

## Literature Review: The Effect of Mediterranean Diet on Lipid Profile and Fasting Blood Glucose in Overweight or Obese

### *Studi Literatur: Pengaruh Diet Mediterania terhadap Profil Lipid dan Glukosa Darah Puasa pada Orang Overweight atau Obesitas*

Gustina Berta Uli<sup>1\*</sup>, Sekar Ramadhanti Asyahir<sup>1</sup>, Leny Budhi Harti<sup>2</sup>

<sup>1</sup>Program Studi Pendidikan Profesi Dietisien, Fakultas Ilmu Kesehatan, Universitas Brawijaya, Indonesia

<sup>2</sup>Departemen Gizi, Fakultas Ilmu Kesehatan, Universitas Brawijaya, Malang, Indonesia

#### ARTICLE INFO

Received: 09-12-2021

Accepted: 04-08-2022

Published online: 03-03-2023

\*Correspondent:

Gustina Berta Uli

[gustinabertauli@gmail.com](mailto:gustinabertauli@gmail.com)



DOI:

10.20473/amnt.v7i1.2023.139-146

Available online at:

[https://e-](https://e-journal.unair.ac.id/AMNT)

[journal.unair.ac.id/AMNT](https://e-journal.unair.ac.id/AMNT)

Keywords:

Mediterranean diet, Lipid profile, Fasting blood glucose, Overweight, Obesity

#### ABSTRACT

**Background:** National Basic Health Research or Riset Kesehatan Dasar in 2018 stated that obesity in Indonesia had reached 21.8%. Being overweight and obese are among the risk factors that increase various health problems, including dyslipidemia and type 2 diabetes mellitus; hence, lifestyle changes are needed, one of which is through dietary modification. The Mediterranean diet is said to improve the lipid and glucose profiles of overweight or obese people.

**Objectives:** This literature study aimed to determine the effect of the Mediterranean diet on lipid profiles and blood glucose levels of overweight or obese people.

**Methods:** This research was conducted using the literature review method on two databases that consist of Pubmed and Cochrane, with specific keywords: "Mediterranean Diet," "Obese," "Overweight," "Lipid," dan "Glucose." The inclusion criteria in this study were articles that have been through peer review and proven that the articles are credible nationally and internationally. In addition, the literature was published in the last ten years, from 2012 to 2022, with RCT research design, using English or Indonesian, >18 years old subjects classified as obese or overweight, and can be accessed online. Meanwhile, the exclusion criteria for this study were literature using pregnant women as a subject, <18 years old subjects, and a non-RCT method study.

**Discussion:** Mediterranean diet is a type of diet that consumes foods high in monounsaturated fatty acid, polyunsaturated fatty acid, and soluble fiber. According to the results of this literature review, these nutrients improve lipid profiles in obese and overweight people. The Mediterranean diet's antioxidant composition and low glycemic index were also found to lower fasting blood glucose levels. In addition, carbohydrate control and physical activity are associated with fluctuation in insulin sensitivity that can affect fasting blood glucose levels in obese and overweight people.

**Conclusions:** It was found that some literature stated that the Mediterranean diet could lower the levels of LDL, triglycerides, and total cholesterol, increase HDL levels and lower fasting blood glucose levels.

#### INTRODUCTION

According to the World Health Organization (WHO), obesity and overweight are abnormal or excessive fat accumulation conditions that can cause various health problems<sup>1</sup>. Health problems caused by obesity and overweight include chronic diseases, such as heart disease and stroke, which are one of the world's most significant causes of death. Apart from heart disease and stroke, obesity and being overweight can also be risk factors for diabetes and its complications. Based on the 2018 Indonesian Basic Health Research (Riskesdas), the prevalence of obesity in Indonesia reached 21.8%<sup>2</sup>.

The results of previous studies stated that people with obesity have higher glucose levels than non-obese. This condition is due to the relationship between

obesity, insulin resistance, and pro-inflammatory adipokines, which cause changes in the distribution of body fat resulting in changes in the body's metabolism and can cause changes in blood glucose levels<sup>3</sup>. Obesity is associated with high levels of triglycerides (TG), cholesterol, and LDL (Low-Density Lipoprotein) and low levels of HDL (High-Density Lipoprotein), which is then referred to as dyslipidemia. Treatment for people with obesity can be started with diet modifications, health education, and medicines<sup>4</sup>.

One type of diet that can be an option for overweight and obese people is the Mediterranean Diet (MedDiet)<sup>5</sup>. The MedDiet diet is cited as the most effective for preventing obesity-related diseases<sup>5</sup>. The MedDiet is the consumption pattern of the Mediterranean community where most types of food

consist of (a) high plant-based foods, such as fruits, vegetables, nuts, whole grain cereals, and whole grains, (b) the use of fresh food ingredients and local consumption, (c) olive oil as a source of fat intake, (d) consumption of red wine, (e) consumption of fresh fish and seafood, (f) high consumption of dairy products, poultry, eggs, (g) low consumption of red meat and its processed products<sup>6</sup>. MedDiet does not cause weight gain due to the low consumption of fatty foods<sup>7</sup>.

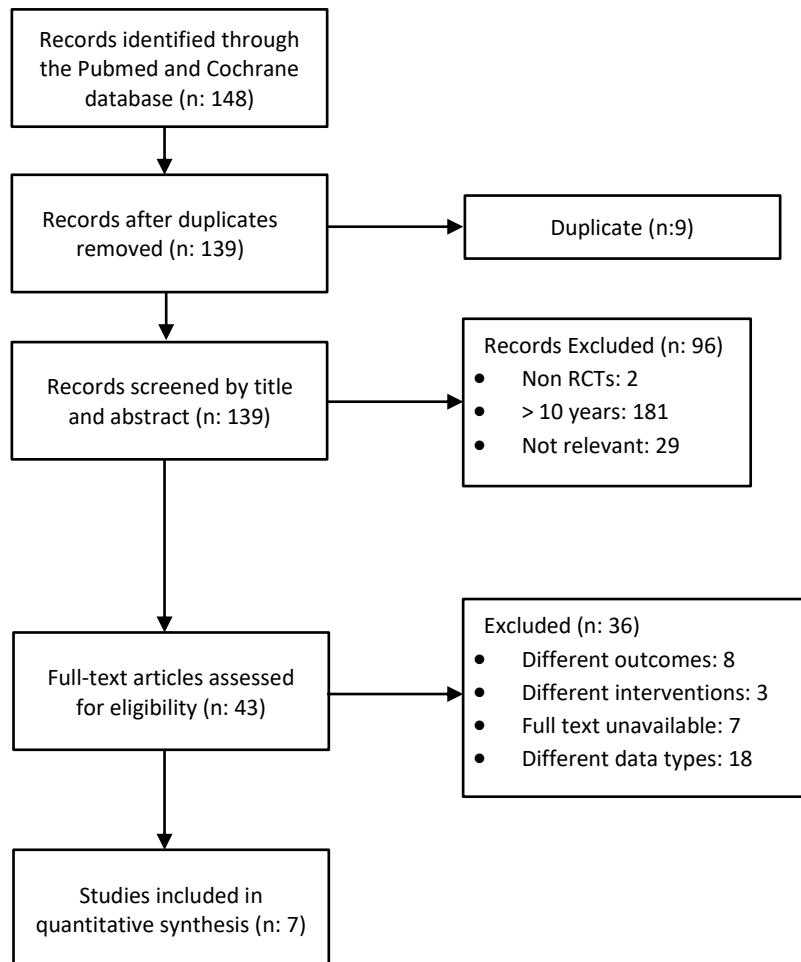
MedDiet provides significantly improves the risk of Cardiovascular Disease (CVD) and supports beneficial effects on blood pressure, insulin sensitivity, lipid profile, lipoprotein particles, inflammation, oxidative stress, and carotid atherosclerosis<sup>7</sup>. By repairing adipose tissue, MedDiet can also improve blood glucose control in obese people<sup>8</sup>.

Given the many risks of obesity for various chronic diseases, a literature review is needed to determine the Mediterranean diet's effect on lipid profiles and fasting blood glucose levels in people with overweight or obese.

**METHODS**

This study used a literature study or literature review using two databases, Pubmed and

Cochrane, with the keywords "Mediterranean Diet," "Obese," "Overweight," "Lipid," and "Glucose." The inclusion criteria in this literature study were: (1) literature that has gone through peer review, (2) has been proven credible nationally and internationally, (3) published in the last ten years, 2012-2022, (4) a Randomized Controlled Trial (RCT) research, (5) using English or Indonesian subjects > 18 years old, (6) classified as obese or overweight, and (7) literature can accessed online. The exclusion criteria for this literature were a literature that used pregnant women aged <18 years and methods outside of RCTs. The literature search used the Boolean Search technique with keywords; Mediterranean Diet AND Obese OR Obesity OR Overweight AND Lipid Profile OR Lipid OR Glucose. The literature found will be reviewed first and will be used if the literature can answer several research questions, such as "What is the meaning of MedDiet?", "How can MedDiet affect lipid profile levels in overweight or obese people?" "How can MedDiet affect blood glucose levels in overweight or obese people?". The PRISMA diagram of the literature search strategy used in this study is presented in Figure 1.



**Figure 1.** Literature search process

## RESULTS AND DISCUSSION

Based on the results of literature selection through two databases, seven articles met the inclusion criteria: three discussing lipid profiles, two discussing fasting blood glucose, and two discussing these two variables and their relation to MedDiet.

### The Effect of the Mediterranean Diet on the Lipid Profile of Overweight or Obese People

Five articles were reviewed regarding the effect of the Mediterranean Diet (MedDiet) on lipid profiles in subjects who were overweight or obese. Most of the articles indicated an improvement in lipid profiles in subjects who were overweight or obese who were given MedDiet. MedDiet is a diet rich in vegetables, and there is an increased consumption of poultry and fish and restrictions on red meat<sup>9</sup>.

Obesity is closely related to dyslipidemia, in which LDL, cholesterol, and triglyceride (TG) levels are high but low HDL. One of the causes of dyslipidemia is the high consumption of saturated fat sources. Thus, running the MedDiet by consuming foods high in Polyunsaturated Fatty acids (PUFA) and fiber can help to improve lipid profiles in people with dyslipidemia. Handayani et al. stated that decreased TG levels and increased HDL levels were based on the influence of Omega-3 fatty acids (PUFA) obtained when consuming fish or olive oil<sup>10</sup>. PUFA are fatty acids that contain more than two double bonds, which have an essential role in transport and fat metabolism, immune function, and maintenance of cell membranes. This finding is supported by research conducted by Casas et al. by dividing subjects into three groups randomly, the MedDiet group supplemented with 50 ml extra virgin oil/day (MedDiet+EVOO), the MedDiet group supplemented with 30 g of mixed nuts/day (MedDiet+ nuts), and a low-fat diet control group with type 2 diabetes mellitus or >2 CVD risk factors. The study results in the third and fifth years showed a decrease in TG, total cholesterol, and LDL levels and an increase in HDL levels in the MedDiet+EVOO and MedDiet+nuts groups<sup>11</sup>. Venturini et al. explained that EVOO could provide an antioxidant effect because it contains polyphenols and monounsaturated fatty acids (MUFA). Besides, EVOO can fight against LDL oxidation and act as a chain-breaking antioxidant for lipid peroxidation<sup>12</sup>. Altamimi et al. stated that nuts contain high PUFA, especially in Hazelnuts, and high MUFA, especially in Walnuts. Peanuts have a higher content of protein and fiber than tree nuts. The relationship between hypocholesterolemia and fiber is that fiber can bind bile acids to reduce serum cholesterol and ferment in the large intestine to produce acetate, propionate, and butyrate, which can inhibit cholesterol synthesis<sup>13</sup>.

Ryan et al. conducted a study on non-diabetic subjects diagnosed with Non-alcoholic Fatty Liver Disease (NAFLD) and randomly divided them into two groups, MedDiet and a low-fat, high-carbohydrate diet for six

weeks. This study showed that subjects who received MedDiet experienced a decrease in TG levels, but there was no significant change in HDL levels. The literature explains that MedDiet contains high MUFA, which can reduce LDL and TG oxidation and increase HDL<sup>14</sup>. MUFA is a fatty acid with one carbon double bond and can be found in olive oil, soybean oil, and others. A high intake of phytosterols from nuts, seeds, vegetables, and fruits is essential in lowering plasma cholesterol levels to compete with cholesterol absorption in the intestine<sup>15</sup>. This finding was supported by research conducted by Bekkouche et al., where all subjects were given guidance to increase physical activity for at least 30 minutes a day, but the group interventions were encouraged to consume whole grains, olive oil, fish, fruits, vegetables, nuts, and linseed grains. The results of this study stated that there were significant differences in the MedDiet group compared to the control group, namely a decrease in TG and cholesterol levels in subjects who adhered to the MedDiet and recommended lifestyle changes<sup>16</sup>. The source and short length of the carbon chain from fatty acids will affect the process and results—body fat metabolism.

Research by Vitale et al. on subjects with overweight or obese was divided into two intervention groups, the MedDiet, and Western diet (control) groups, for eight weeks. The MedDiet group was designed to eat fruit and vegetables (at least five servings, ~500 g/day) and nuts (30 g/day), replacing cereal products with whole grains (at least two servings, ~200 g/day), meat and meat-derived products with legumes and fish (at least two servings, ~300g/week of fish and three servings, ~300g/week of legumes), butter and other condiments containing EVOO. Subjects were encouraged to consume meat, dairy products, and eggs only once/a week. The study showed a significant reduction in LDL levels, and TG and total cholesterol levels tended to be lower after eight weeks of intervention compared to the control group. However, there was no difference in HDL levels<sup>17</sup>. Low cholesterol levels in the group of people on MedDiet occurred because the diet was rich in water-soluble fiber from whole grains, nuts, and fruits. Water-soluble fiber reduces the absorption of cholesterol and bile acids in the small intestine.

Comparisons between the MedDiet and low-fat diets were also studied by Ristic-Medic et al., which resulted in reduced TG, LDL, and cholesterol levels in both groups and more HDL increases in the MedDiet compared to the low-fat group. Thus, it can be said that MedDiet can contribute more to treatment because it can reduce saturated fatty acids and increase MUFA, PUFA, and fatty liver index (FLI) in patients with Non-alcoholic Fatty Liver Disease (NAFLD)<sup>9</sup>. The study by Damasceno et al. stated that there was a decrease in LDL levels after undergoing a MedDiet accompanied by good physical activity<sup>18</sup>. A summary of the literature search results for this study is shown in Table 1.

**Table 1.** Summary of articles findings

Researcher and Year	Title and Research Sample	Method	Results & Conclusions
Casas et al., 2016	<p><b>Title</b> Long-term immunomodulatory effects of a Mediterranean diet in adults at high risk of cardiovascular disease in the PREvención con Dieta MEDiterránea (PREDIMED) randomized controlled trial</p> <p><b>Subject</b> Atherogenesis patients with obesity and overweight</p>	<p><b>Design</b> Parallel-group, single-blind, multi-center, randomized, controlled 5-y clinical trial</p> <p><b>Intervention</b> 160 samples were divided into three groups, group 1 MedDiet with extra virgin olive oil (EVOO), group 2 MedDiet with nuts, and group 3 low-fat diet</p>	<p><b>Results</b> Compared to baseline, at years 3 and 5, both MedDiet groups experienced increases in HDL cholesterol (<math>\geq 8\%</math>) and decreases in blood pressure (<math>&gt; 4\%</math>), total cholesterol, LDL cholesterol, and triglyceride concentrations.</p> <p><b>Conclusion</b> The MedDiet EVOO and the nuts group experienced a decrease in TG levels, and total cholesterol, and an increase in HDL concentrations</p>
Ryan et al., 2013	<p><b>Title</b> The Mediterranean diet improves hepatic steatosis and insulin sensitivity in individuals with non-alcoholic fatty liver disease</p> <p><b>Subject</b> People with obese and overweight with Non-alcoholic Fatty Liver Disease (NAFLD) without diabetes</p>	<p><b>Design</b> A randomized, cross-over intervention study</p> <p><b>Intervention</b> The 12 samples were divided into two groups, the MedDiet group and low-fat-low-carbohydrate (RLRK) group</p>	<p><b>Results</b> There was a non-significant decrease in triglyceride concentrations in the MedDiet group, which was neither seen in the RLRK group nor the RLRK group there was a significant change in HDL cholesterol in both diet groups</p> <p><b>Conclusion</b> There were no significant changes in TG and HDL for both diet groups</p>
Bekkouche et al., 2013	<p><b>Title</b> The Mediterranean diet adoption improves metabolic, oxidative, and inflammatory abnormalities in Algerian metabolic syndrome patients</p> <p><b>Subject</b> Obese and overweight people with metabolic syndrome</p>	<p><b>Design</b> Randomized controlled trial</p> <p><b>Intervention</b> The sample was divided into two groups: the MedDiet group with lifestyle education for three months (36 samples) and the control group that was only given lifestyle education (18 samples).</p>	<p><b>Results</b> Significant reduction in TG, cholesterol, and fasting blood glucose levels in the MedDiet+lifestyle change education group with a p-value <math>&lt; 0.05</math></p> <p><b>Conclusion</b> Lifestyle education interventions based on nutrition education can increase metabolism, improve inflammation from metabolic syndrome, and significantly improve lipid profiles and GDP.</p>
Vitale et al., 2020	<p><b>Title</b> Acute and chronic improvement in postprandial glucose metabolism by a diet resembling the traditional Mediterranean dietary pattern: Can SCFAs play a role?</p> <p><b>Subject</b></p>	<p><b>Design</b> Randomized, controlled, parallel-group design</p> <p><b>Intervention</b> 29 samples were divided into two groups, MedDiet and Western-type diet (control),</p>	<p><b>Results</b> LDL levels in the MedDiet group were significantly lower than the control group (<math>p=0.041</math>), with lower triglycerides (<math>p=0.07</math>), while there was no difference in HDL</p> <p><b>Conclusion</b> The MedDiet group experienced a significant reduction in LDL levels, and TG</p>

Researcher and Year	Title and Research Sample	Method	Results & Conclusions
	<i>Overweight</i> or obesity	for eight weeks	levels and total cholesterol tended to be lower. There was no difference in HDL levels.
Ristic-Medic et al, 2020	<b>Title</b> Calorie-restricted Mediterranean and low-fat diets affect fatty acid status in individuals with non-alcoholic fatty liver disease <b>Subject</b> <i>Overweight</i> or obesity	<b>Design</b> Randomized controlled trial <b>Intervention</b> 24 samples were randomly assigned to a low-fat diet or MedDiet for 3 month	<b>Results</b> In the MedDiet group, TG, cholesterol, LDL, HDL, and fasting blood glucose levels experienced significant improvements with a p-value<0.05. Compared to the low-fat diet, significant differences were found in HDL and TG with p=0.041 and p=0.041, respectively. <b>Conclusion</b> Decreased levels of LDL, TG, cholesterol, fasting blood glucose, and increased HDL levels in the MedDiet group showed significant differences in HDL and TG in the MedDiet and Low-Fat diet groups.
Pellegrini et al. 2020	<b>Subject</b> Patients who recovered from breast cancer with nutritional status of obesity and overweight.	<b>Design</b> Randomized open-label pilot intervention trial <b>Intervention</b> A Total of 34 samples were given MedDiet for four months with the addition of probiotics for the first two months in the intervention group, and MedDiet in the control group	<b>Results</b> The p-value = 0.0025 for fasting blood glucose in the intervention group after four weeks of treatment. <b>Conclusion</b> A significant decrease in fasting blood glucose levels before and after the administration of MedDiet. MedDiet+Probiotic significantly lowers fasting blood glucose levels
Tricò et al., 2021	<b>Title</b> Effects of Low-Carbohydrate versus Mediterranean Diets on Weight Loss, Glucose Metabolism, Insulin Kinetics and $\beta$ -Cell Function in Morbidly Obese Individuals <b>Subject</b> Obese people with a high risk of diabetes	<b>Design</b> Parallel-arm, open, randomized clinical trial <b>Intervention</b> Samples were divided into Low-Carbohydrate diet (LC) and MedDiet groups, with the composition of the LC diet being 30% carbohydrates, 30% protein, and 40% fat and the MedDiet composition being 55% carbohydrates, 15% protein, and 30% fat. Samples were observed for 28 days	<b>Results</b> The mean $\pm$ SD for fasting blood glucose after 28 days in the LC diet group was $5.6 \pm 0.5$ , and in MedDiet, $5.5 \pm 0.7$ , with a p-value> 0.05 <b>Conclusion</b> There was no significant difference in fasting blood glucose between the MedDiet and low-carbohydrate diet groups

### The Effect of the Mediterranean Diet on Fasting Blood Glucose in Overweight or Obese People

Four of the seven selected articles presented in table 1 examined the effect of MedDiet on fasting blood glucose in overweight and obese people. All four articles showed that MedDiet could reduce fasting blood glucose levels in overweight or obese people. Research conducted by Bekkouche et al. stated that administering MedDiet by reducing intake of saturated fatty acids, cholesterol, and carbohydrates, as well as providing educational interventions on physical activity and suitable cooking methods in people with metabolic syndrome showed a significant difference in fasting blood glucose if compared to the group of people without metabolic syndrome, with a  $p$ -value  $< 0.05$ . Carbohydrate intake correlates with increased fasting blood glucose. In obese people, fiber has benefits such as slowing gastric emptying, helping the digestive process, and reducing hunger. So metabolizing carbohydrates into blood sugar can be slowed down by consuming high-fiber foods such as MedDiet. Lifestyles, such as carbohydrate intake and increased physical activity, are associated with fluctuations in insulin sensitivity. Obesity is considered to have the most influence on the development of metabolic syndrome because adipose tissue that accumulates in obese people affects the secretory metabolism of various hormones, glycerol, and other substances in the body of overweight or obese people<sup>19</sup>. Examples are the hormones leptin, cytokines, adiponectin, and various pro-inflammatory substances participating in the release of nonesterified fatty acids (NEFAs) where in people with obesity, these substances are found to be elevated and associated with insulin resistance and  $\beta$ -cell dysfunction<sup>20</sup>.

Both adults and children with fatty liver show abnormal glucose levels and fat metabolism<sup>9</sup>. Early clinical manifestations of Non-alcoholic Fatty Liver Disease (NAFLD) are an accumulation of triglycerides in the liver followed by insulin resistance, which is thought to be caused by many factors, such as a high-energy diet, low physical activity, and genetics<sup>21</sup>. A study by Ristic-Medic et al. in obese and overweight people with NAFLD who were given a calorie restriction intervention on a MedDiet or a low-fat diet resulted in a significant decrease in fasting blood glucose in both diet groups. This condition is because MedDiet, a diet high in MUFA, is one of the diets that can reduce serum Alanine Aminotransferase (ALT) levels. Serum ALT is a marker of liver damage, so a decrease in serum ALT can indicate an improved liver function in NAFLD patients. In addition, a high-MUFA diet has been shown to improve postprandial glucose levels and lower LDL concentrations and triglycerides but without a concurrent increase in HDL<sup>22</sup>.

Pellegrini et al., who examined the composition of the gut microbiota after administering MedDiet and probiotics to obese people who recovered from breast cancer, resulted in a significant decrease in fasting blood glucose levels. Not only when combined with probiotics, but MedDiet was also found to reduce fasting blood glucose levels significantly<sup>23</sup>. The MedDiet is characterized as a diet high in nuts, fruit, fiber, and olive oil, moderate consumption of dairy products, and low consumption of red meat and processed meat<sup>16</sup>. Lipid

fractions from nuts and olive oil, which are sources of ingredients from MedDiet, contain high levels of antioxidants, which can reduce oxidative stress, where oxidative stress is commonly found in hyperglycemia sufferers<sup>24</sup>.

Previous research conducted by Shai et al. stated that MedDiet could induce more balanced weight loss compared to a low-fat diet with the same calorie restriction. On the other hand, more significant changes in plasma insulin and insulin resistance over 24 months were found in non-diabetic subjects following a low-carbohydrate diet, but the numbers were smaller compared to type 2 diabetes mellitus (DM) patients following MedDiet<sup>25</sup>. Research by Trico et al. in subjects with obesity and at risk of diabetes resulted in no significant difference in fasting blood glucose between giving a low-carbohydrate, high-protein diet and MedDiet to overweight or obese subjects. However, there was a significant improvement in insulin sensitivity in fasting conditions from both intervention groups<sup>26</sup>. The Prevencion con Dieta Mediterranea (PREDIMED) study states, MedDiet enriched with olive oil or nuts was associated with a reduced incidence of diabetes by as much as 52% after four years of monitoring in non-diabetic subjects<sup>27</sup>.

The limitations of this literature review were that it only used two databases, the languages used are only Indonesian and English, and there are differences in the comorbidities of the subjects in each article.

### CONCLUSIONS

MedDiet can reduce LDL, triglycerides, total cholesterol, and fasting blood glucose levels and increase HDL levels in overweight or obese people. This condition can be caused by high consumption of unsaturated fatty acids (MUFA and PUFA), fiber, low glycemic index, and antioxidants which are MedDiet criteria. High fiber consumption from whole grains, legumes, vegetables, and fruit can reduce cholesterol absorption and improve the lipid profile. Meanwhile, high consumption of MUFA is said to improve postprandial glucose levels and reduce LDL and triglyceride concentrations. In addition to dietary changes, the risk of complications from being overweight or obese can be reduced by adding daily physical activity. It is necessary to improve their diet to prevent complications in people with overweight or obese. Commitment is needed in undergoing lifestyle improvements, one of which is to adopt the Mediterranean diet to get benefits and improve lipid and glucose profiles to reduce the risk of diseases such as dyslipidemia and diabetes mellitus. Further experimental research is needed regarding the effect of MedDiet on people with overweight or obese without comorbidities to avoid bias.

### ACKNOWLEDGEMENTS

The author would like to thank the lecturers of the Dietitian Profession Study Program, Universitas Brawijaya, for their suggestions and input so that the writing of this literature review can be completed properly.

**Conflict of Interest and Funding Disclosure**

All authors have no conflict of interest in this article. This article was self-funded.

**REFERENCES**

1. World Health Organization. Obesity and overweight. (2018). Available at: <http://www.who.int/news-room/factsheets/detail/obesity-and-overweight>. (Accessed: 28th September 2021).
2. Health Research and Development Agency, Ministry of Health, Republic of Indonesia. RISKESDAS National Report 2018. (2018). Available at: <https://dinkes.kalbarprov.go.id/wp-content/uploads/2019/03/Laporan-Riskesda-2018-Nasional.pdf>. (Accessed: 28th September 2021)
3. Frühbeck, G., Méndez-Giménez, L., Fernández-Formoso, JA, Fernández, S. & Rodriguez, A. Regulation of Adipocyte Lipolysis. *Nutrition Research Reviews*. **27**, 63–93 (2014).
4. Jiménez, JM et al. Changes in Lipid Profile, Body Weight Variables and Cardiovascular Risk in Obese Patients Undergoing One Gastric Bypass Anastomosis. *International Journal of Environmental Research and Public Health*. **17**, 5858 (2020).
5. Romagnolo, DF, Selmin, OI Mediterranean Diet and Prevention of Chronic Diseases. *Nutr. today*. **52**, 208-222 (2017).
6. Martinez-González, MA et al. Benefits of the Mediterranean Diet: Insights from the {PREDIMED} Study. *Progress in Cardiovascular Disease*. **58**, 50–60 (2015).
7. Esposito, K., Kastorini, CM, Panagiotakos, DB & Giugliano, D. Mediterranean Diet and Weight Loss: Meta-Analysis of Randomized Controlled Trials. *Metabolic Syndrome and Related Disorders*. **9**, 1–12 (2011).
8. Mielniczek, K. The Influence of The Mediterranean Diet on Glucose Metabolism. *Journal of Education, Health and Sport*. **11**, 430–433 (2021).
9. Ristic-Medic, D. et al. Calorie-restricted Mediterranean and Low-Fat Diets Affect Fatty Acid Status in Individuals with Non-Alcoholic Fatty Liver Disease. *Nutrients*. **13**, 15 (2020).
10. Handayani, DR & Rakhmat, II Characteristics, Nutritional Status, and Lipid Profile of Dyslipidemia Patients with a Mediterranean Diet. *AtlantisPress*. **37**, 10–15 (2021).
11. Casas, R. et al. Long-term Immunomodulatory Effects of a Mediterranean Diet in Adults at High Risk of Cardiovascular Disease in the Prevention of the Mediterranean Diet in a Randomized Controlled Trial. *The Journal of Nutrition*. **146**, 1–10 (2016).
12. Venturini, D., Simão, ANC, Urbano, MR & Dichi, I. Effects of Extra Virgin Olive Oil and Fish Oil on Lipid Profile and Oxidative Stress in Patients with Metabolic Syndrome. *Nutrition*. **31**, 834–840 (2015).
13. Altamimi, MA, Zidan, S. & Badrasawi, M. Effects of Tree Nut Consumption on Serum Lipid Profile in Hyperlipidemic Individuals: A Systematic Review. *Nutrition and Metabolic Insights*. **13**, 1–10 (2020).
14. Ryan, MC et al. The Mediterranean Diet Improves Hepatic Steatosis and Insulin Sensitivity in Individuals with Non-Alcoholic Fatty Liver Disease. *Journal of Hepatology*. **59**, 138–143 (2013).
15. Tosti, V., Bertozzi, B. & Fontana, L. Health Benefits of the Mediterranean Diet: Metabolic and Molecular Mechanisms. *The Journals of Gerontology*. **73**, 318–326 (2018).
16. Bekkouche, L., Bouchenak, M., Malaisse, W. & Yahia, D. The Mediterranean Diet Adoption Improves Metabolic, Oxidative, and Inflammatory Abnormalities in Algerian Metabolic Syndrome Patients. *Hormone and Metabolic Research*. **46**, 274–282 (2014).
17. Vitale, M. et al. Acute and Chronic Improvement in Postprandial Glucose Metabolism by a Diet Resembling the Traditional Mediterranean Dietary Pattern: Can SCFAs play a role? *Clinical Nutrition*. **40**, 428-37. (2020).
18. Damasceno, NRT et al. Mediterranean Diet Supplemented with Nuts Reduces Waist Circumference and Shifts Lipoprotein Subfractions to a Less Atherogenic Pattern in Subjects at High Cardiovascular Risk. *Atherosclerosis*. **230**, 347–353 (2013).
19. Algoblan, A., Alalfi, M. & Khan, M. Mechanism linking diabetes mellitus and obesity. Diabetes, Metabolic Syndrome, and Obesity: *Targets and Therapy*. **587** (2014).
20. Karpe, F., Dickmann, JR & Frayn, KN Fatty Acids, Obesity, and Insulin Resistance: Time for a Reevaluation. *Diabetes*. **60**, 2441–2449 (2011).
21. Anania, C., Perla, FM, Olivero, F., Pacifico, L. & Chiesa, C. Mediterranean Diet and Non-Alcoholic Fatty Liver Disease. *World Journal of Gastroenterology*. **24**, 2083–2094 (2018).
22. Schwingshackl, L., Strasser, B. & Hoffmann, G. Effects of Monounsaturated Fatty Acids on Glycemic Control In Patients With Abnormal Glucose Metabolism: A Systematic Review And Meta-Analysis. *Ann Nutr Metab*. **58**, 290–296 (2011).
23. Pellegrini, M. et al. Gut Microbiota Composition After Diet and Probiotics in Overweight Breast Cancer Survivors: A Randomized Open-Label Pilot Intervention Trial. *Nutrition*. **74**, 110749 (2020).
24. Ejtahed, HS et al. Probiotic Yogurt Improves Antioxidant Status in Type 2 Diabetic Patients. *Nutrition*. **28**, 539–543 (2012).
25. Shai, I. et al. Weight Loss with a Low-Carbohydrate, Mediterranean, or Low-Fat Diet. *New England Journal of Medicine*. **359**, 229–241 (2008).
26. Tricò, D. et al. Effects of Low-Carbohydrate Versus Mediterranean Diets on Weight Loss, Glucose Metabolism, Insulin Kinetics and Beta-

Cell Function in Morbidly Obese Individuals.  
*Nutrients*. 13, 1345 (2021).

27. Salas-Salvadó, J. et al. Erratum. Reduction in the Incidence of Type 2 Diabetes with the Mediterranean Diet: Results of the Reus Nutrition Intervention Randomized Trial. *DiabetesCare*. **41**, 2259–2260 (2011).