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Comparison of high sensitive c reactive protein levels between metabolically healthy and unhealthy obese

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Introduction: Overweight and obesity are associated with risks of several comorbidities, yet not all individuals with obesity condition having equal metabolic risks, suggesting the presence of a subgroup known as metabolically healthy obese (MHO) and metabolically unhealthy obese (MUHO). Obesity is characterized by chronic low-grade inflammation, with C-reactive Protein (CRP) serving as a key inflammatory marker. Research on high-sensitivity CRP (hs-CRP) levels across different obesity categories, especially MHO and MUHO, remains limited.
Aim: This study aims to compare hs-CRP levels across various levels of obesity, particularly in MHO and MUHO individuals.
Methods: This analytical cross-sectional study included subjects aged 18-60 from Denpasar with a BMI over 25 kg/m2. Subjects with chronic or acute inflammatory conditions were excluded. Comparative tests were utilized for analysis.
Results: The study comprised 40 men and 20 women with an average age of 35.6 years. Of these, 35% were classified as MHO and 65% as MUHO. The analysis revealed no significant difference in hs-CRP levels between the MHO and MUHO groups ($p = 0.108$), likely due to similar age and BMI distributions resulting in comparable levels of inflammation.
Conclusion: The analysis demonstrated no significant variation in hs-CRP levels between MHO and MUHO groups.

Keywords: hs-CRP, MHO, MUHO.

INTRODUCTION

Obesity is a global health problem that affects not only developed countries, but also developing countries. Obesity is not only associated with an increase in the incidence of metabolic and cardiovascular diseases, but will also have an impact on economic sectors where the costs incurred to overcome these problems become very large. For this reason, strategic efforts are needed to overcome the problem of obesity so that mortality and morbidity due to obesity can be suppressed. Obesity is a chronic disease characterized by a pathophysiological process that causes an increase in adipose tissue mass thereby increasing the risk of morbidity and mortality.[1] Both overweight and obesity will increase the risk of various comorbid diseases, such as insulin resistance, type 2 diabetes mellitus, cancer and cardiovascular disease[2]. In obese people develop resistance to the cellular action of insulin with a characteristic reduced ability of insulin to inhibit hepatic glucose synthesis and glucose uptake in fat and muscle. Obesity-related insulin resistance is a major risk for cardiovascular disease and type 2 diabetes mellitus.[2]

However, not everyone with obesity has a high risk of metabolic diseases or death, which suggests there is a group of healthy obese populations called metabolically healthy obese (MHO). MHO has a characteristic of the absence of metabolic disorders such as dyslipidemia, insulin resistance, hypertension.[3] The health of metabolically healthy obese individuals depends largely on their adipogenic potential. Adequate adipogenic capacity will support the energy-buffering activity of adipose tissue, ensuring the protection of metabolic health. However, for each individual, there is a limited capacity for adipogenic processes to take place and limits to which adipose tissue can develop. Once that threshold is exceeded, a critical sequence of events begins, leading to metabolic complications and becoming metabolically unhealthy obese (MUHO).[4]

Some studies show that increased C-reactive protein (CRP) is closely related to obesity. Adipose tissue secretes IL-6 which then contributes to increased CRP in obesity. CRP levels increase in obesity, especially in obese

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with metabolic disorders, and decrease with diet for weight loss in obese women. In a study of a weight loss program for 2 months, it was found that weight loss, followed by a significant decrease in CRP.[5] In the study, Lavanya and colleagues found that there was a positive correlation between BMI and High-Sensitivity C-Reactive Protein (hs-CRP). The average hs-CRP levels are higher in obese and overweight compared to normal BMI.[6] Bevita and colleagues in their research found that there was a significant increase in hs-CRP in individuals with type 2 DM when compared to people without type 2 DM. Increased hs-CRP was also found in obese people with type 2 diabetes compared to obese people without type 2 diabetes.[7] Until now, there has been limited research on hs-CRP levels at various levels of obesity, especially in MHO and MUHO.

This study examined the comparison of hs-CRP levels at various levels of obesity, especially in MHO and MUHO.

MATERIALS AND METHODS

This study used an analytical cross-sectional design. The research was conducted at the Diabetes Center of RSUP Prof. dr. I G.N.G. Ngoerah Denpasar and at Prodia Denpasar Clinical Laboratory in 2020 with consecutive sampling. This study has been approved by research ethics commission number 776/UN14.2.2.VII.14/LT/2020. The subjects of this study were adult at aged 18-60 years who met the criteria for obesity with a body mass index of ≥ 25 kg / m^2 and were willing to sign informed consent.

Metabolically healthy obesity (MHO) is a clinical concept that subgroup of people with obesity who do not show cardiometabolic abnormalities. There is no standardized definition for enforcing MHO. MHO is defined by the absence of metabolic disorders and cardiovascular disease, type 2 DM, dyslipidemia, hypertension, and atherosclerotic cardiovascular disease (ASCVD) in people with obesity.[7] Metabolically unhealthy obesity (MUHO) is defined as the presence of metabolic and metabolic disorders characterized by two or more of the following criteria: triglycerides >150 mg/dL (1.7 mmol/L) or being treated 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 increased HDL-C levels; systolic blood pressure >130 mmHg or diastolic blood pressure >85 mmHg or being treated for hypertension, fasting blood sugar >100 mg/dL (5.6 mmol/L), or T2DM.[8]

The exclusion criteria in this study are all subjects who suffer from acute infectious/inflammatory diseases, suffer from severe chronic diseases (such as kidney, liver, lung and heart disease) and malignancy, are receiving anti-diabetic drug therapy both oral and injection. Sixty subjects were enrolled in this study.

The data analysis used in this study is a descriptive analysis carried out to describe the basic characteristics of each variable and group as well as frequency distribution in the form of average and standard deviation of hs-CRP levels and comparison of average hs-CRP levels in the MHO and MUHO groups. Furthermore, a normality test was carried out and continued with comparative analysis using the Mann-Whitney test because the data was not normally distributed.

RESULTS

The subjects consisted of 40 men and 20 women. The average age was 35.6 years. There were 21 samples (35%) classified as MHO, and 39 samples (65%) classified as MUHO. The sample characteristics of the examination of several parameters can be seen in table 1.

The results of the analysis showed no significant difference in hs-CRP levels between the MHO and MUHO groups ($p = 0.108$).

DISCUSSION

Some studies show that increased CRP is closely related to obesity. Adipose tissue secretes IL-6 which then contributes to increased CRP in obesity. CRP levels decrease with diet for weight loss in obese women. In a study of 227 healthy obese women, 199 people completed a weight loss program for 2 months, it was found that the average weight loss from 65.8 to 62.8 kg ($p < 0.001$), followed by a significant decrease in CRP from an average of 0.63 mg /L to 0.41 mg / L ($p < 0.001$).[5] In vitro studies and animal experiments have also shown that TNF-α is an important component of insulin resistance. TNF-α will increase in the adipose tissue of obese mice and interfere with sensitivity to insulin. Obesity can cause chronic inflammation by stimulating adipocyte tissue to express more cytokines. There is a significant relationship between levels CRP with body mass index (BMI).[8] CRP is synthesized in hepatocyte cells in response to IL-6 stimulation, and levels are found to be increased in obese populations.[9] A study conducted by Jager in 1999 found in 2484 individuals where CRP levels as an early marker of cardiovascular events and associated with the incidence of obesity.[10] Research by *Bennet et. al.* in 2014 in Jamaica, Central America, found an increase in CRP levels associated with obesity and components of metabolic syndrome.[11-13]

High-sensitivity C-reactive Protein (hs-CRP) is a marker of systemic inflammation that has been extensively studied in various health conditions. While hs-CRP is commonly associated with cardiovascular risk, its relationship with diabetes is less clear. One possible explanation for the lack of a strong association between hs-CRP and diabetes is the multifactorial nature of diabetes development. Diabetes is a complex metabolic disorder influenced by

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Table 1. Sample Characteristics

No	Variable	Average (±SD) MHO (n=21)	Average (±SD) MUHO (n=39)	Average (±) Total (n=60)
1	Age	34.62 (7.201)	36.13 (8.285)	35.6 (7.894)
2	Height	163.71 (9.572)	166.13 (7.420)	165.28 (8.238)
3	Weight	80.43 (11.591)	83.56 (13.260)	82.47 (12.691)
4	Body mass index	30.00 (3.500)	30.16 (3.254)	30.10 (3.313)
5	Waist circumference	96.62 (6.614)	100.13 (8.417)	98.90 (7.957)
6	Fasting blood glucose	94.00 (4.743)	96.44 (10.133)	95.58 (8.668)
7	Systolic blood pressure	120.48 (6.690)	122.05 (5.221)	121.50 (5.771)
8	Diastolic blood pressure	75.7143 (5.07093)	77.9487 (6.14709)	77.1667 (5.84885)
9	HDL levels	51.52 (5.344)	39.74 (7.074)	43.87 (8.603)
10	Triglyceride levels	97.14 (25.572)	179.77 (111.763)	150.85 (99.228)
11	hs-CRP levels	3.7429 (3.85092)	2.1026 (2.16946)	2.6767 (2.94632)

HDL: high density lipoprotein; hs-CRP: high sensitive C-Reactive Protein; MHO: metabolically healthy obese; MUHO: metabolically unhealthy obese

Table 2. Mann Whitney Analysis

	hs-CRP levels	p-value
MUHO	3.7429 (3.85092)	0.108
MHO	2.1026 (2.16946)	

factors such as insulin resistance, beta-cell dysfunction, genetic predisposition, and lifestyle factors. In contrast, hs-CRP primarily reflects systemic inflammation and may not directly capture the specific pathways involved in diabetes pathogenesis. Furthermore, studies have shown that while hs-CRP is a valuable marker for predicting cardiovascular risk, its utility in predicting diabetes risk is less consistent. For example, the study by Pradhan et al. (2001) highlighted the association of hs-CRP with cardiovascular risk but did not find a significant correlation with the development of diabetes.[14] Similarly, the meta-analysis by Ridker et al. (2005) suggested that while hs-CRP is useful for assessing cardiovascular risk, its relationship with diabetes risk remains uncertain.[15] These findings suggest that while hs-CRP is a valuable marker for certain health outcomes, its association with diabetes may be influenced by the complex interplay of various factors involved in diabetes pathophysiology. Further research is needed to elucidate the specific mechanisms underlying the relationship between hs-CRP levels and the development of diabetes.

In line with our study, no significant difference was found in high-sensitivity C-reactive Protein (hs-CRP) levels between the metabolically healthy obese (MHO) and metabolically unhealthy obese (MUHO) groups. This is likely due to the minimal difference in average age and body mass index of the subjects in the MHO and MUHO groups, indicating that metabolic differences have not greatly affected hs-CRP levels in individuals within these groups. As a result, the inflammatory response remains relatively consistent in both the MHO and MUHO cohorts.

The study's limitations include a small sample size, potential lack of generalizability due to the specific location, variability in defining metabolically healthy obesity (MHO), a cross-sectional design offering a snapshot rather than longitudinal data, and lack of adjustment for confounding factors like diet and physical activity.

CONCLUSION

The results of the analysis showed no significant difference in hs-CRP levels between the MHO and MUHO groups.

CONFLICT OF INTERESTS

The authors have stated that they have no competing interests.

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ETHICS CONSIDERATION

This study has been approved by research ethics commission number 776/UN14.2.2.VII.14/LT/2020.

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AUTHOR CONTRIBUTIONS

IMPD: main author and corresponding author; IMSS: co-author; IBAN: co-author; WG: co-author; MRS: co-author; AAGB: co-author; KS: co-author. All of the authors collaborated in the study design, execution, and follow-up of the clinical cases, data analysis and results formulation, and writing of the publication. All authors have authorized the submission of the work. The manuscript has neither been published nor submitted elsewhere for publication. The final manuscript was reviewed and approved by all writers.

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