https://doi.org/10.31689/rmm.2023.30.4.335

ORIGINAL PAPERS

Monocyte to HDL Cholesterol Ratio (MHR) and Monocyte to Lymphocyte Ratio (MLR) in Overweight and Obese Women

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Abstract

Background: The prevalence of obesity and overweight in Indonesian women will continue to increase. Obesity and overweight conditions are often associated with low-grade inflammatory conditions and metabolic syndrome. The ratio of monocytes to HDL cholesterol (RMH) and the ratio of monocytes to lymphocytes (RML) are easy tests to monitor inflammation associated with increased body mass index and cardiovascular disorders due to metabolic syndrome.
Objective: To analyze the differences in RMH and RML in obese and overweight women.
Methods: The cross-sectional study was conducted in the outpatient laboratory at the Diponegoro National Hospital (RSND). This study included 55 overweight women (BMI 25.00 – 29.99 kg/m2) and 55 obese women (BMI ≥ 30 kg/m2), healthy, aged 25-45 years. Research subjects were excluded with the criteria of not having hypertension, liver disorders, and diabetes mellitus. RMH is obtained by dividing the absolute monocyte count by HDL cholesterol. RML is obtained by dividing the absolute monocyte and lymphocyte counts. Monocyte and lymphocyte numbers were obtained by examining a Complete Blood Count (CBC) using an automatic hematology analyzer. HDL cholesterol levels were measured by enzymatic methods using a clinical chemistry analyzer. Statistical analysis with the Mann-Whitney test.
Results: There is a difference in RMH between obese and overweight women (p = 0.003). There was no difference in RML (p = 0.342) between the two groups.
Conclusion: Obese women have a significantly higher RMH than overweight. RMH can be used as an assessment of inflammatory conditions and is used as a clinical alert for various health problems in obese and overweight women.

Keywords: obesity, overweight, MHR, MLR

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BACKGROUND

Obesity is a complex and multifactorial health problem that occurs throughout the world[1], including in Indonesia. Obesity and overweight defined as excess or abnormal fat condition that affects health. Data from the World Health Organization (WHO) for 2021 shows that the number of adults who are overweight in Indonesia has doubled in the last 20 years. Data from Basic Health Research (RISKESDAS) in 2018 shows an increase in the prevalence of obesity in Indonesia from 14.8% (2013) to 21.8%[2]. The prevalence of obesity in women is higher than in men[3]. WHO data for 2015 shows that overweight in adulthood reached 2.3 billion people[4]. Overweight is found more in women[4]. The prevalence of overweight is higher than obesity.

Excess body weight and high body mass index (BMI) are also associated with various health problems, including an increased risk of insulin resistance (IR), type 2 diabetes, non-alcoholic fatty liver disease (NAFLD), atherosclerosis, dyslipidemia, degenerative disorders, including dementia, airways, and even malignancy[5]. Obesity and overweight are associated with a low-grade chronic inflammatory state characterized by abnormal cytokine production, increased acute phase proteins and activation of inflammatory signaling pathways[6]. Several studies have shown an increase in inflammatory markers in obese patients[7]. The inflammatory process causes endothelial dysfunction. Endothelial dysfunction is an early process of the development of atherosclerosis in obesity[8].

High calorie intake that exceeds energy needs will trigger an increase in fat storage in the body[9]. Dyslipidemia in obesity is in the form of increased triglycerides (TG) and free fatty acids, decreased high density lipoprotein (HDL) cholesterol with HDL dysfunction and normal or slightly increased low-density lipoprotein (LDL) cholesterol with increased small dense LDL[10]. Hypercholesterolemia can increase production Proinflammatory cytokines especially interleukin-1α, tumor necrosis factor-α, C-reative protein (CRP) thus triggering oxidative stress, due to an increase in free radicals from lipid peroxidation reactions. Pro inflammatory cytokine secretion in hypercholesterolemia conditions activates inflammatory cells, especially monocytes.

Previous studies have shown that monocyte levels are higher in obesity than populations with normal body mass index (BMI) because they play a role in chronic inflammatory processes along with adipocytokines[11]. Inflammatory cells such as lymphocytes and macrophages have been shown to infiltrate adipose tissue in obesity[12]. Monocyte-to-LDL ratio was also previously studied in the occurrence of cardiovascular disease[13]. The ratio of monocytes to HDL cholesterol (RMH) has been reported as a new predictor and prognostic indicator of mortality and morbidity in many diseases[12]. RMH was also found to correlate with CRP levels in disease-related chronic inflammation, such as cardiovascular disease, kidney disease, aortic aneurysm, intracerebral hemorrhage, hypertension, and metabolic syndrome[12]. The ratio of monocytes to HDL cholesterol (RMH) can be prognostic for cardiovascular disorders and is relatively easy to perform[9]. HDL cholesterol levels are lower in the obese group than the normal group[14]. A study by Septiyanti et al., 2020 showed that there was no difference in HDL levels between obesity and normal BMI[15].

Studies in recent decades have shown that both adults and children are obese with increased total leukocytes which appear to be mostly related to monocytes; however, other types of leukocytes such as lymphocytes also increased[16]. The leukocyte count is an indicator of inflammation where the ratio of monocytes to lymphocytes (RML) is a marker of inflammation in various conditions including tumors, obesity, cardiovascular disease and other diseases[17]. In addition to monocytes, lymphocytes also increase in the obese population[11]. Increased RML also occurs in cardiovascular disorders[18]. RML is a simple, inexpensive, and reproducible index of the number of monocytes and lymphocytes in the peripheral blood[18]. RML levels have never been studied in obese and overweight women, so the researchers wanted to see the difference.

METHOD

This research is an analytic observational with a cross-sectional approach. The sample is healthy overweight and obese women who voluntarily come to the outpatient laboratory at the Diponegoro National Hospital (RSND) Semarang. BMI inclusion criteria (overweight = 25-29.99 kg/m2; obesity = ≥ 30 kg/m2), age 25 - 45 years and willing to participate in the study. Subjects who had a history of liver disease, heart problems, diabetes mellitus were excluded from this study.

BMI is calculated by dividing body weight in kilograms by TB in meters squared, RMH is obtained by dividing the absolute monocyte count by HDL choles-

terol. RML is obtained by dividing the absolute monocyte and lymphocyte counts. Monocyte and lymphocyte counts were obtained through a Complete Blood Count (CBC) examination using the Sysmex XS-500i automatic hematology analyzer. HDL cholesterol levels were measured using a clinical enzymatic method using the Indiko chemistry analyzer clinical tool.

Data analysis included descriptive analysis (distribution, frequency and mean) and different test. Univariate analysis was performed on each variable to determine the characteristics of the sample. The data normality test was carried out with the Kolmogorov-Smirnov method. The different test uses the Mann-Whitney U test.

Ethical clearance was obtained from the Medical and Health Research Ethics Committee, Faculty of Medicine, Diponegoro University Semarang, No: 32/EC/KEPK/FK-UNDIP/III/2020.

RESULT

Total 110 women that met the criteria participated in the study. The distribution of subject characteristics is presented in Table 1.

Table 1. Characteristic Subject

Variable (n= 110)	Obesity (n = 55)	Overweight (n = 55)	p^*
	Median (min – max)	Median (min – max)	
Age (years)	35 (25-45)	34 (25-45)#	0,291 μ
Height (m)	1,585 (1,45-1,695)	1,605 (1,47-1,665)	0,555 μ
Weight (kg)	73,2 (63-126,6)	66,5 (60-81,8)	0,005 μ*
BMI (kg/m2)	33,9 (30-52)#	28 (25,3-29,8)	0,000μ*
HDL (mg/dL)	48 (26-71)	55 (5-102)	0,029 μ*
Lymphosite count (uL)	30 (19-44)	31 (21-45)	0,013 μ*
Monocyte count (uL)	6 (3 -9)#	6 (3-10)#	0,709μ

The number of samples in each group is 55 women with the same age range. The obese group had a lower median HDL (48 mg/dL) than the overweight group (HDL = 55 mg/dL). This is in contrast to the median body weight (73.2 kg), BMI (33.9 kg/m2) which was higher in the obese group than the overweight group (body weight = 66.5 kg, BMI = 28 kg/m2). The number of lymphocytes was higher in the overweight group than the obese group. There was no difference in the number of monocytes between the two groups.

Analysis of the differences in RMH and RML in obese and overweight women used the non-parametric Mann-Whitney U test of difference. The different test can be seen in Table 2.

Table 2. MHR and MLR difference between obese and overweight group

Variable (n= 110)	Obese (n = 55) Median (min – max)	Overweight (n = 55) Median (min – max)	p^*
MHR	9,32 (2,91-18,65)	6,9 (3,91–19,09)#	0,003*
MLR	5 (3 – 8,8)	5 (3 – 14)#	0,342

Notes : #Data does not normally distribute (p<0,05);
*p< 0,05= significant

The results of data analysis using the Mann – Whitney test showed that there were significant differences in the RMH parameter (p = 0.003) in obese and overweight women. There was no significant difference in the RML parameter (p = 0.342) in obese and overweight women.

DISCUSSION

Obesity in women is 28.6% which has the potential to cause various health problems such as diabetes mellitus, dyslipidemia, atherosclerosis and metabolic syndrome[19]. WHO 2014 data shows a prevalence of overweight 39% and obesity 13%[15].

Respondent obese group in this study had a higher RMH (p=0.003) than the overweight group. Akin *et al.*, 2018 study also stated that RMH was higher in obese women with polycystic ovary syndrome[12]. Stefano *et al.*, 2020 study showed higher RMH in populations with metabolic syndrome[20]. Monocyte ratio and HDL cholesterol (RMH) are associated with waist circumference, BMI and metabolic syndrome[20].

Low-grade inflammation is a condition that occurs in obesity[21]. Divas *et al*,. 2020 explained that monocytes experienced the highest increase in the obese group[11]. It is possible that there is increased infiltration of monocytes into adipose tissue, so that the number of monocyte types will also be higher. In accordance with the research of Vuong *et* al. 2014 proved that monocytes play an important role in the chronic inflammatory process caused by obesity[11]. Abnormal adipose production, adipokine secretion, oxidative stress and dysregulated proinflammatory responses in muscle and liver tissue contribute to the development of the metabolic syndrome. The secretion of proinflammatory cytokines in hypercholesterolemia activates inflammatory cells, especially monocytes, macrophages and lymphocytes[9]. Increased levels of C-reactive protein in obesity and overweight also stimulate endothelial cells to release Intercellular Adhesion Molecule-1 (ICAM-1), Vascular Cell Adhesion Molecule-1 (VCAM-1) and Monocyte Chemoattractant Protein-1. Release of Intercellular Adhesion Molecule-1 (ICAM-1), Vascular Cell Adhesion Molecule-1 (VCAM-1), Monocyte Chemoattractant Protein-1 (MCP-1) and increased free radicals (ox-LDL) can increase monocyte adhesion and infiltration against endothelial cells[9].

Interleukin-6 and Tumor Necrosis Factor-α have a negative correlation with High Density Lipoprotein (HDL) levels[9]. The mechanism of low HDL can also be caused by an increase in the release of proinflammatory cytokines, especially Interleukin-6, where these cytokines play a role in the process of inhibiting the action of the enzyme lipoprotein lipase in the blood circulation[22].

There was no difference in the monocyte to lymphocyte ratio (RML) in the obese group in the overweight group (p = 0.342). The results of this study are different from that of Stefano et al. 2020 that RML is lower in the group with metabolic syndrome than controls[20]. Research by Lin Yan Juan *et al*., 2018 showed in aortic dissection patients with metabolic syndrome that there was no difference in monocyte levels, but lymphocyte levels were different in the group that had died from cardiogenic shock[23], Research by Okty *et al*. 2021 stated that RML has a weak correlation with central obesity[24] Research from Putu et al,. 2021 showed no difference in RML in the controlled and uncontrolled type 2 diabetes mellitus group[25]. This study explains that RML is more useful for assessing complications of diabetes mellitus. the occurrence of metabolic syndrome at the onset of obesity[11]. Lymphocytes are also often associated with increased levels of adiponectin[21]. Increased levels in monocytes and lymphocytes increase in inflammatory conditions. This is explained in the research by Diva et al, 2020 that monocytes, lymphocytes and neutrophils have increased in the obese population[11]. In the overweight population it is also possible that inflammation occurs due to an increase in adipose tissue so that there is no difference in RML with the obese group. RML did not differ between the two groups, which could be due to the increase in lymphocyte and monocyte numbers which did not differ between the two groups. There was no difference in RML in the overweight and obese groups, possibly due to the weak correlation with obesity.

This study has not been able to determine the exact number of lymphocytes and monocytes in both groups.

CONCLUSION

Obese women have significantly higher RMH than overweight. RMH can be used as an assessment of inflammatory conditions in obese and overweight women. Obese and overweight women have no difference in RML. RML could not explain the inflammatory condition in both groups.

References

1. Aji NJ, Fitriani A. Role of Calcium on Vitamin D absorbtion among diabetic patient. Muhammadiyah J Nutr Food Sci. 2022;2(2)
2. Mahwati Y, Nurrika D. Obesity Indicators and C-reactive Protein in Indonesian Adults (≥ 40 years): The Indonesian Family Life Survey-5 2014–2015. Kesmas Natl Public Heal J. 2020;15(3):169–74.
3. Vaamonde JG, Álvarez-Món MA. Obesity and overweight. Med. 2020;13(14):767–76.
4. Noer ER, Rose S, Fajrani AM, Rachma DE, Limijadi EKS, Fitranti DY. High Waist to Height ratio (WHtR) Worsens Inflammatory And Adiposity Profiles In Adult Women With Abdominal Obesity. Jurnal Gizi dan Dietetik Indonesia (Indonesian Journal of Nutrition and Dietetics).2022;10(1):30-36.
5. Spyridaki EC, Avgoustinaki PD, Margioris AN. Obesity, inflammation and cognition. Curr Opin Behav Sci [Internet]. 2016;9(Figure 1):169–75. Available from: http://dx.doi.org/10.1016/j.cobeha.2016.05.004
6. Castro AM, Macedo-de la Concha LE, Pantoja-Meléndez CA. Low-grade inflammation and its relation to obesity and chronic degenerative diseases. Rev Médica del Hosp Gen México [Internet]. 2017;80(2):101–5. Available from: http://dx.doi.org/10.1016/j.hgmx.2016.06.011
7. Bhattacharjee R, Alotaibi WH, Kheirandish-Gozal L, Capdevila OS, Gozal D. Endothelial dysfunction in obese non-hypertensive children without evidence of sleep disordered breathing. BMC Pediatr. 2010;10.

8. Hasanah FH. Korelasi Jumlah Sel Monosit Dengan Kadar Kolesterol Total Pada Pasien Hiperkolesterolemia Di Rumah Sakit Xkota Kediri. J Wiyata. 2016;3(1):23–30.
9. Klop B, Elte JWF, Cabezas MC. Dyslipidemia in Obesity: Mechanisms and Potential Targets. Nutrients. 2013;5(4):1218–40
10. Humaira DI, Berawi KN, Morfi CW. Hubungan Obesitas Sentral dengan Hitung Jenis Leukosit pada Laki-Laki Dewasa di Lingkungan Universitas Lampung The Relation Between Central Obesity and Differential Count in Male With Obesity in Lampung University. 2020;10(April):43–8.
11. Jia C, Anderson JLC, Gruppen eg, Bakker SJL, Dulaaert RPF, Tietge UJF. High-Density Lipoprotein Anti-Inflammatory Capacity and Incident Cardiovascular Events. Circulation. 2021;143:1935–1945. DOI: 10.1161/CIRCULATIONAHA.120.050808.
12. Jaywant DJ , Bhalerao A , Ratnaparkhi V , Nisale S, Shamraj P, Kulkarni U , et al. Lipid Profile of the Patient with Acute Coronary Syndromes Undergoing Coronary Angiography (CAG) in Rural Costal Region of Maharashtra. Medicina Moderna - Modern Medicine. 2021; 28 (4): 397-400. https://doi.org/10.31689/rmm.2021.28.4.397
13. usta a, avci e, bulbul cb, kadi h, adali e. the monocyte counts to HDL cholesterol ratio in obese and lean patients with polycystic ovary syndrome. Reprod Biol Endocrinol. 2018;16(1):1–8.
14. KSL E, AP P, BW I. HUBUNGAN KADAR HbA1c DENGAN PERSENTASE MONOSIT PADA OBESITAS. Media Medika Muda [Online]. 2019 Oct;3(2). Retrieved from: https://ejournal2.undip.ac.id/index.php/mmm/article/view/6050.
15. Arisoy A, Altunkas F, Karaman K, Karayakall M, Çelik A, Ceyhan K, et al. Association of the Monocyte to HDL Cholesterol Ratio with Thrombus Burden in Patients with ST-Segment Elevation Myocardial Infarction. Clin Appl Thromb. 2017;23(8):992–7.
16. Sitepu JN. Hubungan Indeks Massa Tubuh Dengan Profil Lipid Serum Sebagai Faktor Risiko Penyakit Kardiovaskuler Pada Mahasiswa Universitas HKBP Nommensen. Nommensen J Med [Internet]. 2017;3(1):7–13. Available from: https://uhn.ac.id/files/akademik_files/1804200832_2017_Nommensen Journal of Medicine Vol 3 No 1 Juli 2017_6.
17. Septiyanti S, Seniwati S. Obesity and Central Obesity in Indonesian Urban Communities. J Ilm Kesehat. 2020;2(3):118–27.
18. Yoshimura A, Ohnishi S, Orito C, Kawahara Y, Takasaki H, Takeda H, et al. Association of peripheral total and differential leukocyte counts with obesity-related complications in young adults. Obes Facts. 2015;8(1):1–16.
19. Yue S, Zhang J, Wu J, Teng W, Liu L, Chen L. Use of the monocyte-to-lymphocyte ratio to predict diabetic retinopathy. Int J Environ Res Public Health. 2015;12(8):10009–19.
20. Alfhili MA, Alsughayyir J, Basudan AM, Alsubki R, Alqahtani S, Awan ZA, et al. Monocyte–Lymphocyte Ratio and Dysglycemia: A Retrospective, Cross-Sectional Study of the Saudi Population. Healthcare. 2022;10(11):2289.
21. Harbuwono DS, Pramono LA, Yunir E, Subekti I. Obesity and central obesity in indonesia: Evidence from a national health survey. Med J Indones. 2018;27(2):53–9.
22. Battaglia S, Scialpi N, Berardi E, Antonica G, Suppressa P, Diella FA, et al. Gender, BMI and fasting hyperglycaemia influence Monocyte to-HDL ratio (MHR) index in metabolic subjects. PLoS One. 2020;15(4):1–15.
23. Ikeda Y, Hisakawa N, Ohguro T, Nishiuchi J, Kumon Y. Differential white blood cell count and metabolic syndrome in Japanese men. Atherosclerosis [Internet]. 2016;252(2016):e181–2. Available from: http://dx.doi.org/10.1016/j.atherosclerosis.2016.07.846
24. Han SN, Leka LS, Lichtenstein AH, Ausman LM, Schaefer EJ, Meydani SN. Effect of hydrogenated and saturated, relative to polyunsaturated, fat on immune and inflammatory responses of adults with moderate hypercholesterolemia. J Lipid Res [Internet]. 2002;43(3):445–52. Available from: http://dx.doi.org/10.1016/S0022-2275(20)30151-6
25. Zhang Z, Hu Q, Hu T. Association of lymphocyte to monocyte ratio and risk of in-hospital mortality in patients with cardiogenic shock: A propensity score matching study. Int J Gen Med. 2021;14:4459–68.
26. Prahalnitya O, Hendrianingtyas M. Correlation of Waist Circumference with Monocyte Lymphocyte Ratio, Hemoglobin, and Hba1c in Obesity. Pakistan J Med Heal Sci. 2021;15(7):2036–8.
27. Adnyani PY, Mahartini NN, Herawati S, Mulyantari NK, Lestari AAW. Comparison of neutrophil to lymphocyte ratio (NLR) and lymphocyte to monocyte ratio (LMR) values in controlled and uncontrolled type 2 diabetes mellitus (t2dm) patient. Bali Med J. 2021;10(2):798–801.
28. Adnyani PY, Mahartini NY, Herawati S, Mulyantari NK, Lestari AAW. Comparison of Neutrophil to Lymphocyte Ratio (NLR) and Lymphocyte to Monocyte Ratio (LMR) values in Controlled and Uncontrolled Type 2 Diabetes Mellitus (T2DM) Patient. Bali Med J.2021;Vol 10 No.2:798-801.