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Original Article

Differences in Mediterranean diet adherence on lipid profile and plasma atherogenic index in dyslipidemia patients

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ABSTRACT

Dyslipidemia is lipid metabolism disorder as indicated by increase in total cholesterol, triglycerides, Low Density Lipoprotein (LDL) and decrease in High Density Lipoprotein (HDL). Riset Kesehatan Dasar (RISKESDAS) Database in 2018 showed 12.6% Indonesian population aged 55-64 years had high cholesterol and very high LDL and triglycerides. The Mediterranean diet is non-pharmacotherapeutic treatments in the form of nutrition therapy for dyslipidemic patients. This study aimed to determine differences of adherence to the Mediterranean diet on lipid profile and Plasma Atherogenic Index (PAI) in dyslipidemic patients at a private clinic in Bandung. It used an observational analytic method with a prospective cohort of 30 dyslipidemia patients. Sampling was done by systematic random sampling technique. The subjects were divided into 3 categories based on adherence, namely low, medium and high, then lipid profile examination and PAI were assessed at the end of the month. Total cholesterol, LDL, HDL data were analyzed using Anova and Post Hoc Tukey while triglycerides and PAI were analyzed using Kruskal Wallis and Mann Whitney. Adherence to the Mediterranean diet showed significant results on total cholesterol (p=0.007), LDL level (p=0.019), HDL level (p=0.006), triglycerides (p=0.005) and PAI (p=0.036). The result was associated due to the influence of food content rich in monounsaturated fatty acids (MUFA), polyunsaturated fatty acids (PUFA), phytosterols and polyphenols that affect the levels of lipid profiles and PAI.

Keyword: Adherence, dyslipidemia, lipid profile, Mediterranean diet, Plasma Atherogenic Index

INTRODUCTION

Dyslipidemia is a lipid metabolism disorder as indicated by an increase in plasma cholesterol, triglyceride and *Low Density Lipoprotein* (LDL) cholesterol accompanied by a decrease in *High Density Lipoprotein* (HDL) cholesterol.[1,2] The incidence of dyslipidemia today is 80% related to changes in lifestyle and eating patterns such as increased consumption of saturated and trans fatty foods, obesity, smoking and lack of physical activity or what is commonly called a sedentary lifestyle, coupled with the main risk factors are increasing age and gender, especially women, which will affect the lipid profile due to decreased liver function and the occurrence of hormonal imbalances which affect the lipid metabolism process.[3] Dyslipidemia is a modifiable risk factor for atherosclerosis, stroke and other cardiovascular diseases.[4] Lipid profiles in the form of LDL, HDL and total cholesterol can be used as a parameter to assess the risk of coronary heart disease (CHD), namely by calculating the logarithm of the division between triglycerides and HDL which is called the Plasma Atherogenic Index (PAI). The assessment index can assess the risk of CHD with a greater predictive value than only assessing the lipid profile level. [5,6]

The main management of dyslipidemia prioritizes non - pharmacotherapeutic therapy, where this can be achieved by implementing a Mediterranean diet which is known to be high in consumption of MUFA and PUFA unsaturated fats, polyphenols and phytosterols as recommended by *the American Heart Association* (AHA) or *American College of Cardiology* (ACC) as a good diet to lower lipid profile levels and risk of cardiovascular disease.[7,8,9] The Mediterranean diet is one of the traditional diets originating from European communities in the Mediterranean region, where these communities have the highest life expectancy in the world and are a population with low morbidity and mortality from heart disease. Foods consumed in this Mediterranean diet include high consumption of fruits and vegetables, nuts, cereals, fish, olive oil, moderate consumption of red wine and low consumption of red meat and dairy products.[10,11] Things that need to be considered besides the food component in the application of the Mediterranean diet is adherence to the diet itself, where this adherence can be assessed by the *Alternate Mediterranean Diet* (aMED) score.[12,13]

Previous study has shown that the Mediterranean diet can reduce levels of lipid profiles such as total cholesterol, LDL, triglycerides and increase HDL levels, which of these conditions will reduce the risk of CHD. Study on adherence to the Mediterranean diet in Indonesia has never been carried out, so that makes authors interested in taking the title of differences in the level of adherence of the Mediterranean diet to lipid profile levels and plasma atherogenic index in dyslipidemic patients.

The objective of this study is to determine differences of adherence to the Mediterranean diet on lipid profile and Plasma Atherogenic Index (PAI) in dyslipidemic patients. The hypothesis of this study is that there are differences in the level of adherence of the Mediterranean diet to total cholesterol, LDL, HDL, triglycerides and PAI in dyslipidemic patients.

METHODS AND SUBJECT

The study design used observational analytical methods with the principle of a prospective cohort to determine differences in the level of adherence of the Mediterranean diet to the lipid profile and plasma atherogenic index in dyslipidemic patients. Adherence to the Mediterranean diet will be assessed with an aMED score which will be described through food composition and assessed using the *Food Frequency Questionnaire* (FFQ).

The population in this study were dyslipidemic patients at the clinic in Bandung City from November to December 2021 and were members of the Program Pengelolaan Penyakit Kronis (Prolanis)

which consisted of men and women ≥ 40 years old who had previously been given education regarding adherence in carrying out Mediterranean diet. The inclusion criteria for this study were dyslipidemic patients who received regular treatment and were willing to be research subjects with total cholesterol levels 200 mg/dL, LDL 130 mg/dL, HDL 40 mg/dL and triglycerides 150 mg/dL [7] Calculation of the sample size is calculated by the formula for the sample size of the cohort study so that as many as 30 samples were obtained. The sampling method was carried out using a *systematic random sampling technique*, namely the selection of samples systematically at random with certain intervals where in this study 4 times were taken in 1 month.

This research begins with the selection of the clinic in Bandung City as a research site, preparation of research subjects, preparation of tools and materials, then giving *informed consent* to research subjects to examine lipid profiles. Patients who meet the inclusion criteria will then be given *informed consent* again to administer the FFQ which will be randomized 4 times within a period of 30 days. The results of the FFQ questionnaire assessment will be combined so that it will describe the food consumption of the research subjects for 1 month. Each food component that is assessed from the FFQ will look for its median value which will be used as a standard to determine the adherence of research subjects with each food component eaten, then its adherence will be assessed based on the aMED score. After 1 month of assessment, there will be a re-examination of the lipid profile and calculation of the PAI value of the research subject while still taking into account the COVID-19 health protocol. This assessment of adherence to the Mediterranean diet was carried out on research subjects who already knew and practiced the Mediterranean diet based on educational results from the clinic.

The lipid profile level of the subject is known based on laboratory examination where the sample used comes from venous blood which will then be centrifuged to get the serum. The blood serum will then be mixed with the reagents and the absorbance readings with standard and blank solutions are taken using a spectrophotometer.

Assessment of eating patterns was carried out using the FFQ tool. The FFQ assessment consists of several food components which will later be calculated for the median overall dietary value of each component to serve as a reference for assessing adherence to the Mediterranean diet.tool *food model* to determine the serving size of each food component. Adherence to the Mediterranean diet was assessed using the aMED score which was assessed based on the median food consumption of the study subjects. The level of adherence is divided into 3 categories, namely a score of 0-3 as low adherence, 4-6 as moderate adherence and 7-9 as high adherence.[12,14]

Lipid profile data and the results of the PAI calculations were tested for normality first with the Shapiro-Wilk test because the amount of data was less than 50 then homogenity test was carried out with the Levene. If the data were normally distributed, they would be analyzed with Anova followed by Post Hoc Tukey test. However, if the data were not normally distributed, they would be analyzed by Kruskal Wallis test followed by Mann Whitney test to determine differences in the level of adherence of the Mediterranean diet to lipid profile and IAP. The significance criteria was described by p-value, where $p<0.05$ indicated significant and $p>0.05$ indicated statistically insignificant. The analysis was carried out using a statistical program SPSS version 23. This study was approved by the Health Research Ethics Commission of Jenderal Achmad Yani University with ethical approval number 056/UM2.11/2021.

RESULT AND DISCUSSION

The results showed that 30 subjects who had met the inclusion criteria were divided

into three categories of adherence to the Mediterranean diet, namely low adherence, moderate adherence, and high adherence through the AMED score. The lipid profile and PAI were recalculated at the end of the month.

After the data tested by *Saphiro Wilk* and homogenity test of *Levene* showed that total cholesterol, LDL and HDL were normally distributed (p>0.05) so that the *Anova* was carried out followed by the *Post Hoc Tukey test* while triglycerides and PAI were not normally distributed (P< 0.05) so that the *Kruskal Wallis* followed by the *Mann Whitney test.*

Age and Gender Characteristics

The characteristics of the subjects in this study had an average age of 54.63 years with a median of 55.50 years and a standard deviation of 8.54 years. The youngest age in the study was 40 years old and the oldest was 71 years old.

Increasing age is one of the main risk factors in the occurrence of lipid profile abnormalities. This can occur due to various factors, but the main factor causing the increase in lipid profile with increasing age is due to decreased liver function, which is the most important organ in the process of lipid metabolism. This process occurs due to morphological changes in the sinusoidal endothelium structure in the liver, which can cause disturbances in liver function such as impaired lipoprotein placement, decreased endocytosis, decreased blood flow to the liver and an imbalance in the metabolic processes of chylomicron remnants and triglycerides in the liver.[15,16]

Characteristics of the subjects based on gender were found to be more suffered by women, namely as many as 21 people with a percentage of 70% compared to men, namely as many as 9 people with a percentage of 30%.

The prevalence of dyslipidemia is more common in women than men. This is influenced by hormonal changes that decrease in a woman's life cycle called menopause, which causes estrogen levels in the body to decrease. During the transition towards menopause, there will be a decrease in the hormone estrogen, starting from the depletion of ovarian follicles starting at the age of approximately 30 to 40 and continuing until finally having no follicles at all and menopause occurs.[17] Estrogen has an influence on many organs that contribute to the occurrence of CHD, one of which is through the regulation of lipid metabolism in the liver. When there is a decrease in estrogen levels, it will cause the accumulation of lipid profiles such as triglycerides, total cholesterol and LDL which is a risk for dyslipidemia and can cause complications such as CHD.[18]

Level Of Adherences To The Mediterranean Diet

Research subjects were divided into 3 categories of adherence, each with 7 subjects with low adherence, 16 subjects with moderate adherence, and 7 subjects with high adherence.

Table 1. Level Of Adherences To The Mediterranean Diet

Categories	Frequency	Percentage
Low (0-3)	7	23,3
Moderate (4-5)	16	53,3
High (≥ 6)	7	23,3
Total	30	100.00

Differences In The Level Of Adherence To The Mediterranean Diet To Total Cholesterol, LDL and HDL In Dyslipidemia Patients

The results of the *ANOVA* showed that there was a significant relationship between adherence to the Mediterranean diet and total cholesterol (p=0.007<0.05), LDL (p=0.019<0.05), and HDL (p=0,006<0,05) in dyslipidemic patients. The *Post Hoc Tukey* comparison test showed that there were significantly different results between high and low adherence with total cholesterol (p = 0.005 <0.05), between high and low adherence with LDL (p = 0.019<0.05), and between high and low adherence with HDL (p = 0.005<0.05).

Table 2. Anova Test of Total Cholesterol, LDL, HDL

Mediterranean diet adherence	**Total cholesterol (mg/dL)**			*p-value*
	N	Mean	SD	
Low	7	225,43	38,23	0,007
Moderate	16	191,86	3,76	
High	7	178,14	7,27	
	LDL (mg/dL)			*p-value*
	N	Mean	SD	
Low	7	139,00	20,72	0,019
Moderate	16	125,14	2,48	
High	7	116,43	5,32	
	HDL (mg/dL)			*p-value*
	N	Mean	SD	
Low	7	52,00	7,57	0,006
Moderate	16	45,00	0,82	
High	7	42,43	1,72	

Table 3. Post Hoc Tukey Test Of Total Cholesterol, LDL, HDL

Categories	**Adherence level**	**p-value**	**Conclusion**
Total cholesterol	High vs Moderate	0,162	Unsignificantly different
	High vs Low	0,005	Significantly different
	Moderate vs Low	0,094	Unsignificantly different
LDL	High vs Moderate	0,057	Unsignificantly different
	High vs Low	0,019	Significantly different
	Moderate vs Low	0,580	Unsignificantly different
HDL	High vs Moderate	0,179	Unsignificantly different
	High vs Low	0,005	Significantly different
	Moderate vs Low	0,076	Unsignificantly different

Differences In The Level Of Adherence To The Mediterranean Diet To Trygliceride and PAI In Dyslipidemia Patients

The results of the *Kruskal Wallis* showed that there was a significant relationship between adherence to the Mediterranean diet with trygliceride (p=0,005<0,05) and PAI (p=0,036<0,05) in dyslipidemic patients. The *Mann Whitney* comparison test on trygliceride showed there were significantly different results between high adherence and low adherence (p = 0.004 < 0.05) and between high

adherence and moderate adherence (p = 0.015 < 0.05) and The *Mann Whitney* comparison test on PAI showed there were significantly different results between high adherence and low adherence (p = 0.011 < 0.05) and between high adherence and moderate adherence (p = 0.039 < 0.05).

Table 4. Kruskal Wallis Test of Trygliceride and PAI

Mediterranean diet adherence	**Trygkiceride (mg/dL)**			*p-value*
	N	Mean	SD	
Low	7	155,43	72,30	0,005
Moderate	16	107,57	8,06	
High	7	97,86	17,39	
	PAI (mg/dL)			***p-value***
	N	Mean	SD	
Low	7	0,45	0,13	0,036
Moderate	16	0,38	0,03	
High	7	0,36	0,07	

Table 5. Mann Whitney Test Of Trygliceride and PAI

Categories	**Adherence level**	**p-value**	**Conclusion**
Trygliceride	High vs Moderate	0,015	Significantly different
	High vs Low	0,004	Significantly different
	Moderate vs Low	0,055	Unsignificantly different
PAI	High vs Moderate	0,039	Significantly different
	High vs Low	0,011	Significantly different
	Moderate vs Low	0,452	Unsignificantly different

The benefit between adherence to the Mediterranean diet and total cholesterol was obtained from the high consumption of legumes, nuts, whole grains, vegetables and fruits that are rich in dietary fiber. The content of water-soluble fiber such as fructans and inulin will reduce the absorption of cholesterol from food and bile. In addition, the high intake of phytosterols obtained from these food components also plays an important role in reducing cholesterol, namely competing with cholesterol absorption in the intestine.[19,20] The results of this study according to the results of research conducted by Schwingshack L, et al. in 2019 was found the adherence of Mediterranean diet could reduced total cholesterol that was obtained from the benefits of Mediterranean diet itself, which are rich in fiber and phytosterols.[19]

The relationship between adherence and LDL levels was obtained from the content of foods in the Mediterranean diet that are rich in MUFA, which are found in olive oil. This benefit is derived from the MUFA mechanism that affects apoproteins in the liver, where MUFA will reduce levels of apoprotein C-III mRNA which is an apoprotein for the formation of LDL and VLDL precursors. As a result of the decrease in apoproteins, the concentration of VLDL in the blood will decrease, thereby lowering LDL levels as well. In addition, other benefits are obtained from the content of the Mediterranean diet which is rich in phytosterols and fiber, both of which reduce the absorption of cholesterol in the intestine so that it will increase the absorption of

LDL by the liver.[21,22] This result according to the result of research conducted by Hannon BA, et al. in 2017 where the composition of MUFA in the Mediterranean diet will be related to LDL levels obtained from the main component in the Mediterranean diet, namely olive oil as a source of unsaturated fat that is rich in MUFA content.[23]

The result between adherence and HDL was not in accordance with research conducted by Hernaez, et al. 2014 and Cruces EG, et al. 2021 which shows the results that the Mediterranean diet increases and affects HDL levels.[24,25] The relationship between adherence to the Mediterranean diet and HDL levels occurs because of MUFA effect derived from olive oil, whole wheat and nuts which increase HDL levels through several mechanisms such as increasing cholesterol efflux capacity, decreasing CETP enzymes and increasing LCAT enzymes which will cause HDL to increase. increase. The influence of the Mediterranean diet on HDL can also occur based on its function, namely an increase in function as an antioxidant and a decrease in HDL reduction, so that it will protect from the risk of dyslipidemia and its complications in the form of CHD.[24,25]

Triglycerides would decrease through mechanisms arising from PUFA, especially group (ω) 3 in the Mediterranean diet which has the effect of inhibiting the de novo synthesis process / *de novo lipogenesis* where this condition will cause a decrease in free fatty acid synthesis so that it will decrease synthesis of triglycerides. PUFA group (ω) 3 fatty acids are important as body intake because they cannot be synthesized in the human body. For example, group (ω) 3 consists of alpha linoleic acid, which is generally sourced from fish or seeds.[19,23,26] This result according to the result of research conducted by Schwingshack L, et al. In 2019, where the higher adherence to the Mediterranean diet shows triglyceride levels, mainly due to PUFA components that can affect the triglyceride formation process.[19]

The PAI is a logarithm calculation of the ratio between triglycerides and HDL. The lower the triglyceride level and the higher the HDL level, the lower the PAI results will be, which indicates a lower risk of CHD. This relates to the effect of adherence to the rich Mediterranean diet on the reduction of triglyceride levels and an increase in HDL levels. HDL also has a function as an antioxidant and a vasoprotector which will increase the synthesis of NO which functions as a vasodilator, thereby reducing the risk of damage to the vascular endothelium as one of the risks of CHD.[21,27] In a study conducted by Van HL, et al. 2016 states that the higher adherence to the Mediterranean diet, shows a reduced risk of CHD. This theory is in accordance with the results of the study where increased adherence to the Mediterranean diet showed a more significant reduction in the risk of CHD compared to low adherence. The higher the adherence to the Mediterranean diet, the lower the risk of CHD as described by the PAI value.[9]

This study has some limitation, so the authors assess there are suggestions that need to be considered, namely the need for further research on adherence to the Mediterranean diet with a period of more than 1 month, the need for research on adherence to the Mediterranean diet assessing eating patterns using *24h food recall* to describe more representative eating pattern, the need for research on adherence to the Mediterranean diet on lipid profile and PAI in dyslipidemia associated with factors influencing outcomes such as physical activity and medication.

CONCLUSION

The characteristics of patients who followed the Mediterranean diet were 54.63 years on average, with the youngest being 40 years old and the oldest 71 years old, with a female sex percentage of 70% more

and divided into three categories, namely the low adherence category of 7 people, 16 people moderate and 7 people high. There was a significant relationship between adherence to the Mediterranean diet on total cholesterol levels with P=0.007, LDL P=0.019, HDL P=0.006, triglycerides P=0.005 and PAI P=0.036. The result showed that total cholesterol, LDL, HDL, trygliceride and PAI are better on a higher level than those on a lower adherence of adherence to the Mediterranean diet.

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DECLARATION OF INTERESTS

The authors declared that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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