disease has a positive correlation with the improvement of LDL cholesterol levels.\textsuperscript{50} Soluble fiber has a positive effect on apoB levels in respect of preventing cardiovascular disease. ApoB is the dominant lipoprotein component in LDL particles, which is also found in VLDL and IDL. ApoB have been proposed as a marker to quantitate the atherogenic damage, due to the fact that it is the component constituent of the atherogenic particles; hence, plasma apoB levels reflect the total numbers of atherogenic particles.\textsuperscript{25,51} Research on the association of ApoB levels and dietary fibers intake shows controversial results (Table 3). This may be due to differences in the characteristics of the subject, especially in the source of food and metabolism in the body in various populations.

Two studies did not find associations between dietary fiber and serum apoB, while other seven found the association. Dietary fiber has been widely reported to be involved in the metabolism of serum cholesterol (both atherogenic and non-atherogenic) and blood pressure; hence, the deficiency of dietary fiber intake is believed to contribute to the epidemic of cardiovascular diseases. Several factors including nutritional status, dietary diet pattern, age, gender, physical activity, and smoking habits might influence the relationship between dietary fiber and serum apoB; thus, explaining the different results. The clinical utility of apoB is of the most value in populations such as those with obesity and type 2 diabetes in whom the risk of CVD is elevated.\textsuperscript{58} Trapping of apoB particles drives the atherosclerotic process from beginning to end.\textsuperscript{59} Cholesterol is a critical component of the apoB particles within the arterial wall. The mass of cholesterol within plasma does correlate positively with the number of apoB particles within plasma. But variance in the mass of cholesterol per apoB particle produces variance in the relation between cholesterol and apoB and therefore a difference in the relation of each to risk.\textsuperscript{60} EAS and EFLM accept that cardiovascular risk relates more closely to apoB than to LDL-C/non-
HDL-C; therefore, the clinical utility of apoB exceeds LDLC/non-HDL-C.\textsuperscript{61,62}

Unfortunately, there are still few studies that did not find associations between dietary fiber and serum apoB one of which is study by Ho et al.\textsuperscript{53}. Interestingly study by Ho et al.\textsuperscript{53} showed that konjac glucomannan did not appear to significantly affect the overall effect estimate for apoB, the reduction of 0.05 g/L is higher than that reported in the previous reported meta-analysis of oats (−0.03 g/L) and barley (−0.03 g/L) β-glucans by Ho et al.\textsuperscript{55}. Therefore, more studies are required to better understand the role of konjac glucomannan and β-glucans on apoB, specifically the mechanism of which causing the results to be distinctive.

**Conclusion**

The results of the studies on the relationship between dietary fibers and serum apoB levels have been inconsistent; while some studies found the negative correlation between dietary fibers and serum apoB levels, others did not. Dietary fiber has been widely reported to be involved in the metabolism of serum cholesterol (both atherogenic and non-atherogenic) and blood pressure; hence, the deficiency of dietary fiber intake is believed to contribute to the epidemic of cardiovascular diseases. Several factors including nutritional status, dietary diet pattern, age, gender, physical activity, and smoking habits might influence the relationship between dietary fiber and serum apoB; thus, explaining the different results. More studies are required in the future for better understanding on the effect of dietary fiber on the level of serum apoB; hence, the risk of cardiovascular diseases.

**Table 1.** Dietary fiber content of various food sources\textsuperscript{24}

| Food Sources       | Soluble Dietary Fiber (g/100 g) | Insoluble Dietary Fiber (g/100 g) | Total  |
|--------------------|---------------------------------|-----------------------------------|--------|
| **Fruits (raw)**   |                                 |                                   |        |
| Apple with skin    | 0.70                            | 2.00                              | 2.70   |
| Banana             | 0.58                            | 1.21                              | 1.79   |
| Grape              | 0.24                            | 0.36                              | 0.60   |
| Mango              | 0.69                            | 1.08                              | 1.76   |
| Orange             | 1.37                            | 0.99                              | 2.35   |
| Pear with skin     | 0.92                            | 2.25                              | 3.16   |
| Pineapple          | 0.04                            | 1.42                              | 1.46   |
| Strawberry         | 0.60                            | 1.70                              | 2.30   |
| Watermelon         | 0.13                            | 0.27                              | 0.40   |
| **Beans (cooked)** |                                 |                                   |        |
| Black beans        |                                 |                                   | 8.7    |
| Red beans          | 1.36                            | 5.77                              | 7.13   |
| **Nuts**           |                                 |                                   |        |
| Almonds            |                                 |                                   | 12.3   |
| Peanuts            |                                 |                                   | 8.1    |
| **Vegetables (cooked)** |                               |                                   |        |
| Broccoli           | 1.85                            | 2.81                              | 4.66   |
| Carrot             | 1.58                            | 2.29                              | 3.87   |
| Lettuce (raw)      |                                 |                                   | 1.3    |
| Corn               |                                 |                                   | 2.0    |
| Mushroom           |                                 |                                   | 2.4    |
| Cooked potatoes with skin |                         |                                   | 2.31   |
| Steamed potato, skinless |                      |                                   | 2.05   |
| **Grains and Products** |                             |                                   |        |
| Rice (cooked)      |                                 |                                   |        |
| White              |                                 |                                   | 0.3    |
| Food Sources             | Soluble Dietary Fiber (g/100 g) | Insoluble Dietary Fiber (g/100 g) | Total |
|--------------------------|---------------------------------|-----------------------------------|-------|
| Red Bread                | 1.8                             |                                    |       |
| White Bread              | 2.4                             |                                    |       |
| Wheat                    | 6.8                             |                                    |       |
| Cereal (cold)            |                                 |                                    |       |
| All rice bran            | 29.3                            |                                    |       |
| Raisin skin              | 11.1                            |                                    |       |
| Corn flakes              | 2.5                             |                                    |       |
| Wheat biscuits           | 10.6                            |                                    |       |

Table 2. Recommended fiber intake in Indonesia and the United States

| Gender  | Age (year) | Recommended fiber intake (gram) | Indonesia | United State |
|---------|------------|---------------------------------|-----------|--------------|
| Man     | 19 – 29    | 37                              | 38        |              |
|         | 30-49      | 36                              |           |              |
|         | ≥ 51       |                                  |           |              |
| Woman   | 19 – 29    | 32                              | 25        |              |
|         | 30-50      | 30                              |           |              |
|         | ≥ 51       |                                  | 21        |              |

Table 3. Characteristics of studies on the association between apoB and dietary fibers

| Author                  | Study Design                              | Subjects                                                                 | Results/Conclusion                                                                                     |
|-------------------------|-------------------------------------------|-------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------|
| Yulia et al. (2016)     | Double blind randomized clinical trial with parallel design | 28 individuals with obese I (BMI of 25-29.9 kg/m²), aged 30-50 years.  | *Psyllium husk* fiber 8.4 g/day and low-calorie balanced diet 1200 kcal/day in obese I individuals did not reduce apoB level in 4 weeks |
| Ho et al. (2017)        | Meta-analysis study                       | 12 publications (n = 370) were included. Six trials reported on apoB (n = 162). | Results from 6 studies did not show any effect of konjac glucomannan, a viscous soluble fiber, on apoB |
| Antoniazzi et al. (2019)| Population-based observational study      | 190 individuals with heterozygous familial hypercholesterolemia          | Inverse association was encountered between fibers with ApoB                                          |
| Ho et al. (2016)        | Meta-analysis study                       | Fifty-eight trials (n 3974) retrieved from MEDLINE, Embase, CINAHL and Cochrane CENTRAL assessing the effect of oat β-glucan diets compared with controlled diets apoB. | *Oat β-glucan, a viscous, soluble fibre, has a lowering effect on apoB*                                |
| Rakvaag et al. (2019)   | Double-blind, randomized, controlled, parallel intervention study | 73 subjects with abdominal obesity (abdominal circumference ≥80 cm for women or ≥94 cm for men) age ≥40 years. | Low-fiber cereal consumption for 12 weeks reduced fasting apolipoprotein B. |
| Author                  | Study Design                              | Subjects                                                                 | Results/Conclusion                                                                 |
|------------------------|-------------------------------------------|----------------------------------------------------------------------------|------------------------------------------------------------------------------------|
| Frondelius et al. (2017) | Population-based cohort                   | 74,318 healthy individuals, men and women aged 44–74 years between 1991 and 1996 | There was a significant correlation between dietary fiber intake and apolipoprotein B. |
| Ramos et al. (2011)      | Randomized, parallel-design study with blinded endpoints | Subjects with primary hypercholesterolemia (n=116).                        | ApoB levels in the group fed with fiber significantly lower after after 12 weeks.     |
| Anggadiredja et al. (2020) | Double-blind, randomized, parallel-group study | 50 hypercholesterolemic participants (fasting LDL-c concentration of > 130 mg/dL), 18 years of age | Four weeks of fibers supplement treatment significantly affects apolipoprotein B levels. |
| Jovanovski et al. (2018) | Meta-analysis study                        | 28 trials (n = 1924) retrieved from Medline, EMBASE, CINAHL, and the Cochrane Central Register of Controlled Trials | Supplementation of Psyllium fiber effectively improves apoB (95% CI: -0.08, -0.03 g/L; P < 0.0001) |

Conflict of Interest

Authors declared no conflict of interest regarding this article.

Open Access

This article is distributed under the terms of the Creative Commons Attribution 4.0 International Licence (http://creativecommons.org/licenses/by/4.0/), which permits unrestricted use, distribution, and reproduction in any medium, provided you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if changes were made.

References

1. Slavin JL, Lloyd B. Health Benefits of Fruits and Vegetables. Adv Nutr. 2012; 3:506–16.
2. Arfines PP, Luglio HF, Kusumawardani N. Prevalence and Lifestyle Risk Factors of Overweight and Obesity Among Indonesian Adolescents: An Analysis of Global School-Based Health Survey 2007 and 2015. Adv Heal Sci Res 2019; 22:512–8.
3. Putri MF. The use of coconut dregs flour as food fiber and its application to oyster mushroom (reviewed from its nutrition). AIP Conf Proc 2018;1941(1):020026.
4. Bodhini D, Gaal S, Shatwan I, Ramya K, Ellahi B, Surendran S, et al. Interaction between TCF7L2 polymorphism and dietary fat intake on high density lipoprotein cholesterol. PLoS ONE 2017; 12(11): e0188382.
5. Komarayanti S, Suharso W, Herrianto E. Business of Local Fruit and Vegetables in Jember District as a Support of Food Security, Indonesia. Budapest Int Res Critics Inst Humantit Soc Sci 2018;1:208–24.
6. Kalmpourtzidou A, Eilander A, Talsma EF. Global Vegetable Intake and Supply Compared to Recommendations: A Systematic Review. Nutrients 2020; 12:1558.
7. Barber TM, Kabisch S, Pfeiffer AFH, Weickert MO. The Health Benefits of Dietary Fibre. Nutrients 2020; 12:3209.
8. Lockyer S, Spiro A, Stanner S. Dietary fibre and the prevention of chronic disease – should health professionals be doing more to raise awareness? Nutr Bull 2016; 41:214–31.
9. Sánchez-Muniz FJ. Dietary fibre and cardiovascular health. Nutr Hosp 2012; 27:31–45.
10. Reynolds A, Mann J, Cummings J, Winter N, Mete E, Te Morenga L. Carbohydrate quality and human health: a series of systematic reviews and meta-analyses. Lancet 2019; 393:434–45.
11. Mozaffarian D, Benjamin EJ, Go AS, Arnett DK, Blaha MJ, Cushman M, et al. Heart Disease and Stroke Statistics-2016 Update: A Report From the American Heart Association. Circulation 2016;133(4):e38-360.
12. Kaptoge S, Pennells L, De Bacquer D, Cooney MT, Kavousi M, Stevens G, Riley LM, Savin S, Khan T, Altay S, et al. World Health Organization cardiovascular disease risk charts: revised models to estimate risk in 21 global regions. Lancet Glob Heal 2019; 7:e1332–45.
13. Winoto PMP, Ahsan A, Nasution TH. Analysis of Risk Factors Related to Recurrence of Coronary Heart Disease. World J Adv Healthc Res 2019; 3:84–8.
14. Pencina MJ, Navar AM, Woydyla D, Sanchez RJ, Khan I, Elassel J, D’Aostino RB, Peterson ED, Snideman AD. Quantifying Importance of Major Risk Factors for Coronary Heart Disease. Circulation 2019; 139:1603–
Autophagy. PLoS One 2013; 8:e57590.

Andreo U, Guo L, Chirieac D V., Tuyama AC, Clerc F, Reiding KR, Jansen BC, Kammeijer GSM, Jiménez-Mora MA, Mendivil CO. ApoE and apoc-III-defined HDL subtypes: a descriptive study of their lecithin cholesterol acyl transferase and cholesteryl ester transfer protein content and activity. Lipids Health Dis 2020; 19:106.

Anggadiredja K, Ufamy N, Amali L. Ameliorating Effects of Four Nutritional Approaches to Lower Triglycerides. Nutrients 2019; 11:1297.

Bodt A, Wuhrer M. Human plasma protein N-glycosylation. Glycoconjug J 2016; 33:309–43.

Boyle SW, Cui SW. An introduction: Evolution and finalisation of the regulatory definition of dietary fibre. Food Hydrocoll 2011; 25:139–43.

Borg M, Ernberg I, Fröndelius K, Ernst Y, Aberg-Lindstrom M, Sellstrom M, Ekborg O, Torzilli A, Mattson SA, Kiviniemi A, Kröller M, Fagerberg L, Ohlson I, Jönsson J. Total carbohydrate intake with cardiovascular disease and mortality in 18 countries from five continents (PURE): a prospective cohort study. Lancet 2017; 390:2050–62.

Creswell JW, Phillips GO, Cui SW. An introduction: Evolution and finalisation of the regulatory definition of dietary fibre. Food Hydrocoll 2011; 25:139–43.

Dhingra D, Michael M, Rajput H, Patil RT. Die finalisation of the regulatory definition of dietary fibre. Phillips GO, Cui SW. An introduction: Evolution and finalisation of the regulatory definition of dietary fibre. Food Hydrocoll 2011; 25:139–43.

Dhingra D, Michael M, Rajput H, Patil RT. Die finalisation of the regulatory definition of dietary fibre. Phillips GO, Cui SW. An introduction: Evolution and finalisation of the regulatory definition of dietary fibre. Food Hydrocoll 2011; 25:139–43.

Dong J, Kongsuen T, Devaraj S, Hoefner DM, Warnick GR. Apolipoprotein B and cardiovascular disease risk: Position statement from the AACC lipoproteins and vascular diseases division working group on best practices. Clin Chem 2009; 55:407–19.

Doonan LM, Fisher EA, Brodsky JL. Can modulators of apolipoproteinB biogenesis serve as an alternate target for cholesterol-lowering drugs? Biochim Biophys Acta - Mol Cell Biol Lipids 2018; 1863:762–71.

Donaghedea J, Ufamy N, Amalia L. Ameliorating Effects of Four-Week Fiber-Multivitamin Combination Treatment on Low-Density Lipoprotein Cholesterol, Owen JS, Simons JP, Khoo B. Exon Skipping of Hepatic APOB Pre-mRNA With Splice-switching Oligonucleotides Reduces LDL Cholesterol In Vivo. Mol Ther 2013; 21:602–9.

Dzau VJ, Kass DA, de Lemos JA, Elam MB, Capra JA, Ford JD, Criqui MH. Recommendations for use of non-HDL cholesterol or non-HDL-C for risk of coronary heart disease in healthy individuals: the EPIC-Norfolk prospective population study. Eur J Clin Invest 2013; 43:1009–15.

Feingold KR, Grunfeld C. Introduction to Lipids and Lipoproteins. 2000.

Fleming TE, Dana T, Sacks FM, Kwan BCH, Kronenberg F, Beddhu S, Cheung AK, Zinsmeister AR, Kannel WB, Howard BV, Knopp RH, Daviglus ML, O’Meara ES, Furberg CD, Mallette M, Larson MG, Feinleib M, Kuller LH, Muller JE, Miller ME, Kastanjé JJP, Wareham NJ, Boekholdt SM, Khaw K-T. Non-HDL cholesterol vs. Apo B for risk of coronary heart disease in healthy individuals: the EPIC-Norfolk prospective population study. Eur J Clin Investig 2013; 43:1009–15.
Total Cholesterol, and Apolipoprotein B Profiles in Hypercholesterolemic Participants. J Diet Suppl 2020; 17:173–83.

46. Anagnostis P, Stevenson JC, Crook D, Johnston DG, Godsland IF. Effects of gender, age and menopausal status on serum apolipoprotein concentrations. Clin Endocrinol (Oxf) 2016; 85:733–40.

47. Jain RB. Impact of smoking on the observed levels of apolipoprotein B: Data from NHANES 2007–2012. Environ Toxicol Pharmacol 2017; 53:227–33.

48. Wang Y, Xu D. Effects of aerobic exercise on lipids and lipoproteins. Lipids Health Dis 2017; 16:1–8.

49. Yazdani R, Marefati H, Shahesmaeili A, Nakhaei S, Bagheri A, Dastoorpoor M. Effect of Aerobic Exercises on Serum Levels of Apolipoprotein A1 and Apolipoprotein B, and Their Ratio in Patients with Chronic Obstructive Pulmonary Disease. Tanaffos 2018; 17:82–9.

50. Ross I. Plantago ovata Forsk. Dalam: Thau A, editor. Medicinal Plants of the World: Chemical Constituents, Traditional and Modern Medicinal Uses. Humana Press Inc 2009; :426.

51. Boyd S. Krauss Food and The Nutrition Process. 2011.

52. Yulia RN, Tambunan V, Prijanti AR. Pengaruh Suplementasi Serat Psyllium husk dan Diet Rendah Kalori Seimbang terhadap Kadar Apo B Penyandang Obes I. Arsip Gizi dan Pangan 2016; 1:121–8.

53. Ho HVT, Jovanovski E, Zurbau A, Blanco Mejia S, Sievenpiper JL, Au-Yeung F, Jenkins AL, Duvnjak L, Leiter L, Vuksan V. A systematic review and meta-analysis of randomized controlled trials of the effect of konjac glucomannan, a viscous soluble fiber, on LDL cholesterol and the new lipid targets non-HDL cholesterol and apolipoprotein B. Am J Clin Nutr 2017; 105:1239–47.

54. Antoniazzi L, Arroyo-Olivares R, Bittencourt MS, Tada MT, Lima I, Jannes CE, Krieger JE, Pereira AC, Quintana-Navarro G, Muñiz-Grijalvo O, et al. Association of dietary components with dyslipidemia and low-grade inflammation biomarkers in adults with heterozygous familial hypercholesterolemia from different countries. Eur J Clin Nutr 2019; 73:1622–5.

55. Ho HVT, Sievenpiper JL, Zurbau A, Blanco Mejia S, Jovanovski E, Au-Yeung F, Jenkins AL, Vuksan V. The effect of oat β-glucan on LDL-cholesterol, non-HDL-cholesterol and apoB for CVD risk reduction: a systematic review and meta-analysis of randomised-controlled trials. Br J Nutr 2016; 116:1369–82.

56. Rakvaag E, Fuglsang-Nielsen R, Bach Knudsen KE, Landberg R, Johannessen Hjelholt A, Sondergaard E, Hermansen K, Gregersen S. Whey Protein Combined with Low Dietary Fiber Improves Lipid Profile in Subjects with Abdominal Obesity: A Randomized, Controlled Trial. Nutrients 2019; 11:2091.

57. Jovanovski E, Yashpal S, Komishon A, Zurbau A, Blanco Mejia S, Ho HVT, Li D, Sievenpiper J, Duvnjak L, Vuksan V. Effect of psyllium (Plantago ovata) fiber on LDL cholesterol and alternative lipid targets, non-HDL cholesterol and apolipoprotein B: a systematic review and meta-analysis of randomized controlled trials. Am J Clin Nutr 2018; 108:922–32.

58. Kohli-Lynch CN, Thanassoulis G, Moran AE, Sniderman AD. The clinical utility of apoB versus LDL-C/non-HDL-C. Clin Chim Acta 2020; 508:103–8.

59. Sniderman AD, Thanassoulis G, Glavinovic T, Navar AM, Pencina M, Catapano A, Ference BA. Apolipoprotein B Particles and Cardiovascular Disease. JAMA Cardiol 2019; 4:1287.

60. Sniderman AD, Couture P, Martin SS, DeGraaf J, Lawler PR, Cromwell WC, Wilkins JT, Thanassoulis G. Hypertriglyceridemia and cardiovascular risk: a cautionary note about metabolic confounding. J Lipid Res 2018; 59:1266–75.

61. Langlois MR, Nordestgaard BG, Langsted A, Chapman MJ, Aakre KM, Baum H, Borén J, Bruckert E, Catapano A, Cobbaert C, et al. Quantifying atherogenic lipoproteins for lipid-lowering strategies: consensus-based recommendations from EAS and EFLM. Clin Chem Lab Med 2020; 58:496–517.

62. Mach F, Baigent C, Catapano AL, Koskinas KC, Casula M, Badimon L, Chapman MJ, De Backer GG, Delgado V, Ference BA, et al. 2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk. Eur Heart J 2020; 41:111–88.