Rahmawati_Obesity_Effect_on_Homeostasis.pdf

by Rahmawati Minhajat

Obesity Effect on Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) Value in Various Metabolic Syndrome (MS) Components

Syahrir Parawansyah*,[1], Husaini Umar*, Makbul Aman Mansyur*, Syakib Bakri*, Hasyim Kasim*, Himawan Sanusi*, Rahmawati Minhajat* and Arifin Seweng**

*Department of Internal Medicine, Faculty of Medicine, Hasanuddin University, Makassar, Indonesia., **Department of Biostatistics, Faculty of Public Health, Hasanuddin University, Makassar, Indonesia.

ABSTRACT Insulin resistance plays a major role in the pathophysiology of MS. HOMA-IR has proven to be a strong examination to assess insulin resistance. Differences in the prevalence of the MS are also caused by the diagnostic criteria used. Obesity is an absolute requirement for the criteria for MS according to the IDF compared to other components, while NCEP ATP III only requires the number of components. The purpose of this study was to determine the effect of obesity on HOMA-IR values on various components of the MS. The study was cross-sectional, in healthy male subjects aged 40-65 years. The research was conducted at various health facilities in Makassar. Subjects were assessed for blood pressure, abdominal circumference, fasting blood sugar, HDL cholesterol, triglycerides and HOMA-IR. Tertile 3 HOMA-IR is considered as insulin resistance. Then the samples were divided into five groups based on obesity and the number of MS components (including the NCEP ATP III and IDF criteria) and compared each HOMA-IR with the non-obese + group without other MS components (reference group). Of the total 102 samples that took part in the study, the increase in the proportion of subjects suffering from insulin resistance was by the number of components of MS that were disrupted and the presence of obesity. HOMA-IR values in Obese subjects + 2-4 components of the MS were significantly higher than the reference group. HOMA-IR values in Obese + 0-1 subjects in the MS component were significantly higher than the reference group, and HOMA-IR values in Non-Obese + 1- 3 subjects in the MS were not significantly different from the reference group. Obesity (whether accompanied by or without other components of the MS) is very influential on the value of HOMA-IR.

KEYWORDS Obesity, HOMA-IR, Metabolic Syndrome

Introduction

Insulin resistance plays a major role in the pathophysiology of MS. Insulin resistance is often associated with visceral adiposity, glucose intolerance, hypertension, dyslipidemia, hyperglycemia, endothelial dysfunction, and an increase in inflammatory markers [1]. Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) has proven to be a strong check for insulin resistance. However, several studies have shown that there is a large variability in the HOMA-IR level threshold to define IR [2], [3]. Understanding the pathogenesis of insulin resistance is becoming increasingly important as a guide to future therapy as well as health and economic policies [4].

DOI:10.5455/IJMRCR.Obesity-Effect-on-HOMA-IR-Value
First Received: April 15, 2019
Accepted: May 11, 2019
Manuscript Associate Editor: Ivan Inkov (BG)

[1]Syahrir Parawansyah; Department of Internal Medicine, Faculty of Medicine, Hasanuddin University, Jalan Perintis Kemerdekaan Km. 11 Tamalanrea, Makassar, 90245, Indonesia.; Email: syach028@gmail.com

Table 1 Description of HOMA-IR and MS Components.

	Variable	N	%
Blood pressure	<130/85	28	27.5
	≥ 130/85	74	72.5
Fasting glucose	Fasting glucose <100mg/dL	63	61.8
	Fasting glucose Fasting glucose ≥ 100mg/dL	39	38.2
HDL	HDL≥ 40	57	55.9
	HDL<40	45	44.1
TG	TG<150	46	45.1
	TG≥ 150	56	54.9
Obesity	Non-Obese	30	29.4
	Obese	72	70.6
HOMA-IR	Tertile I (0.36 – 0.76)	36	35.3
	Tertile II (0.77 – 2.64)	32	31.4
	Tertile III (2.65 – 7.48)	34	33.3
Obese and components of MS	Obese + 2-3-4 components	58	56.9
	Non obese + 1-2-3 components	20	19.6
	Obese + 0-1 components	14	13.7
	Non obese + 3 components	6	5.9
	Non obese + 0 components	4	3.9

Table 2 Distribution of Obese and various components of MS Based on insulin resistance.

Group	Obese and MS other components		Insulin Resistance		Total
			Non-IR	IR	
1	Obese + 2-3-4 components	n	30	28	58
		%	51.7 %	48.3 %	100.0 %
2	Non obese + 3-4 components	n	5	1	6
		%	83.3 %	16.7%	100.0 %
3	Obese + 0-1 components	n	9	5	14
		%	64.3 %	35.7 %	100.0 %
4	Non obese + 1-2 components	n	20	0	20
		%	100.0 %	0.0 %	100.0 %
5	Non obese + 0 components	n	4	0	4
		%	100.0 %	0.0 %	100.0 %
Total		n	68	34	102
		%	66.7 %	33.3 %	100.0 %

The prevalence of MS always varies in each region, depending on geographical and sociodemographic factors, as well as the diagnostic criteria used. MS Criteria NCEP ATP III and IDF are criteria for MS, which are often used mainly in the Asian region [5]. Several studies compare the components of MS, including regarding differences between MS definition criteria between NCEP ATP III and IDF especially in predicting diabetes mellitus and disease cardiovascular [6], [7], [8]. Obesity by IDF is absolute requirement criteria for MS whereas NCEP ATP III only requires several components [9], [10]. This study aims to look at the effect of obesity on HOMA-IR on various components of MS required by NCEP ATP III and The IDF, in healthy adult men.

Material and Methods

This study was an observational study with a cross-sectional study, which was conducted at various health facilities in Makassar, Indonesia, from March to September 2018.

Study population

Male subjects, aged 40-65 years, not taking anti-diabetic, anti-dyslipidemia, anti-hypertension drugs and or at least stopped taking the drug for more than a month, outpatients, did not appear to be sick and were willing to take the study.

Ethics Statement

The study was approved by the Ethics Committee of Faculty of Medicine Hasanuddin University. Written informed consent was obtained from each participant.

Data collection

Sampling was obtained by examining blood pressure, waist circumference, fasting blood sugar, HDL cholesterol, triglycerides and HOMA-IR. Tertile 3 HOMA-IR is considered as insulin resistance. Abnormalities of the results of examination are included in the components of the MS, including the component of obese (waist circumference ≥ 90 cm), component of increased triglycerides (≥ 150 mg / dL), component of HDL cholesterol reduction (<40 mg / dL), component of increased blood pressure (≥ 130/85 mmHg), and components of fasting blood sugar disorders (≥ 100 mg / dL). Then divided into five groups based on obesity and the number of components of the MS. Group I: Obese + 2,3, and 4 other components of the MS, Group 2: Non-obese + 3-4 components of other MSs, Group 3: Obese + 0-1 components of other MSs, and Group 4: non obese + 1 and 2 other components of the MS. Then compared each average HOMA-IR with group 5: non obese + without other MS components (reference group).

Statistical analysis

All data were analysed using SPSS statistical software (version 22.0). Statistical analysis performed is descriptive statistical calculations, frequency distribution and independent-t statistical tests. All reported p values; values <0.05 were considered statistically significant.

Results

One hundred two male subjects obtained were aged between 40-65 years, with a mean of 51 ± seven years in Makassar. The mean waist circumference is 93.23 ± 10 cm, and HOMA-IR is 2.18 ± 1.8. Based on tertile HOMA IR values, the subjects were considered Insulin Resistance (IR) if they had HOMA-IR values IR≥2.65. (Table 1) The increase in the proportion of subjects suffering from RI was by the number of components of MS that were disrupted and the presence of obesity. The highest proportion of IR subjects was found in group I (obese plus 2 or more other MS components), which was 48.3%. Whereas from 24 of group 4 subjects (not obese and only 0, 1 or 2 other MS components), all of them did not suffer from IR (0.0%).(Table 2)

Comparison of HOMA-IR values based on obesity and MS component, with Non Obese + 0 MS Components as control (reference group), it was found that the HOMA-IR values in group 1 (Obese subjects with 2.3 and 4 other MS components) were significantly higher, which is 2.79 compared to 0.59 (p <0.001), the HOMA-IR value in group 2 (Obese subjects + 0 and 1 other MS component) is significantly higher, which is 2.00 compared to 0.59 (p <0.05), and the HOMA-IR values in group 3 (Non Obese subjects with 1, 2 and 3 other MS components) were not significantly different from the reference group (each with p> 0.05). So from the results of this comparison, it was found that Obese subjects (whether accompanied or without a disturbing component of MS) had significantly higher HOMA-IR values than Non-Obese subjects. (Table 3)

Discussion

In the obese group with 2 or more components the MS definition of IDF criteria while in the non-obese group with 3 or more components is the definition of the MS criteria NCEP ATP III (modification 2005) without obese [9], [10]. The proportion of IR and HOMA-IR values in obese groups with 2 or more components higher than non-obese groups with 3 or more components. This shows that the criteria of the MS IDF have a higher HOMA-IR value than the modified without obese ATP III. Chackrewarthy et al (2013) [11], obtained from 1358 healthy men aged 30-65 years, indicating that HOMA-IR in male subjects with MS (NCEP ATP III without obese) was higher than that of MS IDF (Obese + min 2 component of MS), which is 2.49 ± 1.5 vs 4.05 ± 5.7. This shows that obesity contributes to increased insulin resistance in MS IDF subjects compared to ATP III without obese. In contrast to Bhowmik et al (2015) study [12], from 863 healthy men over the age of 20 in rural Bangladesh, showed no difference between HOMA-IR in male subjects with MS (NCEP ATP III without obese) compared to criteria IDF (Obese + min 2 components of MS) namely 2.9 (2.7-3.2) vs 2.9 (2.6-2.9), the difference in these results is thought to be caused by differences in the study population. This shows that ethnicity and subject metabolic conditions also determine the HOMA-IR value.

In this study, the proportion of subjects suffering from IR was by the existence of obesity and the number of components of MS that were disrupted. HOMA-IR 2.65 cut-off in this study was taken from tertile 3 HOMA-IR, several previous population-based studies have shown a cut off of HOMA –IR based on a percentile (60th-90th) [3]. One of them was by researcher Do et al. (2010) [13], in Thailand in 738 subjects aged ≥35 years, with a normal Body Mass Index and fasting blood sugar, getting a cut off value of 1.55. But another study in Italy by Miccoli et al. (2005) [14] in healthy adult subjects got a cut-off value of 2.5. The impact of obesity and the number of components on HOMA-IR has supported previous studies of Lina Y et al. (2009) [16] in 137 obese male subjects in Indonesia showing a positive correlation between HOMA-IR and central obese (r = 0.29, p = 0.001) with an average HOMA-IR of 1.9 ± 1.1. Research in the SMART Study (2011) [16] examined 2611 subjects, 70% of which

Table 3 Description of HOMA-IR and MS Components.

Variable		N	%
Blood pressure	<130/85	28	27.5
	≥ 130/85	74	72.5
Fasting glucose	Fasting glucose <100mg/dL	63	61.8
	Fasting glucose Fasting glucose ≥100mg/dL	39	38.2
HDL	HDL≥ 40	57	55.9
	HDL<40	45	44.1
TG	TG<150	46	45.1
	TG≥ 150	56	54.9
Obesity	Non-Obese	30	29.4
	Obese	72	70.6
HOMA-IR	Tertile I (0.36 – 0.76)	36	35.3
	Tertile II (0.77 – 2.64)	32	31.4
	Tertile III (2.65 – 7.48)	34	33.3
Obese and components of MS	Obese + 2-3-4 components	58	56.9
	Non obese + 1-2-3 components	20	19.6
	Obese + 0-1 components	14	13.7
	Non obese + 3 components	6	5.9
	Non obese + 0 components	4	3.9

were adult men with arterial artery disorders aged 59.6 ± 10.4. It was found that the greater the number of components of the subject MS, the greater the HOMA-IR will increase ($p < 0.001$).

From the results of the researchers' investigation, there are no comparative data on obese grouping and various components of the MS as was done in this study. The results showed that obesity was a major factor in increasing HOMA-IR and insulin resistance. These results also support IDF criteria which require absolute obesity in the definition of MS. Central obesity is an example of body fat accumulation which is dangerous because lipolysis in this area is very efficient and is more resistant to the effects of insulin than adipocytes in other regions. Adipose tissue also makes and releases some adipocytokines. The most important adipocytokine is TNF-α, which has the role of inducing insulin resistance through Glucose Transporter 4 (GLUT 4) and increasing the release of free fatty acids. [17]

This study concludes that obesity, whether accompanied by or without other components of the MS, is very influential on the value of HOMA-IR and can even be said that obesity is a significant risk factor for insulin resistance. This study cannot only show a comparison in terms of the proportion of the number of subjects and the value of HOMA-IR at one time, while the component of MS is something dynamic over time, so it cannot show a causal relationship. Therefore, it is recommended that obese people over 40 years should be screened for MS, and also because IDF criteria (requires obesity) have a higher relationship with insulin resistance, so it is suitable for clinical and research related to insulin resistance.

References

1. Lann D, LeRoith D. Insulin resistance as the underlying cause for the metabolic syndrome. Med Clin North Am. 2007; 91:1063–77.

2. Antuna-Puente B, Disse E, Rabasa-Lhoret R, et al. How can we measure insulin sensitivity/resistance? Diabetes Metab. 2011; 37:179–88.

3. Gayoso-Diz, et al. Insulin resistance (HOMA-IR) cut-off values and the metabolic syndrome in a general adult population: effect of gender and age: EPIRCE cross-sectional study. BMC Endo Disord. 2013; 13:47.

4. Samuel, V. T. & Shulman, G. I. Mechanisms for Insulin Resistance: Common Threads and Missing Links. Cell, 2012;148, 852-871.

5. Aryal N, Wasti SP. The prevalence of metabolic syndrome in South Asia: a systematic review. Int J Diabetes Dev Ctries. 2016;36(3):255–62.

6. Sulistiowati E, Sihombing M. NCEP-ATP III and IDF criteria for metabolic syndrome predict type 2 diabetes mellitus. Univ Med. 2016; 35:46-55.

7. Pokharel DR, Khadka D, Sigdel M, et al. Prevalence of metabolic syndrome in Nepalese type 2 diabetic patients according to WHO, NCEP ATP III, IDF and Harmonized criteria. J Diabetes Metab Disord. 2014; 13:104.

8. Sav H, Mousa U, Koseoglular O, et al. The NCEP ATP III criteria may overestimate the diagnosis of metabolic syndrome in obese and overweight adolescents. Endo Abs. 2015;37. EP122.

9. American Heart Association; National Heart, Lung, and Blood Institute. Diagnosis and management of the metabolic syndrome: an American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement. Circulation. 2005; 112 (17): 2735-52.

10. Alberti KG, Zimmet P, Shaw J. Metabolic syndrome: a new world-wide definition: a consensus statement from the International Diabetes Federation. Diabet Med. 2006; 23(5):469-80.

11. Chackrewarthy S, Gunasekera D, Pathmeswaren A, et al. A Comparison between Revised NCEP ATP III and IDF Definitions in Diagnosing Metabolic Syndrome in an Urban Sri Lankan Population: The Ragama Health Study. ISRN Endocrinol. 2013; 32:176.

12. Bhowmik B, Afsana F, Siddiquee T, et al. Comparison of the prevalence of metabolic syndrome and its association with diabetes and cardiovascular disease in the rural population of Bangladesh using the modified National Cholesterol Education Program Expert Panel Adult Treatment Panel III and International Diabetes Federation definitions. J DiabetesInvestig.2015;6(3):280-8.

13. Do HD, Lohsoosthorn V, Jiamjarasrangsi W, Lertmaharit S, Williams MA. Prevalence of insulin resistance and its relationship with cardiovascular disease risk factors among Thai adults over 35 years old. Diabetes Res Clin Pract. 2010; 13:303–308.

14. Miccoli R, Biamchi C, Odoguardi L. Prevalence of the metabolic syndrome among Italian adults according to ATPII definition. Nutr Metab Cardiovasc Dis. 2005;13:250–254. DOI: 10.1016/j.numecd.2004.09.002.

15. Lina Y, Lawrence GS, Wijaya A, et al. Fibroblast Growth Factor 21 (FGF21), Free Fatty Acid (FFA), High Sensitivity C-reactive Protein (hsCRP) and Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) Among Indonesian Obese Non-Diabetic Males. InaBJ. 2009:1(3):76-80.

16. Verhagen SN, Wassink AM, van der Graaf Y, Gorter PM, Visseren FL. Insulin resistance increases the occurrence of new cardiovascular events in patients with manifest arterial disease without known diabetes. The SMART study. Cardiovascular diabetology. 2011 Dec;10(1):100.

17. Ritawaty R, Sukmawati IR, Patellongi I. Pathomechanism of insulin resistance in men with central obesity: correlation of GGT, GPx, hs-CRP and plasma total cysteine. The Indonesian Biomedical Journal. 2013 Aug 1;5(2):101-6.

Rahmawati_Obesity_Effect_on_Homeostasis.pdf

ORIGINALITY REPORT

%19	%12	%15	%9
SIMILARITY INDEX	INTERNET SOURCES	PUBLICATIONS	STUDENT PAPERS

PRIMARY SOURCES

1	www.ejmanager.com Internet Source	%3
2	"Posters", Diabetic Medicine, 12/2006 Publication	%1
3	univmed.org Internet Source	%1
4	link.springer.com Internet Source	%1
5	acrabstracts.org Internet Source	%1
6	bmcendocrdisord.biomedcentral.com Internet Source	%1
7	doaj.org Internet Source	%1
8	Jorge Navarro, Josep Redón, Luis Cea-Calvo, José V. Lozano et al. "Metabolic syndrome, organ damage and cardiovascular disease in treated hypertensive patients. The ERIC-HTA	%1

study", Blood Pressure, 2009
Publication

9	repo.unand.ac.id Internet Source	%1
10	"Abstracts of the EASD, Stockholm 2010", Diabetologia, 2010 Publication	%1
11	mafiadoc.com Internet Source	%1
12	"Study of the Risk Factors of Colorectal Adenoma in Women", Health Evaluation and Promotion, 2010 Publication	%1
13	Submitted to Universitas Hasanuddin Student Paper	%1
14	"Track 1 – Track 5", International Journal of Obesity, 05/2008 Publication	%1
15	"42nd EASD Annual Meeting of the European Association for the Study of Diabetes", Diabetologia, 2006 Publication	%1
16	ec.bioscientifica.com Internet Source	<%1
17	O. E. Johansen, K. I. Birkeland, E. Orvik, Ø.	<%1

Flesland et al. "Inflammation and coronary angiography in asymptomatic type 2 diabetic subjects", Scandinavian Journal of Clinical and Laboratory Investigation, 2009
Publication

---

18 Sawaek Weerakiet, Pongamon Bunnag, Bunyong Phakdeekitcharoen, Surapee Wansumrith et al. "Prevalence of the metabolic syndrome in Asian women with polycystic ovary syndrome: Using the International Diabetes Federation criteria", Gynecological Endocrinology, 2009
Publication
<%1

---

19 2016.wco-iof-esceo.org
Internet Source
<%1

---

20 Ajay Duseja, Ashim Das, Reena Das, R. K. Dhiman, Y. Chawla, A. Bhansali, Naveen Kalra. "The Clinicopathological Profile of Indian Patients with Nonalcoholic Fatty Liver Disease (NAFLD) is Different from That in the West", Digestive Diseases and Sciences, 2007
Publication
<%1

---

21 journals.ssu.ac.ir
Internet Source
<%1

---

22 journals.plos.org
Internet Source
<%1

23	Submitted to Monash University Sunway Campus Malaysia Sdn Bhd Student Paper	<1%
24	Submitted to University of Brighton Student Paper	<1%
25	Submitted to University of Westminster Student Paper	<1%
26	Császár, Albert, Ede Kékes, Tánja Abel, Renata Papp, István Kiss, and Sándor Balogh. "Prevalence of metabolic syndrome estimated by International Diabetes Federation criteria in a Hungarian population", Blood Pressure, 2006. Publication	<1%
27	Nurullah Çelik, Nesibe Andıran. "The relationship between serum phosphate levels with childhood obesity and insulin resistance", Journal of Pediatric Endocrinology and Metabolism, 2011 Publication	<1%
28	mdpi.com Internet Source	<1%
29	"Abstracts", Diabetologia, 2005 Publication	<1%
30	"Abstracts of the 10th Metabolic Syndrome Symposium", Obesity Reviews, 2014. Publication	<1%

31	Submitted to Indian Institute of Management Calcutta Student Paper	<%1
32	Aaron L. Slusher, Chun-Jung Huang. "Association of pentraxin 3 with insulin resistance and glucose response following maximal aerobic exercise in obese and normal-mass individuals", Canadian Journal of Physiology and Pharmacology, 2016 Publication	<%1

EXCLUDE QUOTES	ON	EXCLUDE MATCHES	< 5 WORDS
EXCLUDE BIBLIOGRAPHY	ON		