KESANS: International Journal of Health and Science
e-ISSN: 2808-7178, p-ISSN: 2808-7380
Web: http://kesans.rifainstitute.com/index.php/kesans/index

Relationship of Nutrient Intake and Physical Activity with Metabolic Conditions in Obesity

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Article Information
Submitted: **13 April 2024**
Accepted: **15 April 2024**
Online Publish: **20 April 2024**

Abstract
Introduction: *Obesity is a risk factor for several chronic diseases, including hypertension, cardiovascular disease, type 2 diabetes mellitus (T2DM), dyslipidemia, and other metabolic disorders. Despite the frequent association of obesity with various chronic diseases, not all obese individuals experience these conditions.* ***Method:****A subgroup of this population is referred to as metabolically healthy obese (MHO). The prevalence of MHO among obese individuals is approximately 30-40%. The potential causes of the transition from MHO to metabolically unhealthy obesity (MUO) are linked to weight gain, aging, and unhealthy lifestyle. This study employed a cross-sectional observational design involving healthcare professionals with obesity at Prof. dr. I.G.N.G Ngoerah Denpasar Central General Hospital.* ***Result and Discussion:*** *The research was conducted at the Diabetes Center and the Clinical Pathology Laboratory of Prof. dr. I.G.N.G Ngoerah Denpasar Central General Hospital from May to October 2023. Total of 72 obese subjects were consecutively recruited for this study. Among these, the majority were male with 38 individuals (52.8%), while 34 were female (47.2%). Out of these, 47 individuals (65.3%) were classified as MHO, and 25 individuals (34.7%) as MUO. The analysis indicated no significant correlation between total caloric intake, protein, and carbohydrate intake with metabolic conditions (p >0.05). High fat intake was significantly associated with an increased risk of poor metabolic conditions in obese individuals (RP = 1,429, p = 0.038). Low physical activity was positively correlated with poor metabolic conditions in obesity (PR = 7,418, p = 0.004).* ***Conclusion:*** *This study showed that High Fat Diet and low physical activity increase risk MUO event in obesity. However, there is no significant association between total caloric intake, carbohydrate, and protein intake with metabolic conditions.*
Keywords: Metabolically Healthy Obese; Metabolically Unhealthy Obese; Nutrient Intake; Physical Activity;

How to Cite **Adhika Tri Putra Sugiharta, I Made Pande Dwipayana, Gde Ngurah Indraguna Pinatih/Relationship of Nutrient Intake and Physical Activity with Metabolic Conditions in Obesity, Vol. 3, No. 7, 2024**
DOI https://doi.org/10.54543/kesans.v3i7.290
e-ISSN/p-ISSN **2808-7178 / 2808-7380**
Published by **Rifa'Isntitute**

Introduction

Obesity is one of the non-communicable diseases that become an epidemic throughout the world. About one-third of the world's population is obese. By 2030, an estimated 38% of the adult population worldwide will suffer *overweight* and the other 20% is obese. Obesity is generally defined as an excess body weight caused by an imbalance between calories in and out, this results in the accumulation of fat in adipose tissue. Obesity is characterized by a body mass index of ≥ 25 kg/m^2 (WHO, 2000)

Obesity is a risk factor for several chronic diseases including hypertension, cardiovascular disease, type 2 diabetes mellitus (DMT2), high cholesterol and other metabolic diseases. In obese patients, the process of atherosclerosis occurs through several mechanisms including an increase in oxidative stress due to the accumulation of fat tissue, endothelial dysfunction, and fat accumulation resulting in the release of *proinflammation* which induces atherosclerosis. In addition, in obese patients there is an obstacle to glucose uptake in fat and muscle which is one of the causes of DMT2 (Lovren, Teoh, & Verma, 2015)

Although obese people are often associated with several chronic diseases, not all obese people experience these diseases. This group of populations is called metabolically healthy *obese* (MHO). There is no universal definition in defining an MHO, some studies define MHO as the absence of metabolic disorders and cardiovascular disease, type 2 diabetes, dyslipidemia, hypertension, and atherosclerotic cardiovascular disease (ASCVD).

Based on the criteria put forward by Wildman in 2008 MHO is defined if not more than two of the following criteria: Triglycerides >150 mg/dL (1.7 mmol/L) or are on medication for hypertriglyceridemia; HDL-C: <40 mg/dL (1.03 mmol/L) in men and <50 mg/dL (1.29 mmol/L) in women or on medication for elevated HDL-C levels; Blood pressure: systolic ≥130 mmHg or diastolic ≥85 mmHg or moderate in the treatment of hypertension; Fasting blood sugar (GDP) ≥100 mg/dL (5.6 mmol/L), or DMT2. This population is believed to be metabolically healthy individuals even though it is said to be obese (Wildman et al., 2008)

The prevalence of MHO sufferers among obese people is around 30-40%. The prevalence of people with MHO in China was found to be around 4.2% among 24.3% of obese people. About 13.3% of MHO sufferers were found among the 28.1 percent obese in India and Asia. A meta-analysis of 12 cohort studies and 7 intervention studies found the prevalence of people with MHO to be around 35%. In general, people with MHO are more common in women than men and decrease with age (Bluher, 2020). These individuals have good insulin sensitivity, no high blood pressure, which explains the low incidence of type 2 diabetes and cardiovascular disease (Hruby & Hu, 2015)

The difference between people with healthy metabolic obesity and unhealthy metabolic obesity is still unclear. In several studies conducted in the UK reported that 44.5% of MHO sufferers became MUO within 8 years (Hamer, Bell, Sabia, Batty, & Kivimaki, 2015). In addition, nearly 50% of participants in the *Multi-Ethnic Study of*

Atherosclerosis (MESA) who were previously MHO progressed to MUO within 12 years. The results of this study are also supported by a meta-analysis of 12 studies on more than 5900 participants followed in 3-10 years, showing that almost half of all participants previously classified as MHO progressed to MUO. Based on these data, the thre is great possibility of MHO transitioning into MUO (Hruby & Hu, 2015)

The possible causes of the change from MHO to MUO are associated with weight gain, aging, and unhealthy lifestyles. Until now, there has been no research that can distinguish lifestyle is a major factor between MHO and MUO, but poor lifestyles such as lack of physical activity, smoking habits, and lack of nutritional intake are believed to increase the risk of MHO becoming MUO (Hamer et al., 2015)

Several studies examine the relationship between daily nutrient intake in the form of macro and micronutrients, sleep duration, physical activity and genetics can affect the development of healthy metabolic individuals to unhealthy (Hankinson et al., 2013). Research conducted by Philips, et al (2013) concluded that MHO survivors have a healthier nutritional intake compared to MUO sufferers. Another study conducted in Poland concluded that people with MHO have a higher intake of nutrients in the form of fish consumption, and grains without going through more whole grain processing and low sugar intake compared to patients with metabolic syndrome (Suliga, Kozie, Cie la, & G uszek, 2015). The conclusion of this study is different from research conducted by in America by Hankinson in 2013, where there was no difference in the intake of macronutrients and micronutrients in the form of fat, protein, carbohydrates, fiber, iron in patients with MHO and MUO (Hankinson et al., 2013)

Obesity is a risk factor for metabolic diseases, so it is necessary to prevent MHO from developing into MUO. Risk factors for the development of MHO into MUO include poor nutritional intake and lack of physical activity. Weight gain can be influenced by factors that can be changed such as diet and physical activity levels. These two factors are considered intermediate factors that can be modified. Overweight and obesity are characterized by an excess amount of body fat. Body fat mass increases when energy intake exceeds energy expenditure (Oussaada et al., 2019)

Until now, there have been few studies exploring between nutritional intake and physical activity in people with MHO and MUO, especially in Indonesia. Therefore, this study aims to investigate the connection between nutrient intake and physical activity in patients with MHO and MUO.

Method

This study aimed to investigate the relationship between nutrient intake, physical activity, and metabolic conditions in individuals with obesity. Conducted as a cross-sectional study, it included 72 obese patients observed at the Diabetes Center, Prof. Dr. I.G.N.G. Ngoerah Hospital in Denpasar, between May and October 2023.

Eligible participants were healthcare professionals aged 18-45 years who met the obesity criterion of a body mass index (BMI) $\geq$ 25 kg/m^2. Each participant provided

informed consent before inclusion in the study. Individuals were excluded if they had acute infectious or inflammatory diseases or malignancies.

The study utilized primary data on total caloric intake, carbohydrate, protein, and fat consumption, along with physical activity levels in obese patients. Measurement scales included numeric scales for calories and nutrient intake and categorical scales for classifying metabolic obesity status. Corellation between nutrient intake, physical acitivty, and metabolic conditions was analyzed using Chi-Square test. Multiple logistic regression was carried out to determine the effect of confounding variables.

Result and Discussion

Result

In this study, a total of 72 obese participants were recruited consecutively. Among them, 38 were male (52.8%) and 34 were female (47.2%). Of the participants, 47 (65.3%) were classified as having metabolically healthy obesity (MHO), while 25 (34.7%) were classified as having metabolically unhealthy obesity (MUO). The detailed characteristics of the study subjects are presented in Table 1.

Table 1 Characteristics of Reasearch Participants (N=72)

No	Variable	Median	Standard Deviation	Min	Max
1.	Age (years)	31.24	4.452	22	44
2.	Triglycerides (mg/dL)	126.38	93.93	32	416
3.	HDL (mg/dL)	45.58	9.06	18	67
4.	BP Systolic (mmHg)	118.34	12.44	100	160
5.	BP Diastolic (mmHg)	71.04	9.63	60	95
6.	Fasting Blood Sugar (mg/dL)	94.75	29.19	75	265
7.	Height (cm)	166.33	9.085	149	189
8.	Body Weight (kg)	83.06	16.64	56	150
9.	BMI (kg/m^2)	29.86	4.42	25.16	46.3
10.	Total Caloric Intake (kcal)	1744.9	270.88	1190	2607
11.	Protein Intake (gr)	64.5	15.84	37.02	167.2
12.	Fat Intake (gr)	56.54	13.16	35.03	117.7
13.	Carbohydrate Intake (gr)	247.78	40.77	141.6	338.3
14.	Physical Activity (METs/week)	1438.5	990.34	291	4293

Information:
HDL: High-Density Lipoprotein; BP: Blood Pressure; BMI: Body Mass Index; METs: Metabolic Equivalents

Based on the classification in table 2 it was found that the majority of subjects had good metabolic conditions where triglyceride, HDL and fasting blood sugar levels were normal. In addition, the majority of subjects also had normal systolic and diastolic pressure.

Table 2 Characteristics of Metabolic Conditions, Nutritional Intake, and Physical Activity (N=72)

Triglycerides	**Frequency**	**Percentage %**
Normal	53	73.6
High	19	26.4
HDL		
Normal	42	58.3
Low	30	41.7
Fasting Blood Glucose		
Normal	66	81.7
High	6	8.3
Systolic Blood Pressure		
Normal	64	88.9
High	8	11.1
Diastolic Blood Pressure		
Normal	65	90.3
High	7	9.7
Total Caloric Intake		
Not excessive	34	47.2
excessive	38	52.8
Protein Intake		
Not excessive	48	66.7
excessive	24	33.3
Fat Intake		
Not excessive	25	34.7
excessive	47	65.3
Carbohydrate Intake		
Not excessive	54	75
excessive	18	25
Physical Activity		
Low-Moderate	54	76.4
High	18	23.6

Information:
HDL: High-Density Lipoprotein

Based on table 2, total calories and excess fat intake were obtained as much as 52.8% (32 people) and 65.3% (47 people) respectively. The protein and carbohydrate intake of most subjects was not excessive, namely as many as 58 people (66.7%) and 54

people (75%). Based on this study, it was found that most subjects had a low-moderate level of physical activity, which was 76.4% (54 people).

Table 3 Relationship Between Total Caloric Intake, Protein, Fat, and Carbohydrate Consumption and Metabolic Conditions in Obesity (N=72)

Total Caloric Intake	MHO	MUO	PR	p	95% CI
Not excessive	20	14	0.828	0.277	0.58-1.17
excessive	27	11			
Protein Intake					
Not excessive	30	18	0.882	0.484	0.63-1.23
excessive	17	7			
Fat Intake					
Not excessive	21	5	1.429	0.038*	1.04-1.96
excessive	26	20			
Carbohydrate Intake					
Not excessive	34	20	0.475	0.872	0.61-1.24
excessive	13	5			

Information: *Significant p<0.05
OR: Odd Ratio; CI: Confidence Interval, PR: Prevalence Ratio.

The study revealed there were no significant relationship between total caloric intake, protein intake, or carbohydrate intake and metabolic conditions in obesity. However, this study show a significant association between fat intake and metabolic conditions. Specifically, higher fat intake was negatively associated with poor metabolic conditions in obesity.

The relationship of metabolic physical activity with metabolic conditions was tested using *the Fisher Exact test* with the calculation of the Prevalence Ratio (RP). The relationship of physical activity with metabolic conditions in obesity can be seen in Table 4.

Table 4 Relationship Between Physical Activity Levels and Metabolic Conditions in Obesity (N=72)

Physical Activity	MUO	MHO	PR	p	95% CI
Low-Moderate	24	31	7.418	0.004*	1.08-50.85
High	1	16			

Information: *Significant p<0.05
MUO: metabolically uhealthy obese, MHO: metabolically healthy obese

The study indicates a significant relationship between physical activity levels and metabolic conditions in obesity. Specifically, low to moderate levels of physical activity were found to be positively associated with poor metabolic conditions in obesity.
Table 5 presents the results of the multivariate analysis using logistic regression, which evaluated the relationship between each independent variable and the occurrence of metabolically unhealthy obesity (MUO) in obese patients. The analysis revealed that fat

intake (p = 0.045, CI95% 1.029-16.106) and physical activity (p = 0.008, CI95% 0.005-0.459) were significantly associated with the incidence of MUO.

Table 5 Multivariate analysis

Variable	Beta Coefficient	95% CI	P
Sex	1.821	1.765 -21.735	0.005*
Fat Intake	1.404	1.029 – 16.106	0.045*
Physical Activity	-3.007	0.005 – 0.459	0.008*

Information: *Significant p<0.05

Discussion

The study found 72 people with obesity of which 47 people (65.3%) belonged to the MHO group and 25 people (34.7%) belonged to the MUO group. The higher proportion of MHO sufferers is in accordance with research conducted by Camhi, et al. where MHO sufferers (80%) are more than MUO sufferers (20%) (Camhi, Crouter, Hayman, Must, & Lichtenstein, 2015). In this study, the majority of patients aged 30 years with male sex as many as 38 people (52.8%) and 34 women (47.2%).

The proportion of male sex is in line with research conducted in Beijing, China where the prevalence of obesity in men is as much as 15.2% while women are 5.3%. The high proportion in men is due to unhealthy lifestyles such as smoking and alcohol consumption (Mathis, Tanaka, & Hiramatsu, 2023). In line with the results of this study, studies in Italy and Estonia show the incidence of MHO is more common in the age range of 18-30 years while the age of >60 years is the least age range (Mathis et al., 2023). Similar results were also obtained from a study in Beijing where MHO is more common at the age of under 45 years and the incidence of MUO begins to occur over the age of 45 years to 65 years (Liu et al., 2019)

The results of the analysis showed that the average Body Mass Index (BMI) of the subjects was 29.86, with average triglyceride levels of 126.38 mg/dL, HDL 45.58 mg/dl, fasting blood sugar 94.75 mg/dL Systolic blood pressure 118.3 mmHg and diastolic 71 mmHg. Based on metabolic characteristics, it was found that the most common MUO criteria were low HDL levels followed by high triglycerides and high blood pressure. Similar results were also found by Camhi, et al. where the majority of subjects had poor HDL triglyceride levels (Camhi et al., 2015)

This result is different from a study conducted in Estonia where the most common metabolic characteristic in MUO is hypertensive hypertension, the second most common metabolic characteristic is high triglyceride levels as much as 39.7%. Research in Norway found hypertension as much as 72.6% and low HDL levels occupy the second place as much as 56.8% (Slagter et al., 2018)

The study found no significant relationship between total caloric intake, protein intake, or carbohydrate intake and metabolic conditions in obese individuals. However, a significant association was identified between fat intake and unhealthy metabolic conditions. The analysis revealed that fat intake had a relative risk (RP) of 1.429 with a significance level of 0.038. This suggests that high fat intake is associated with an

increased risk of poor metabolic conditions in obese individuals. These results underscore the impact of excessive fat consumption on metabolic balance in those with obesity.

Similar results were also stated by Philiips, et al. (2013), In a cross-sectional study of 2047 people in Ireland it was concluded that nutrient intake is not associated with metabolic conditions unless high fat intake has a significant value for metabolic conditions in obese patients ($p< 0.05$) (Slagter et al., 2018), (Phillips et al., 2013). Protein is one component of the diet that plays a role in supplying essential amino acids that play a role in cardiometabolic disease processes. High Protein Diet (HPD) 1.07 – 1.6 g protein/kgBB plays a role in weight loss and reduces metabolic risk factors by increasing satiety, thermogenesis during meals, hepatic gluconeogenesis response, and increased ketogenesis due to higher protein intake (Moon & Koh, 2020). The role of DTP in weight loss and metabolic risk occurs if the individual also decreases total daily calories and carbohydrates, but if this intake is not reduced then the risk of cardiometabolic occurrence will increase (Zhang et al., 2020)

Carbohydrates are a major contributor to total daily calories, especially in Asian populations. Cross-sectional studies in Korea found that carbohydrates were a major contributor to metabolic syndrome (OR 1.34, 95%, CI 1.08–1.66, $p = 0.004$). The high consumption of carbohydrates in this study mainly occurred in groups with low socioeconomic and education levels (Merchant et al., 2009). The findings of this study are different from the results of studies conducted in the United States. The results showed that the risk of metabolic syndrome was higher in those who consumed carbohydrates below the recommendation compared to the group that adhered to the daily recommendation (OR 1.067, CI 95%: 1.063 - 1.071, $p < 0.001$). In addition, the majority of participants in this study were also identified as consuming fat beyond normal limits, resulting in high total daily calories (Dustin et al., 2023)

The incidence of obesity is closely related to higher total calories than calories used. One of the contributing factors in increasing the number of daily calories is a high intake of fat. Several studies have shown that high fat consumption is associated with poor metabolic conditions. Research on rats that consume high fat diet in the long term (10 months) found that high fat diet resulted in increased blood pressure, fasting glucose levels and the pro-inflammatory cytokine IL-6 which are risk factors for metabolic disorders (Delle et al., 2023)

The results of this study are supported by Meta-Analysis research conducted by Lu, et al. revealed that there is a significant relationship between high fat consumption with high levels of triglycerides and low HDL ($p < 0.001$) (Lu, Wan, Yang, Huggins, & Li, 2018). Similar results were also obtained in another meta-analysis study in which obese people who were carried out low-fat nutrition interventions had lower triglyceride levels (–8.38, 95% CI –13.50-3.25; $p=0.001$) and better HDL levels (2.35 mg/dL, 95% CI 1.29-3.42; $P<0.0001$) compared to individuals with high fat consumption (Kadowaki et al., 2023)

High consumption of fat is also associated with impaired glucose intolerance. In a study conducted in Japan, consumption of high fat diet in the short term (6 days) reduced insulin sensitivity by 4% where insulin resistance is a risk of T2DM (Kadowaki et al., 2023). Similar research was also conducted in Indonesia, in obese patients with a family history of T2DM who consumed high-fat diit, there was a decrease in insulin sensitivity, increased triglyceride levels and IL-6 levels which are risk factors for the occurrence of T2DM and metabolic disorders (Budiyati, Purnamasari, Wibowo, Widyahening, & Soewondo, 2023)

The results of this study illustrate the relationship between physical activity levels and metabolic conditions in individuals who are obese. Statistical analysis shows that the Prevalence Ratio (PR) is 7.418 with a significance of 0.004 and a 95% confidence interval between 1.08 to 50.85. These findings suggest that low-moderate levels of physical activity have a positively meaningful association with a greater risk of OMTS in obese people with low-moderate levels of physical activity. These results provide strong support for the importance of adequate physical activity in maintaining metabolic balance and tackling the problem of obesity.

Physical activity plays an important role in maintaining energy balance and body mass, as well as mitigating risk factors for *non-communicable diseases* (NCDs). According to World Health Organization (WHO) recommendations, adult individuals should engage in moderate-intensity physical activity for at least 150 minutes or > 1000 METs in one week. A significantly higher BMI can be suppressed through increased levels of physical activity. The Rotterdam study revealed that participants who were overweight but engaged in low levels of physical activity had a 1.33 to 1.35 times higher risk of cardiovascular disease compared to normal weight participants who had high levels of physical activity (Ikram et al., 2020)

In line with this study, Metabolically Healthy Obese Individuals (OMS) carrying out physical activity for 45 minutes every day have a better metabolic risk and quality of life compared to obese people with OMTS sedentary lifestyles ($P<0.05$). Consistent with these results, a Dutch study of 9270 individuals with obesity found that high physical activity had a 2 times lower risk of MUO (OR 2.02, 95% CI, 1.5-2.71 $p< 0.0001$) (Slagter et al., 2018), (Schwingshackl & Hoffmann, 2013)

Lifestyle modifications involving changes in diet, physical activity, and exercise are considered the foundation of obesity management. Various studies have shown a direct link between sedentary behaviors, such as sleeping, sitting, lying down, and watching television, and increased metabolic risk. Overweight individuals spend more daily time sitting and watching TV compared to normal weight individuals, as well as reduced time for exercise. Experimental studies in humans have indicated that increased sedentary behavior is associated with reduced energy expenditure, development of insulin resistance, and accumulation of belly fat (de Rooij et al., 2016)

Conclusion

This study show significant associations between fat intake and physical activity levels with metabolic conditions in individuals with obesity. In contrast, no significant relationships were found between total caloric intake, carbohydrate and protein intake with metabolic outcomes. These findings emphasize the critical role of dietary fat management and regular physical activity for improving metabolic health in obese individuals.

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