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Obesity Indicators and C-Reactive Protein in Indonesian Adults (More than Equal to 40 Years Old): The Indonesian Family Life Survey 5

Yeni Mahwati[1*], Dieta Nurrika[2,3]

[1]Study Program of Public Health, Sekolah Tinggi Ilmu Kesehatan Dharma Husada, Indonesia
[2]Department of Public Health, School of Health Science Banten, Indonesia
[3]Department of Health Informatics and Public Health, Faculty of Epidemiology, Tohoku University School of Public Health, Japan

Abstract

C-reactive protein (CRP) is the best clinical marker for systemic inflammation. Obesity is associated with increased CRP levels. Systemic inflammation is present before morbidity occurs. This study revealed that the identification of obesity indicators and CRP levels is limited among Indonesians. The present study investigated the associations among obesity indicators (body mass index/BMI, waist circumference/WC, waist-to-hip ratio/WHR, waist-to-height ratio/WHtR, and CRP levels) among Indonesian adults. This cross-sectional study based on Indonesian Family Life Survey 5 in 2014–2015 was conducted among 3,386 adults (≥ 40 years) living in 13 provinces in Indonesia during the study period. All data were collected in 2014. Multiple logistic regression was used to estimate the odds ratio (ORs) and 95% CI for hs-CRP levels on obesity indicators by using underweight (BMI) and normal (WC, WHR, and WHtR) as references. Our multivariable logistic regression analysis indicated that respondents with increased WHR (OR: 1.278, 95% CI: 1.005–1.625, p-value < 0.001) were more likely to have high-risk hs-CRP levels than those with normal WHR. Compared to respondents with normal WHtR, those with increased WHtR were found associated with high-risk hs-CRP levels (OR: 1.980, 95% CI: 1.544–2.541, p-value < 0.001). Therefore, WHR and WHtR can predict central obesity, which is associated with hs-CRP levels.

Keywords: adult, c-reactive protein, obesity

Introduction

Acute-phase C-reactive protein (CRP) is well known as a sensitive marker for systemic inflammation, which is synthesized in the liver; the process is predominately regulated by interleukin-6 (IL-6).[1,2] Previous prospective studies reported that CRP levels are associated with future coronary heart disease risks.[3] Another previous study showed that elevated CRP levels significantly correlate with metabolic abnormality features,[4] such as insulin resistance,[5] and low high-density lipoprotein cholesterol.[6,7] Thus, CRP levels that can assist in predicting future morbidity risks are important.

Obesity is a major public health problem in the world, affecting people in developed and developing countries.[2,8,9] In 2016, 39% of adults aged 18 years and above (39% of men and 40% of women) were overweight; overall, approximately 13% of the world's adult population (11% of men and 15% of women) were obese.[10] Obesity is associated with metabolic syndrome, development of type II diabetes,[11] and coronary heart disease.[12] Inflammation is recently understood as a key pathogenic mechanism in the initiation and progression of cardiovascular disease.[13] Adipose tissue is a passive storage repository for fat, but this tissue also plays an active role in metabolism by producing pro-inflammatory cytokine and IL-6. Given that IL-6 has inflammatory properties and stimulates acute phase protein production in the liver, the release of IL-6 from adipose tissue may induce low-grade systemic inflammation in person with the excess body.[1] Therefore, identifying obesity markers and CRP levels to predict future morbidity risks becomes a great concern in public health.

In Indonesia, the prevalence of obese adults (18 years and older) was 21.8% in 2018, higher than that in 2007 (10.5%) and 2013 (14.8%).[14] In addition, the prevalence of overweight girls (15–18 years) in rural and urban areas was 10%.[15] Moreover, the prevalence of obesity in Indonesia from 1993 to 1997 raised remarkably.[16]

Indonesia has developed a community-based noncommunicable disease control model through Integrated Health Post for Elderly-Chronic Disease for controlling

Correspondence*: *Yeni Mahwati, Study Program of Public Health, Sekolah Tinggi Ilmu Kesehatan Dharma Husada, Terusan Jakarta Street No. 77 Bandung, West Java, Indonesia, E-mail: yenimahwati@stikesdhb.ac.id, Phone: +62-22-7204803*

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risk factors of non-communicable diseases, such as obesity measurement, body fat analysis, blood pressure, and simple lung function (peak flow meter). From the public health perspective, a further understanding of chronic conditions, such as inflammation and obesity, is needed for the effective interventions and optimal predictions for future health care costs. Investigating obesity markers and CRP levels among Indonesian adults are informative for early intervention in future morbidity risks.

However, to our knowledge, only a few studies on obesity markers and CRP levels among Indonesians use the national scale. Azizah and Sulchan,[17] conducted a study on stunted obesity female adolescents in Rural Jepara, Indonesia. They found that the female adolescent inflammation in stunted obesity is not provable. Hastuti, *et al.,*[18] also found increased levels of IL-6 and CRP in the obese group compared with the controls among people/residents of Western Indonesia. These studies did not focus on the relationship between obesity indicators and CRP levels. Therefore, the present study investigated the associations among obesity markers (body mass index/BMI), waist circumference/WC, waist-to-hip ratio/WHR, waist-to-height ratio/WHtR, and CRP levels) among Indonesian adults.

Method

This study used secondary data from the fifth wave of the Indonesian Family Life Survey (IFLS5). The IFLS is an ongoing longitudinal socioeconomic and health survey. It is based on a sample of households representing approximately 83% of Indonesians living in 13 of the nation's 26 provinces. The survey collects data on individual respondents, their families, their households, the communities in which they live, and the health and education facilities they use. The first wave (IFLS1) was administered in 1993 among individuals living in 7,224 households. The IFLS2 sought to re-interview the same respondents four years later. A follow-up survey (IFLS2+) with 25% of the sample was conducted in 1998 to measure the immediate impact of the economic and political crisis in Indonesia. The third wave, IFLS3, was fielded on the full sample in 2000. The IFLS4 was conducted in late 2007 and early 2008 on the same 1993 households and their split-offs. The IFLS5 was fielded in late 2014 and early 2015 on the same set of IFLS households and split-offs: 16,204 households and 50,148 individuals were interviewed.[19] Data from IFLS are publicly available from the Rand Corporation website.

In the present study, respondents were adults aged 40 years and older were interviewed. We excluded those with missing data on height, body weight, waist circumference, hip circumference or high-sensitivity CRP (hs-CRP) level, and other covariates (sex, age, marital status, education, residence, and multimorbidity). The final sample comprised of 3,386 individuals.

The study was based on publicly available de-identified data. All IFLS and procedures are reviewed and approved by the Institutional Review Boards in the United States (at RAND) and in Indonesia at the Universitas Gadjah Mada. Written informed consent was obtained from all respondents prior to data collection.[20]

The BMI, WC, WHR, and WHtR were used as overweight and obesity indicators.[2] Body mass index was computed by dividing weight (kg) by height squared (m^2). Weights were measured to the nearest tenth of a kilogram by using a Camry model EB1003 scale. Heights were assessed to the nearest millimeter by using a Seca plastic height board, Model 213. According to Asian standards by the World Health Organization (WHO), BMI is divided into four categories: underweight (BMI less than 18.50 kg/m^2), normal weight (BMI 18.50–22.99 kg/m^2), overweight (BMI 22.99–24.99 kg/m^2), and obese (BMI 25.00 kg/m^2 and above).[21] The WC was measured in a horizontal plane midway between lowest rib and the iliac crest, and then classified into two groups: normal (WC less than 90 cm for men and WC less than 80 cm for women) and increased (WC 90 cm and above for men and WC 80 cm and above for women).[22] The WHR was calculated as waist circumference divided by hip circumference, and then categorized as: normal (WHR less than 0.9 for men and WHR less than 0.85 for women) and increased (WHR 0.9 and above for men and WHR 0.85 and above for women).[22] The WHtR was calculated as waist circumference (cm) divided by height (cm), and then divided into two groups: normal (0.46 to 0.42) and increased (greater than 0.46).[2]

The CRP concentrations in dried blood spot (DBS) specimens, as the dependent variable, were measured using a hs-CRP ELISA method. Details of the CRP data collection and validation in IFLS 2014 are explained in the IFLS Wave 5 Dried Blood Spot Data User Guide. Concentration values higher than 3 mg/L are considered at high risk.[19,23]

Age was divided into three categories (40–49, 50–59, and 60 years and older). Household location was classified as urban and rural areas. Marital status was categorized as single, married, divorced, or widowed, whereas education level was classified into primary school, secondary school, college, and above. Multimorbidity was based on the number of respondents self-reported diagnoses of chronic non-communicable diseases (NCDs) that were previously made by health professionals. Examples of such NCDs are diabetes, hypertension, heart disease, stroke, lung diseases, asthma, cancer, arthritis, and depression. Multimorbidity was defined as two or more chronic NCDs.[24]

Simple logistic regression was used to compare categorical variables. Those found significant in the bivariate

analysis at the p-value < 0.25 level were entered into multivariate analysis. Multiple logistic regression was used to estimate the odds ratio (ORs) and 95% confidence interval (95% CIs) for hs-CRP levels according to BMI by using underweight as a reference, whereas WC, WHR, and WHtR using normal as reference. First, we built a model that includes all variables found significantly associated with hs-CRP levels. Second, we constructed an adjusted model (Model 1 presented in Table 1) for assessing the relationship between obesity indicators and hs-CRP levels. Model 1 was adjusted by age (40–49, 50–59, greater than 60 years), sex, education (no education, primary school, secondary school, and college and above), marital status (single, married, or divorced/widowed), residence (rural or urban), and multimorbidity (no or yes).

All data were analyzed using a statistical package software. A p-value of 0.05 was considered to indicate statistical significance.

Results

A total of 3,386 participants aged 40 years and over were initially included in this study. Table 1 presents the characteristics of the study population, particularly the overall baseline characteristics of participants according to obesity indicators. Measurements using BMI showed that participants identified as overweight or obese were more than 50% female, aged 40–49 years old, and had high-risk CRP. Moreover, 50.4% were married, 68.3% obtained college or above education, 54.5% were living in urban areas, and 60.1% had multimorbidity. Measurements using WC and WHR indicators revealed the same characteristic pattern in obese/overweight participants: 63.4% and 80.6% were female, 51.9% and 74.5% were aged 50–59 years old, 56.3 and 78.3% had high-risk CRP, 51.8% and 75.1 were divorced or widowed, 47.9% and 70.5% obtained college or above education, 51.3% and 74.1% were living in urban areas, and 61.2% and 82.3% had multimorbidity, respectively. Measurements using WHtR showed that participants identified as overweight or obese were 33.6% female, 32.2% aged ≥ 60 years old, 28.2% had high-risk CRP, 39.5% were single, 30% either had no education or only reached primary school, 32.0% were living in urban areas, and 36.8 % reported multimorbidity.

Table 2 shows the associations among obesity indicators, other covariates, and hs-CRP levels. In the association between BMI and hs-CRP, overweight/obese respondents were likely to be young female (40–49 years old), to have high-risk hs-CRP, to be married, to obtain higher education level (college and above), to live in urban areas, and to have multimorbidity (p-value < 0.001 for all variables). In the association between WC and hs-CRP, respondents with increased WC were likely to have multimorbidity. However, they were less likely to be male, old (age ≥ 60 years), to have normal hs-CRP, to be single, to obtain lower education (no education), and to live in rural areas (p-value < 0.001 for all variables). In the

Table 1. Characteristics of Participants (n = 3,386) by Obesity Indicators in Indonesian Family Life Survey-5 2014–2015

Characteristic	Category	BMI (%)			WC (%)		WHR (%)		WHtR (%)	
		Underweight (n = 477)	Normal (n = 1,275)	Overweight/Obese (n = 1,634)	Normal (n = 1,857)	Increased (n = 1,529)	Normal (n = 1,002)	Increased (n = 2,348)	Normal (n = 2,666)	Increased (n = 537)
Sex	Male	15.8	46.2	38.0	79.9	21.0	43.1	56.9	73.5	26.5
	Female	12.8	31.2	56.0	36.6	63.4	19.4	80.6	66.4	33.6
Age (years)	40–49	7.1	34.9	57.9	54.3	45.7	33.4	66.6	72.8	27.2
	50–59	9.7	35.3	55.1	48.1	51.9	25.5	74.5	69.2	30.8
	≥ 60	20.6	40.6	38.7	59.3	40.7	30.0	70.0	67.8	32.2
CRP	Normal	14.2	39.9	45.8	57.5	42.5	31.5	68.5	86.0	14.0
	High risk	13.5	28.2	58.4	43.7	56.3	21.7	78.3	71.8	28.2
Marital status	Single	21.1	46.1	32.9	71.1	28.9	43.4	56.6	60.5	39.5
	Married	12.3	37.3	50.4	56.6	43.4	30.7	69.3	70.7	29.3
	Divorced or widowed	18.9	38.0	43.1	48.2	51.8	24.9	75.1	66.5	33.5
Education	No education	23.8	42.6	33.6	59.1	40.9	31.3	68.7	68.9	31.1
	Primary school	15.2	39.9	44.9	56.5	43.5	30.5	69.5	68.2	31.8
	Secondary school	9.1	33.9	57.0	52.1	47.9	29.5	70.5	71.0	29.0
	College and above	5.7	26.0	68.3	45.1	57.9	20.3	79.7	73.6	26.4
Residence	Rural	18.4	41.0	40.6	62.5	37.5	34.2	65.8	71.2	28.8
	Urban	10.6	34.9	54.5	48.7	51.3	25.9	74.1	68.0	32.0
Multimorbidity	No	14.6	40.0	45.5	58.6	41.4	32.4	67.6	71.0	29.0
	Yes	12.0	27.9	60.1	38.8	61.2	17.7	82.3	63.2	36.8

Notes: BMI: Body Mass Index; WC: Waist Circumference; WHR: Waist-to-Hip Ratio; WHtR: Waist-to-Height Ratio; CRP: C-Reactive Protein.
[a]underweight (BMI < 18.50 kg/m^2), normal weight (BMI 18.50–22.99 kg/m^2), overweight (BMI 22.99–24.99 kg/m^2), and obese (≥ 25.00 kg/m^2).
[b]normal (WC < 90 cm for men, < 80 cm for women) and increased (WC ≥ 90 cm for men, ≥ 80 cm for women).
[c]normal (WHR < 0.9 for men, WHR < 0.85 for women) and increased (WHR ≥ 0.9 for men, WHR ≥ 0.85 for women).
[d]normal (WHtR 0.46 to 0.42) and increased (WHtR > 0.46).
[e]normal (hs-CRP ≥ 3) and high risk (hs-CRP < 3).

Table 2. C-Reactive Protein by Obesity Indicators (n = 3,386) in Indonesian Family Life Survey-5 2014–2015

Characteristic	Category	BMI		WC		WHR		WHtR	
		Overweight/Obese (%) (n = 1,634)	p-value	Increased (%) (n = 1,529)	p-value	Increased (%) (n = 2,348)	p-value	Increased (%) (n = 537)	p-value
Sex			< 0.001		< 0.001		< 0.001		< 0.001
	Female	56.0		63.4		80.6		33.6	
Age (years)			< 0.001		< 0.001		< 0.005		< 0.050
	50–59	55.1		51.9		74.5		30.8	
	≥ 60	38.7		40.7		70.0		32.2	
CRP			< 0.001		< 0.001		< 0.001		< 0.050
	High risk	58.4		56.3		78.3		28.2	
Marital status			< 0.001		< 0.001		< 0.001		< 0.050
	Married	50.4		43.4		69.3		29.3	
	Divorced or widowed	43.1		51.8		75.1		33.5	
Education			< 0.001		< 0.001		0.090		0.234
	Primary school	44.9		43.5		69.5		31.8	
	Secondary school	57.0		47.9		70.5		29.0	
	College and above	68.3		57.9		79.7		26.4	
Residence			< 0.001		< 0.001		< 0.001		0.051
	Urban	54.5		51.3		74.1		32.0	
Multimorbidity			< 0.001		< 0.001		< 0.001		< 0.001
	Yes	60.1		61.2		82.3		36.8	

Notes: BMI: Body Mass Index; WC: Waist Circumference; WHR: Waist-to-Hip Ratio; WHtR: Waist-to-Height Ratio; CRP: C-Reactive Protein.

Table 3. Logistic Regression between Obesity Indicators and C-Reactive Protein (n = 3,386) in Indonesian Family Life Survey-5 2014–2015

Characteristic	BMI	WC	WHR	WHtR
	Overweight/Obese	Increased	Increased	Increased
Number of participants (n = 3,386)	1,643	1,529	2,348	537
High risk CRP, n (%)	(58.4)	(56.3)	(78.3)	176 (28.2)
Crude	0.829 (0.585–1.176)	1.042 (0.790–1.373)	1.234 (0.968–1.572)	1.845**(1.427–2.386)
Model 1***	0.847 (0.608–1.180)	1.151 (0.888–1.491)	1.278*(1.005–1.625)	1.980**(1.544–2.541)

Notes: BMI: Body Mass Index; WC: Waist Circumference; WHR: Waist-to-Hip Ratio; WHtR: Waist-to-Height Ratio; CRP: C-Reactive Protein.
*Significance at level 0.05; **Significance at level 0.01; ***Model 1 was adjusted for age (40–49, 50–59, ≥ 60 years old), sex, education (no education, primary school, secondary school, college, or above), marital status (single, married, or divorced/widowed), residence (rural or urban), and multimorbidity (no or yes).

association between WHR and hs-CRP, respondents with increased WHR were likely to be female, aged 50–59 years old, to have high-risk hs-CRP, to be divorced or widowed, to live in urban area, and to have multimorbidity. Furthermore, respondents with increased WHtR were less likely to be male, young (aged 40–49 years old), to have normal hs-CRP, to be married, and to not have multimorbidity.

The multiple logistic regression analysis showed significant associations among WHR, WHtR, and hs-CRP (Table 3). Compared with respondents with normal WHR, the multivariate-adjusted OR (95% CI) of the high-risk hs-CRP level was 1.278 (1.005–1.625) for those with increased WHR. With regard to the association between WHtR and hs-CRP, in comparison with respondents with normal WHtR, the multivariate-adjusted OR (95% CI) was 1.980 (1.544–2.541) for those with increased WHtR; Model 1; p-values were < 0.05 and < 0.01 for WHR and WHtR, respectively. However, no association was observed among BMI, WC, and hs-CRP.

Discussion

This study determined the association between obesity indicators and CRP levels among Indonesian adults. The study found that approximately 50% Indonesian adults were overweight or obese, as measured by BMI. All obesity indicators (e.g., BMI, WC, WHR, and WHtR) were associated with hs-CRP levels. WHR and WHtR also associated with high-risk hs-CRP levels after adjusting for age, sex, education, marital status, residence, and multi-morbidity; these findings were in accordance with previous studies.[25-27]

Our findings showed that all obesity indicators were associated with hs-CRP levels. A previous study suggested a positive correlation among BMI, WC, and hs-CRP, whereas WHR is moderately and significantly correlated with hs-CRP.[27] Another study also indicated that CRP increases as WHtR increases.[28] We observed that over-

weight/obese respondents with increased WC and WHR likely have high-risk CRP. Ikeoka, *et al.,*[29] revealed that cytokines and other inflammatory mediators (IL-6-soluble receptors, IL-6 and C-reactive protein) may be involved in the formation of systolic and diastolic ventricular dysfunction, as shown by echocardiography in obese individuals normotensive.

After adjusting for covariates, compared with BMI and WC, the current study indicated that WHR and WHtR are associated with high-risk hs-CRP levels. A previous study suggested that abdominal obesity indicators are better compared to the one with BMI, WHR, and WHtR, which play substantial roles in mortality due to cardio-metabolic diseases.[29] Another study reported that WHR is a reflection of fat distribution in different parts of the body and a good indicator of central obesity that is significantly carried with cardiovascular risk factors.[26] Lee, *et al.,*[30] conducted a meta-analysis among more than 88,000 adults who are mostly from Asian countries. The study suggested that WHtR is the best discriminator for hypertension, diabetes, and dyslipidemia;[30] whereas BMI is the poorest differentiator for cardiovascular risk factors.[31] Another meta-analysis that includes more than 300,000 adults indicates that compared to BMI and WC, WHtR identifies cardio-metabolic risks better.[32] A previous Korean study reported that compared with BMI, WHtR better predicts the presence of metabolic syndrome.[33] A prospective study among the Mongolian men in China indicates that WHtR is a robust predictor of ischemic stroke.[34] Thus, the present study suggests that WHR and WHtR may be used to predict hs-CRP levels related to future morbidity risks.

The association between WHtR and hs-CRP levels have been identified both in Indonesia and other countries. It might be because WHtR is a proxy for central (visceral) adipose tissue, which has recently received attention as a marker of 'early health risk'. Furthermore, abdominal obesity which is defined by WHtR is more effective than BMI to reflects the visceral fat. The WHtR also has been viewed as a simple primary risk assessment tool that identifies more subjects at "cardiometabolic risk" than the combination of BMI and WC. It is suggested that WHtR predicts central obesity, which is associated with hs-CRP levels, is also applied in Indonesia.

The strength of the present study is it used national survey data; hence, the study results are quite representative. However, several limitations are observed, such as 1) the study is cross-sectional; thus, the causal relationships among the observed variables cannot be inferred, 2) Only one hs-CRP measurement was used and thus might not perfectly indicate the long-term inflammatory status of participants.

Conclusion

In summary, BMI, WC, WHR, and WHtR as obesity markers are associated with hs-CRP levels. However, only WHR and WHtR are associated with the high-risk hs-CRP levels. Therefore, WHR and WHtR can predict central obesity associated with hs-CRP levels, which can be used to initiate early prevention for future morbidity risks among Indonesian adults. Furthermore, a longitudinal study is needed to establish the relationship between obesity markers and CRP levels.

Abbreviations

CRP: C-reactive Protein; BMI: Body Mass Index; WC: Waist Circumference; WHR: Waist-to-Hip Ratio; WHtR: Waist-to-Height Ratio; IL-6: Interlukin-6; IFLS: Indonesian Family Life Survey; hs-CRP: High-Sensitivity-C-Reactive Protein; NCDs: Non-communicable Diseases.

Ethics Approval and Consent to Participate

The analyses used secondary data that is publicly available. Ethics approval was obtained by RAND Corporation and Survey Meter who fielded the survey.

Competing Interest

Author declares that there are no significant competing financial, professional, or personal interests that might have affected the performance or presentation of the work described in this manuscript.

Availability of Data and Materials

The dataset is publicly available and can be obtained free of cost upon registration from RAND Corporation's website.

Authors' Contribution

Yeni Mahwati conceived the study, participated in its design and acquired the dataset. Dieta Nurikka contributed to the interpretation of the data. Both authors were involved in the drafting of the manuscript and intellectual content. Both authors have read and approved the final draft.

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