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Association between Dietary Macronutrient Intake and High-Sensitivity C-Reactive Protein Levels among Obese Women in Kuantan, Malaysia

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Abstract

Elevated high-sensitivity C-reactive protein (hs-CRP) levels may be associated with an increased risk of cardiovascular disease (CVD). In general, an individual's dietary intake may influence the hs-CRP level. However, evidence on the influence of dietary macronutrient intake on hs-CRP levels among obese Malaysian women remains fragmented. Therefore, this study aims to investigate the association between the hs-CRP level and dietary macronutrient intake of obese adults living in Kuantan. The assessment of 24-hour dietary recall and venous hs-CRP levels were investigated in 67 women with a body mass index of 27.5 to 39.9 kg/m². The findings revealed that obese women living in Kuantan had elevated hs-CRP levels (median = 7.95 mg/L, IQR = 7.90) and a significant negative correlation between the hs-CRP level and total dietary fiber intake ($r = 0.205$, $p = .014$). In conclusion, this study suggests that certain macronutrients, particularly dietary fiber, seem to be associated with elevated hs-CRP in obese women. Hence, this information could help assess and manage low-grade chronic inflammation and underlying obesity-related conditions.

Keywords: cardiovascular risk, macronutrient intake, C-reactive protein, obesity

Introduction

Cardiovascular disease (CVD) is the worldwide number-one killer of both men and women. The World Health Organization (WHO) reports in 2015, among countries in the Southeast Asian region, the estimated proportionate mortality rate because of ischemic heart disease (IHD) was highest in Malaysia (20.1%), followed by Philippines (15.4%), Singapore (18%), and Thailand (13.7%) [1]. In addition, IHD was the principal cause of death in Malaysia for 10 years, from 2005 to 2014 [2]. Obesity is a risk factor for IHD in adults [3]. In Malaysia, the prevalence of obesity (body mass index [BMI] ≥ 27.5 kg/m²) was higher among women (33.6%) than men (27.8%) [4]. Also, the prevalence of abdominal obesity was higher in women (35.4%) compared with men (11.8%) [4]. Abdominal obesity is characterized by excess visceral fat and is also a prominent risk factor for IHD. Therefore, this study suggested that

Malay women with high BMI are at high risk of premature mortality because of IHD, thus justifying the focus on this population to reduce the mortality rate because of IHD in Malaysia.

The clinical practice guideline (CPG) for the prevention of CVD in women acknowledged that risk classification is a way to reduce the mortality rate because of CVD [5]. Currently, the risk classification of CVD is best measured using the Framingham Risk Score where the 10-year risk of CVD is determined based on several independent risk factors for CVD, including age, total cholesterol and high-density lipoprotein level, systolic blood pressure level, smoking status, and diabetes status [5]. However, the current risk classification method is limited to several independent risk factors for CVD, which may omit other significant risk factors for CVD. Recent evidence suggests that inflammation plays a vital role in the intrinsic part of the pathogenesis of

CVD, especially in obese adults [6,7]. In general, inflammation is a bodily response to infection or tissue damage. In obese adults, excess adipose tissue releases pro-inflammatory mediators, such as tumor necrosis factor- α (TNF- α) and interleukin-6 (IL-6) [7], which subsequently stimulate the production of C-reactive protein (CRP). The continuous production of CRP leads to an elevated CRP level in the body, which is then involved in the pathogenesis of atherosclerosis [8]. Previously, the CRP assay could measure the CRP level in the body up to 10 mg/L. However, the current technology produces a high-sensitivity assay that allows the high-sensitivity CRP (hs-CRP) level to be measured as precisely as 0.5 mg/L [9].

In addition to obesity status, other factors, including diet and lifestyle, may influence the hs-CRP level in an adult. Khayyat-zadeh *et al.* suggested that the hs-CRP level may be associated with dietary macronutrient intake in the Iranian population [10]. In addition, studies by Ning *et al.* and Sutcliffe *et al.* found that dietary fiber intake was significantly associated with lower levels of hs-CRP [11,12]. Furthermore, a 12-week intervention that involved a healthy diet and physical activity program combined with stress reduction significantly reduced the hs-CRP level among obese African-American adults [13]. However, the association between dietary macronutrient intake and serum hs-CRP among Malay obese women in Malaysia remains unclear. Therefore, this study aims to investigate the association between dietary macronutrient intake and the serum hs-CRP level of the study population. This study's findings will help the healthcare professional better understand the significant dietary macronutrient intake that might be associated with an elevated hs-CRP level in Malay obese adults. In turn, findings on the risk classification and the influential dietary macronutrient intake associated with an elevated hs-CRP level may reduce the morbidity and mortality rate because of IHD in women.

Materials and Methods

Study design. This study is a cross-sectional study of Malay women with obesity from suburban areas of Kuantan, Pahang. Pahang is a state located in Peninsular Malaysia.

Participants. A total of 67 participants were recruited in this study. The inclusion criteria were obese women (referring to the cut-off values of BMI in Malaysia ≥ 27.5 kg/m²), aged between 19 and 60 years old, and able to speak and write in Malay or English. In addition, the exclusion criteria included individuals with any self-reported comorbidities, such as type 2 diabetes mellitus (T2DM) or thyroid disorders, pregnant and lactating women, and individuals currently taking medications for chronic and endocrine diseases.

The data collection process started right after the Institutional Research Ethics Committee's ethical approval in December 2015. The data collection procedures were conducted in a primary care clinic in a public university in Kuantan. In the beginning, the researcher conducted a series of health screening activities and posted advertisement materials, including flyers, posters, handbills, and online advertisements via social media networks. The potential participants who responded to the advertisement were pre-screened during telephone inquiries. Then, the eligibility of the participants was assessed based on the inclusion and exclusion criteria. Identification cards were obtained to confirm the participants' identity and age, and their height and weight were also measured to calculate the BMI level.

In addition, the participants were interviewed about their current health status and history of past medical illnesses to ensure that they were free from any chronic diseases, not pregnant, and not taking any medication. All eligible participants were included in the study. A written informed consent form was obtained from the participants as evidence of their willingness to participate in the study. After that, the researcher assessed the dietary macronutrient intake of the participants using the 24-hours dietary recall. A registered nurse was also assigned to obtain 10 milliliters of venous blood from each participant to determine the serum hs-CRP level. The blood samples were sent to the laboratory within two hours to maintain their quality. The concentration of hs-CRP was quantified using a human hs-CRP enzyme-linked immunosorbent assay kit. Before the venipuncture procedure, the participants were called to ensure that they would be free from any acute inflammation (major trauma and infection). CRP is an acute-phase reactant, and its levels increase transiently during an acute inflammation state [14]. Participants were also reminded to fast overnight. Finally, before the data collection process ended, an honorarium was given to the participants as a token of appreciation for their participation in this study.

Instruments and procedure. The dependent variable measured in this study is the hs-CRP level, and the independent variable is dietary macronutrient intake. In determining the hs-CRP level, serum hs-CRP level was obtained from participants by a registered nurse. In general, the hs-CRP level of more than 3 mg/L indicates an elevated hs-CRP level [14]. Nonetheless, for this study, the cut-off value for hs-CRP was determined by referring to the cut-off values stated in the Malaysian CPG of Dyslipidemia, the optimal level of hs-CRP and would be 0.5 mg/L. In contrast, the cut-off point of "elevated hs-CRP level" is more than 1 mg/L [15].

The dietary macronutrient intake of the study population was assessed using 24-hour dietary recall. During the dietary intake recall assessment, each participant was asked to recall all food consumed during the previous day and estimate quantities in standard measures or servings. The raw data from the 24-hour dietary recall were then entered into Nutritionist Pro™ software that converted the raw data into the 10 outcome measures, namely total energy (kcal), protein (g), carbohydrate (g), total fat (g), cholesterol (mg), saturated fat (g), monounsaturated fat (g), polyunsaturated fat (g), total dietary fiber (g), and total sugar (g).

Data analysis. All analysis was performed using SPSS (version 21). Normally distributed data are presented as means ± standard deviations (SD) and non-normally distributed data are presented as medians ± interquartile ranges (IQR). The Spearman’s rho correlation coefficient test was used to determine the association between hs-CRP level and continuous variables. In addition, an independent sample Mann-Whitney test

was used to determine the association between the hs-CRP level and categorical variables. A *p*-value of less than .05 was considered statistically significant.

Results and Discussion

Baseline characteristics of the study population. The demographic characteristics, physical attributes, and the hs-CRP level of the participants are presented in Table 1. On average, the age of the participants was 33 ± 10.11 years. The majority of the participants were married (50.7%), nulliparous (50.7%), employed (49.3%), and a degree holder (37.3%). The physical attributes, including the height and weight of the study population, were 154.93 ± 5.08 cm and 76.05 ± 9.01 kg, respectively. The study population was mainly classified as obese class I with a mean BMI of 31.63 ± 3.39 kg/m². Furthermore, the findings showed that the study participants had elevated hs-CRP levels with a median (IQR) of 7.95 ± 7.90 mg/L.

Table 1. Demographic Characteristics, Physical Attributes, and hs-CRP Level of Study Participants (N = 67)

Variables	Total (N = 67)		Normal hs-CRP (N = 8)		Elevated hs-CRP (N = 59)		<i>p</i>														
	n	%	Mean	SD	n	%		Mean	SD												
Age (years)			33.01	10.11			31.25	11.70												.603	
Employment status																					
Homemaker	12	17.9			1	12.5			11	18.6											
Employed	33	49.3			2	25.0			31	52.5											
Unemployed	1	1.5			0	0			1	1.7											
Student	21	31.3			5	62.5			16	27.1											
Marital status																					
Single	29	43.3			5	62.5			24	40.7											
Married	34	50.7			2	25.0			32	54.2											
Divorced/Widowed	4	6.0			1	12.5			3	5.1											
Monthly income (RM)*			200.00	2500.00			0	2424.00			700.00	2500.00									.223
Parity status																					
Nulliparous	34	50.7			5	62.5			29	49.2											
Primiparous	2	3.0			0	0			2	3.4											
Multiparous	31	46.3			3	37.5			28	47.4											
Educational status																					
Certificates	2	3.0			0	0			2	3.4											
Sijil Pelajaran Malaysia	16	23.9			3	37.5			13	22.0											
Matriculation	14	20.9			3	37.5			11	18.6											
Diploma	6	9.0			0	0			6	10.2											
Degree	25	37.3			2	25			23	39.0											
Masters	4	6.0			0	0			4	6.8											
Height (cm)			154.93	5.08			158.18	3.79			154.49	5.10									.053
Weight (kg)			76.05	9.01			77.11	7.72			75.91	9.22									.726
Body mass index (kg/m²)			31.63	3.39			30.91	3.85			31.73	3.35									.527
Smoking status																					
No	67	100			8	11.9			59	88.1											
Yes	0	0			0	0			0	0											
High-sensitivity CRP level (mg/L)*			5.10	9.50			0.55	0.30			6.50	9.60									.001†

All data is presented in mean and standard deviation, *p*-value using independent sample t-test

* Data is presented in median and interquartile range (IQR), *p*-value using independent samples Mann-Whitney U test

† *P*-value <.05

Furthermore, Table 1 also presents the differences in characteristics of the study participants based on the hs-CRP status. The hs-CRP status was determined using the elevated hs-CRP level's cut-off values at more than 1 mg/L[15]. The findings show that the mean age of obese women with an elevated hs-CRP level was 33.25 ± 9.96 years. Over half of the obese women with elevated hs-CRP were married (50.7%), and the majority of them were employed (49.3%). More than half of those with a normal hs-CRP level were students (62.5%), single (62.5%), and around 31 years old. The findings also showed that obese women with a higher BMI had an elevated hs-CRP level (31.73 ± 3.35 kg/m²) relative to those with normal hs-CRP levels (30.91 ± 3.85 kg/m²).

Dietary intake of the study population. The dietary intake of obese women in this study is described in Table 2. The findings show that the mean total energy gained from the dietary intake among obese women was approximately 1703 ± 678.13 kcal per day. In addition, the mean intake of the essential dietary macronutrients, protein, carbohydrate, and total fat, was 74 ± 33.28 grams per day, 208 ± 98.91 grams per day, and 66 ± 28.71 grams per day, respectively. Moreover, the average intake of saturated, monounsaturated, and polyunsaturated fat was 14.39 ± 9.14 grams per day, 13.81 ± 8.46 grams per day, and 9.92 ± 7.73 grams per day, respectively. The median of the cholesterol and dietary fiber from the dietary intake was 203.6 ± 271.54 mg/L per day and 4.64 ± 5.77 grams per day, respectively. This result demonstrated that obese women in the study consumed an average of 37.1 ± 26.6 grams per day of total sugar from dietary intake. Table 2 also presents the distribution of dietary macronutrient intake defined by the hs-CRP status. The findings show

no statistically significant differences in the dietary macronutrient intake among obese women with normal and elevated hs-CRP (p -value $>.05$). Nevertheless, obese women with an elevated hs-CRP level had a higher daily intake of carbohydrate, saturated fat, and monounsaturated fat than obese women with a normal hs-CRP level.

The association between dietary macronutrient intake and Hs-CRP level. Table 3 shows the association between dietary macronutrient intake and hs-CRP levels among obese women in this study. The results demonstrated a significant negative correlation between the hs-CRP level and total dietary fiber intake ($r = 0.275$, $p = .024$).

Discussion. To our knowledge, this is the first study to describe the association between dietary macronutrient intake and hs-CRP levels among women with obesity living in suburban areas of Kuantan. Our findings showed that obese women in Kuantan are at high risk of CVD based on hs-CRP levels. Hs-CRP level has been suggested as a useful risk marker for CVD because of its role in inflammatory activities in the body and its central role in the pathogenesis of atherosclerosis [19,20]. In particular, the abnormal inflammatory activities, caused by infection, or any trauma to vascular smooth muscle cells, may lead to the pathogenesis of atherosclerosis later progressed to CVD [6]. Thus, based on the level of hs-CRP, one's risk of developing CVD can be determined [8,21]. In this study, most obese women in Kuantan had elevated hs-CRP levels (>1 mg/L). The elevated level of hs-CRP may be influenced by obesity status, as the BMI of the obese women with an elevated hs-CRP level was higher than those with a normal hs-CRP level. Previous scholars have established

Table 2. Dietary Macronutrients Derived from the Dietary Intake of the Study Participants (N = 67)

Variables	Total (N = 67)		Normal hs-CRP (N = 8)		Elevated hs-CRP (N = 59)		p
	Mean	SD	Mean	SD	Mean	SD	
Energy (kcal)	1702.89	678.13	1722.88	705.89	1700.18	680.51	.934
Protein (g)	73.99	33.28	86.82	52.00	72.25	30.14	.248
Carbohydrate (g)	207.83	98.91	206.16	105.77	208.06	98.90	.963
Total fat (g)	65.71	28.71	63.32	22.61	66.03	29.59	.804
Cholesterol (mg)*	203.59	271.54	230.48	326.21	203.59	271.77	.542
Saturated fat (g)	14.39	9.14	11.12	6.62	14.83	9.39	.284
Monounsaturated fat (g)	13.81	8.46	12.93	7.96	13.93	8.59	.757
Polyunsaturated fat (g)	9.92	7.73	11.34	7.08	9.73	7.85	.567
Total dietary fiber (g)*	4.64	5.77	8.31	16.18	4.54	5.55	.315
Total sugar (g)	37.08	26.60	41.04	43.26	36.55	24.01	.657

All data is presented in mean and standard deviation, p -value using independent sample t-test

* Data is presented in median and interquartile range (IQR), p -value using independent samples Mann-Whitney U test

† P -value $<.05$

Table 3. Correlation Analysis Between Dietary Macronutrients Derived from the Dietary Intake and hs-CRP Level of The Study Participants (N = 67)

Variables	Hs-CRP	
	Spearman's rho correlation Coefficient (r)	P-value
Energy (kcal)	0.032	.796
Protein (g)	0.071	.567
Carbohydrate (g)	0.031	.805
Total fat (g)	0.078	.530
Cholesterol (mg)	0.101	.414
Saturated fat (g)	0.162	.190
Monounsaturated fat (g)	0.043	.729
Polyunsaturated fat (g)	-0.067	.588
Total dietary fiber (g)	-0.275	.024†
Total sugar (g)	-0.013	.915

Note: † Correlation is significant ($p < .05$) by Spearman's rho correlation coefficient (2-tailed)

that obesity is a risk factor for the elevated hs-CRP level [19–22]. The pathophysiology behind this phenomenon can be explained by the existence of large adipocytes in obese adults, which promotes macrophage infiltration, resulting in increased CRP [23–25]. In turn, the elevated CRP level leads to chronic low-grade inflammation [26].

The elevated hs-CRP level seen in obese women in this study may also be influenced by their dietary macronutrient intake. This study reported the distribution of the main dietary macronutrients, including carbohydrates, protein, and total fats. These dietary macronutrients are essential for health and wellbeing [27]. Our findings demonstrated that obese women in this study had a higher mean intake of carbohydrate, protein, and total fat than the findings reported in the Malaysian Adults Nutrition Survey (MANS) 2014 [28]. The carbohydrate and total fat intake were higher among obese women with an elevated hs-CRP level, which might have influenced their circulating hs-CRP level. High-carbohydrate intake has an established association with weight gain, reduction in high-density lipoprotein level, and elevated triglyceride level [32,33], which in turn may lead to chronic low-grade inflammation state and metabolic syndrome.

Nevertheless, the precise mechanism involved in reducing inflammation by reducing dietary carbohydrate intake remains unclear [31]. Also, high-fat diets have a proven association with inflammation. In accordance with Welty *et al.*, a high intake of saturated fat may also result in an elevated hs-CRP level because increases in saturated fat from dietary intake have been associated with inflammation [32]. Therefore, an emphasis on reducing the intake of carbohydrates and total fat from the diets of obese women in Kuantan is necessary to combat obesity and to reduce the incidence of CVD in women.

Based on the findings of this study, the hs-CRP level of the obese women in Kuantan was negatively correlated with total daily dietary fiber intake. In other words, a lower fiber intake in the daily diet may influence the hs-CRP level of obese women. In the CPG of T2DM [30], the recommended dietary fiber intake to reduce the risk of T2DM is between 20 to 30 grams per day. In addition, the CPG on the prevention of CVD in women [5] specifies that an intake of soluble dietary fiber intake between 9 to 16.5 grams per day is recommended to reduce the risk of CVD in women. Among the study population, obese women consumed less than the recommended amount of dietary fiber per day.

Further analysis showed that obese women with a greater intake of dietary fiber per day have a normal hs-CRP level than obese women with an elevated hs-CRP level. These findings imply that adequate dietary fiber intake in the daily diet may protect these obese women against CVD. The findings were consistent with a large population study by Khayyat-zadeh *et al.* in which dietary fiber intake was significantly associated with hs-CRP levels among apparently healthy Persian women [10]. The mechanism involved in reducing the hs-CRP level could be attributed to the antioxidant properties of the dietary fiber. In accordance with Saura-Calixto, antioxidants are associated with dietary fiber, and it constitutes a major proportion of the antioxidants present in foods and diets [33]. The proposed mechanism is that the antioxidants neutralize free radicals in the body, thus protecting the body against oxidative stress, inhibiting cardiovascular inflammation [34]. Therefore, the promotion of adequate fiber intake as part of a healthy diet reduces CVD in women and should be intensified.

A sample menu plan for Malaysian adults consists of 20 to 30 grams per day of dietary fiber intake [35].

Nonetheless, the obese women in this study had consumed an average of only five grams of dietary fiber per day. The data also suggest that the hs-CRP level increases as the consumption of the dietary fiber decrease. Therefore, this study implies a great challenge for the nursing profession in promoting dietary fiber intake among obese women. Other emerging countries also experience the challenge of promoting healthy lifestyles because of environmental influences, including limited access to healthy foods, healthy foods being more expensive than unhealthy foods, and lack of exercise[36]. Consequently, this study highlights the vital role that nursing personnel plays in educating obese women in Kuantan about the importance of adequate dietary fiber intake to stabilize hs-CRP levels at an optimum level and reduce the risk of mortality because of IHD.

Several trials from western countries dispute the effect of dietary fiber intake on the hs-CRP level among obese adults. For instance, a randomized controlled trial that compared the effect of meal replacement from a low-fiber food to food with a viscous source of fiber (whole-grain ready to eat oat cereal) found no significant effect on the hs-CRP level among overweight and obese adults in the United States (U.S.) after 12 weeks of the intervention [37]. Moreover, a trial by Hutchins, Brown, and Cunnane reported that daily flaxseed intake (rich in soluble fiber) for 12 weeks among postmenopausal obese women with pre-diabetes in the U.S. did not produce any significant effect on hs-CRP levels[38]. Therefore, this study suggested that increased dietary fiber intake might reduce the hs-CRP level in obese women. However, the evidence regarding the type of food and adequate daily intake is still unclear. Further study regarding the effect of various sources of dietary fiber with different antioxidant capacities on hs-CRP levels among obese women is highly recommended. Also, similar studies with larger sample sizes are highly recommended to clarify the association between hs-CRP levels and dietary fiber intake among apparently healthy obese women.

Nonetheless, there are limitations to this study. Firstly is the small sample size, thus limiting the generalization of the study's findings. In addition, the self-reporting method of this study to collect dietary intake may introduce bias. Also, the menstrual cycle of the participants was not recorded before the hs-CRP level test. Hence, these limitations need to be considered during the interpretation of the findings.

Conclusion

In conclusion, this work found that obese women in Kuantan experience elevated hs-CRP levels. This study also determined that certain macronutrients, particularly dietary fiber, seem to be associated with elevated hs-

CRP in obese women. Hence, this information could be useful in assessing and managing low-grade chronic inflammation and underlying obesity-related conditions.

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