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THE INFLUENCE OF DIETARY COMPOSITION TO METABOLIC SYNDROME INCIDENCE

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ABSTRACT: Metabolic syndrome is a group of several clinical conditions which is related to the prevalence of another disease such as cardiovascular disease, diabetes mellitus (DM) or increased fasting blood glucose level, visceral obesity, hypertension, *etc*. The major factor that affects the metabolic syndrome occurrence is diet composition.This research aimed to determine the influence of diet composition on metabolic syndrome prevalence. This study was performed using *in-vivo* method. The animal was divided into three groups, each administered a different composition of diet, which was high carbohydrate, high lipid, and high protein diet for 42 days. The parameters were body weight, HDL and triglyceride level, blood glucose level, and blood pressure. The results showed that each diet composition affected the glucose, HDL, triglyceride, and blood pressure level differently. The high-fat diet gave the most significant effect in HDL reducing and blood pressure elevation, while the high carbohydrate diet gave the most significant effect in blood glucose and triglyceride level elevation. It could be concluded that the lowest affecting food to metabolic syndrome was the high protein group, while the high fat and high carbohydrate food had higher risk to induce the metabolic syndrome.

INTRODUCTION: Metabolic syndrome (MetS) is a term for a group of certain clinical conditions which can increase cardiovascular disease risk that is diabetes mellitus or increasing in fasting blood glucose level, visceral obesity, dyslipidemia, and hypertension. There are 20-25% of the world's adult population have metabolic syndrome and those with metabolic syndrome are twice as likely to die from and three times as likely to have a heart attack and stroke compared to those without metabolic syndrome.

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In addition, metabolic syndrome raises the fivefold greater risk of diabetes mellitus [1]. MetS is a chronic low-grade inflammation as a result of complex interaction between genetic and environmental factor. Several factors affect the development of MetS are visceral adiposity, insulin resistance, endothelial dysfunction, genetic susceptibility, atherogenic dyslipidemia, elevated blood pressure, hypercoagulable state, and chronic stress [2]. Metabolic syndrome is characterized by at least three of the five criteria according to WHO, IDF and NCEP-ATPIII (the National Cholesterol Education Program - Adult Treatment Panel III), that are central obesity (obesity with abdominal circumference that exceeds 80 cm in women and 90 cm in men), elevated triglyceride levels, decreased HDL-cholesterol, fasting glucose up to 110-126 mg/mL (due to decreased insulin sensitivity), and elevated blood pressure [3, 4, 5].

Metabolic syndrome was said more related to central obesity compared with general obesity. Central obesity was thought to be the main cause of insulin resistance, which was one of the main markers of metabolic syndrome. Furthermore, central obesity could also trigger the release of pro-inflammatory compounds responsible for the diabetes mellitus, hyperlipidemia, and cardiovascular disease occurrence [6].

"Let food be thy medicine and medicine be thy food", a phrase from Hippocrates the Ancient Greek father of modern medicine, was indicated that the idea of a relationship between food and health was not a new one. Carbohydrate, lipid, and protein were the primary nutrients or macronutrients we needed. The difference between these three macronutrients was the total amount of energy. The fat contained 9 kcal/g, while protein and carbohydrate contained 4 kcal/g [7]. These differences would determine the total energy intake per day and thus affected the energy balance that in the end could lead to obesity and metabolic syndrome. For example, a high-fat diet could induce weight gain because of excessive energy intake [8]. On the other hand, carbohydrate was also blamed for the incidence of obesity and metabolic syndrome [9], although it might be because of the wrong choice of the type of carbohydrate [9, 10]. The aim of this study was to evaluate the influence of dietary composition on metabolic syndrome incidence.

MATERIALS AND METHODS:

Animals: Male Wistar mouse 2-3 months old weighing 200-250 g. The animals were kept at standard laboratory conditions at 24-26 °C, humidity 70-75%, and 12 h light/dark cycle. Animals were fed with a treatment diet and water *ad libitum*. The methods in this study were performed in accordance with ethics and guided for animals care and used (139/UN6.KEP/EC/2018).

Administration of Different type Diet Composition in Order to Induce Metabolic Syndrome: Each animals group was fed with 3 different types of diet composition; group 1 was fed with high-fat diet (60% fat), group 2 with high carbohydrate diet (60% carbohydrate), and group 3 with high protein diet (60% protein) for 42 days [11]. The parameters were body weight, insulin sensitivity, blood HDL and triglyceride level, and blood pressure. These parameters were measured at before treatment and at 21, 35, and 42 days during treatment.

Insulin Tolerance Test: Before the study was conducted and at 21, 35, and 42 days after treatment, an insulin tolerance test (ITT) using insulin 0.75 U/kg bw, ip, was performed after 4 hours fasting period. Blood glucose concentration from the tail vein was measured using the Easy Touch® blood glucose meter at 0, 15, 30, 45, and 60 minutes after insulin administration [12].

RESULTS:

Effect of Dietary Patterns to Body Weight: The body weight elevation after 42 days administration of different type of diet was shown in **Table 1**.

TABLE 1: BODY WEIGHT PROFILE DURING 42 DAYS OF DIET ADMINISTRATION

Diet composition	Bodyweight at day- (g)			
	0	21	35	42
High fat	208±9	240±19	241±18	237±13
High protein	197±10	234±26	241±14	241±23
High carbohydrate	212±15	250±16	251±14	256±18

Note: Data are presented as mean ± SD, n=6 mice/group, * means significantly different from high protein group, # means significantly different from high carbohydrate group, $p<0.05$.

Table 1 showed that variation in diet composition, statistically, didn't affect body weight significantly. Although the result showed that high carbohydrate diet gave higher body weight elevation compared to the other groups. And high-fat diet had the lowest effect on body weight.

Effect of Dietary Patterns to HDL Level: The level of HDL during 42 days diet administration was shown in **Table 2**.

TABLE 2: HDL LEVEL DURING 42 DAYS OF DIET ADMINISTRATION

Diet composition	HDL level at day- (mg/dl)			
	0	21	35	42
High fat	24.5 ±5.4	5.3 ±1.5*#	5.2 ±0.7*#	4.5 ±1.2*#
High protein	31 ±11.7	32.6 ±8#	34.5 ±9.6#	35.3 ±8.7#
High carbohydrate	30.7 ±9.1	4 ±0.9*	7.5 ±0.9*	10.3 ±0.9*

Note: Data are presented as mean ±SD, n=6 mice/group, * means significantly different from high protein group, # means significantly different from high carbohydrate group, $p<0.05$.

From **Table 2**, it could be seen that there were differences between groups treated with high fat, high protein, and high carbohydrate diet. The lowest level of HDL was shown by the high-fat group, followed by carbohydrate group, and the highest level of HDL was shown by high protein group. The HDL level was significantly different compared to each other.

Effect of Dietary Patterns to Triglyceride Level: The level of triglyceride during 42 days diet administration was shown in **Table 3**.

TABLE 3: TRIGLYCERIDE LEVEL DURING 42 DAYS OF DIET ADMINISTRATION

Diet composition	Triglyceride level at day- (mg/dl)			
	0	21	35	42
High fat	64.1 ±20.2	106.3 ±7.2*#	92.1 ±40.5*#	103.8 ±4.6*#
High protein	81.4 ±2.5	81.2 ±4.9#	78.6 ±4.0#	82.1 ±1.3#
High carbohydrate	86.3 ±6.1	124.9 ±33.1*	141.3 ±38.8*	130.3 ±32.4*

Note: Data are presented as mean ±SD, n=6 mice/group, * means significantly different from high protein group, # means significantly different from high carbohydrate group, p<0.05.

Table 3 showed that the triglyceride level was also affected by the different composition of the diet. Different from the HDL level, the highest elevation of triglyceride level was shown by the high carbohydrate group, followed by high fat group, and the lowest triglyceride level was shown by high protein group.

Effect of Dietary Patterns to Fasting Blood Glucose Level: The level of fasting blood glucose during 42 days diet administration was shown in **Table 4**.

TABLE 4: FASTING BLOOD GLUCOSE LEVEL DURING 42 DAYS OF DIET ADMINISTRATION

Diet composition	Fasting blood glucose level at day- (mg/dl)			
	0	21	35	42
High fat	88±15	106±27	124±17*	128±4*
High protein	82±14	86±19	98±25	107±15
High carbohydrate	80±6	129±26*	135±20*	129±13*

Note: Data are presented as mean ±SD, n=6 mice/group, * means significantly different from high protein group, # means significantly different from high carbohydrate group, p<0.05.

Table 4 showed a significant difference between high fat and high carbohydrate group compared to high protein group. But there was no significant difference between high-fat diet compared to high carbohydrate diet.

Effect of Dietary Patterns to Blood Pressure: The level of fasting blood glucose during 42 days of diet administration was shown in **Table 5**.

TABLE 5: BLOOD PRESSURE DURING 42 DAYS DIET ADMINISTRATION

Diet composition	Sistol at day- (mmHg)				Diastol at day- (mmHg)			
	0	21	35	42	0	21	35	42
High fat	92±2	114±37*	122±29*	128±24	75±2	85±37	104±21*	109±18*
High protein	97±15	85±2	96±15	103±18	80±16	70±5	77±11	87±17
High carbohydrate	91±3	89±5	99±11	108±20	75±10	72±6	83±13	93±14

Note: Data are presented as mean ±SD, n=6 mice/group, * means significantly different from high protein group, # means significantly different from high carbohydrate group, p<0.05.

Table 5 showed that a high fat diet could significantly increase systolic and diastolic blood pressure, while the high protein and high carbohydrate diet didn't.

DISCUSSION: Body weight was one of the main parameters for metabolic syndrome[1]. But from our study, the different compositions of a diet didn't affect the bodyweight significantly. These data were comparable to another study that showed that dietary intake and physical activity could lead to an improvement in metabolic profile, with or without weight loss [13]. From this study, we could see that body weight could not be used as an absolute mark whether a person had metabolic syndrome or not.

The HDL level was most affected by the high-fat diet compared to the high carbohydrate and high protein diet. HDL is a lipoprotein that is responsible for transporting lipid from peripheral tissue to liver; in other words it responsible for anti-atherogenic activity [14]. The higher the HDL level, the lower the atherogenic risk. Low HDL level, along with high LDL level, could lead to coronary heart disease [15, 16] and cerebrovascular disease [17]. The trans-fatty acid was strongly correlated to the reduction in HDL level [14].

As for the effect on the triglyceride level, the high carbohydrate diet showed the highest elevation compared to the high fat and high protein.

Elevation in triglyceride level was directly affected by the elevation of blood glucose level (hyperglycemia) due to high carbohydrate intake. Hyperglycemia would trigger an increase in insulin requirements resulting in hyperinsulinemia. This condition would eventually cause insulin resistance. Insulin resistance would cause a decrease in the activity of the lipoprotein lipase enzyme, the enzyme responsible for triglyceride transportation to peripheral tissue. The lower the activity of the lipoprotein lipase enzyme, the higher triglyceride level in blood. Then with elevation of triglyceride level, the HDL catabolism would also increase, thus causing a decrease in HDL level [18, 19]. It was proved by the elevation in HDL level of the high carbohydrate group.

According to the blood glucose level, the high fat and high carbohydrate diet were both had the potential to increase blood glucose level compared to the high protein diet. The mechanism of both causing an elevation in blood glucose level was not fully understood, although it was thought by affecting the insulin sensitivity [20, 21].

The high-fat diet was also increasing the blood pressure, while the others didn't. Although, the mechanism of fat-induced hypertension was not fully understood, but another study showed the comparable result [22].

From the data above, it could be seen that different diet composition could affect different parameters of metabolic syndrome. And the metabolic syndrome symptoms were not always accompanied by weight gain or obesity. Although it might be because of the lack of time in this experiment to induce obesity. But in general, the high-fat diet and high carbohydrate diet were more responsible in metabolic syndrome symptom occurrence, while the high protein diet gave the lowest effect in metabolic syndrome.

CONCLUSION: From this experiment, it could be concluded that the lowest affecting food to metabolic syndrome was the high protein group, while the high fat and high carbohydrate food had a higher risk in induce the metabolic syndrome.

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