BLOOD GLUCOSE LEVELS ARE STRONGLY ASSOCIATED WITH VCAM-1 LEVELS IN PATIENTS WITH METABOLIC SYNDROME

(KADAR GLUKOSA DARAH SANGAT TERKAIT DENGAN KADAR VCAM-1 PADA PASIEN DENGAN SINDROM METABOLIK)

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ABSTRACT

Metabolic syndrome is a combination of metabolic risk factors that cause cardiovascular disease. These risk factors include high blood pressure, obesity, low HDL levels, hyperglycemia, and hypertriglyceridemia. This study aims to investigate the relationship between the components of metabolic syndrome and VCAM-1 levels, a marker of endothelial dysfunction, in patients with metabolic syndrome residing in RW 01 Cibeber, Cimahi. The study was conducted using a cross-sectional design with analytical descriptive methods. The respondents were 44 people who were taken by consecutive sampling. The components of the metabolic syndrome based on the NCEP ATP-III criteria include waist circumference, blood pressure, triglyceride levels as measured by the colorimetric GPO-PAP (Glycerol Peroxidase Phosphate Acid) enzymatic test, fasting blood glucose levels using the GOD-PAP (Glucose Aminoantypirin Oxidase-Peroxidase), and HDL cholesterol levels with the Trinder PEG (Polyethylene Glycol) precipitation method. VCAM-1 levels were examined using a quantitative enzyme-linked immunosorbent assay method as a marker of endothelial dysfunction. The results showed that most subjects had three or more of the five components (50%), and more than half of the subjects had high levels of VCAM-1 (63.6%). In addition, there was a significant relationship between the two components of the metabolic syndrome and VCAM-1 levels, namely fasting blood sugar ($p = 0.000$; $r = 0.570$) and triglycerides ($p = 0.001$; $r = 0.501$). Increased

blood sugar causes changes in insulin signaling, interfering with NO production and increasing pro-inflammation, which in turn increases VCAM-1. At high triglyceride levels, it causes oxidative stress, leading to damage to vascular tissue, which in turn increases VCAM-1.
Keywords: cardiovascular disease; E=endothelial dysfunction; metabolic syndrome, VCAM-1

ABSTRAK

Sindrom metabolik (SM) merupakan kumpulan faktor risiko metabolik yang berhubungan terutama pada penyakit kardiovaskular. Faktor risiko tersebut yaitu tekanan darah tinggi, obesitas, HDL rendah, hiperglikemia, dan hipertrigliserida. Penelitian ini bertujuan melihat hubungan komponen sindrom metabolik dengan kadar VCAM-1 sebagai penanda disfungsi endotel pada pasien sindrom metabolik di RW 01 Kelurahan Cibeber Cimahi. Penelitian dilakukan secara cross sectional dengan metode deskriptif analitik. Jumlah responden 44 orang diambil secara consecutive sampling. Kriteria yang digunnakan, yaitu kriteria NCEP ATP-III meliputi lingkar pinggang, tekanan darah, kadar trigliserida yang diukur melalui uji enzimatik kolorimetri GPO-PAP (Glyserol Peroxidase Phospat Acid), kadar glukosa darah puasa dengan metode GOD-PAP (Glucose Oxidase-Peroxidase Aminoantypirin), dan kadar kolesterol HDL dengan metode presipitasi Trinder PEG (Pholyethylene Glycol). Selanjutnya, dilakukan pemeriksaan kadar VCAM-1 dengan metode quantitative enzyme immune-assay sebagai penanda disfungsi endotel. Hasil penelitian didapatkan sebagian besar subjek memiliki tiga dari lima komponen yang ada (50%) dan lebih dari setengah subjek memiliki kadar VCAM-1 yang tinggi (63,6%). Selain itu, terdapat hubungan yang bermakna antara 2 komponen sindrom metabolik terhadap kadar VCAM- 1, yaitu kadar gula darah puasa (P=0,000; r=0,570) dan trigliserida (p=0,001; r=0,501). Gula darah yang meningkat menyebabkan perubahan pensinyalan insulin sehingga mengganggu produksi NO dan meningkatkan pro-inflamasi sehingga VCAM-1 akan meningkat. Pada kadar trigliserida yang tinggi menyebabkan terjadinya stress oksidatif sehingga menyebabkan kerusakan jaringan vaskuler yang akan meningkatkan VCAM-1.

Kata Kunci: d*isfungsi endotel; penyakit kardiovaskular; sindrom metabolik, VCAM-1*

INTRODUCTION

Metabolic syndrome is a cluster of risk factors for cardiovascular and metabolic diseases. These risk factors include insulin resistance, central obesity, dyslipidemia, and hypertension.[1] More than 36 million people die annually from non-communicable diseases (NCDs), and globally, the leading cause of death is cardiovascular disease.[2] Meanwhile, according to the 2018 Basic Health Research (Riskesdas), the incidence of heart and blood vessel disease, the most common cardiovascular disease, in Indonesia, has been increasing year by year.[3] Cardiovascular disease is associated with mortality and morbidity from metabolic syndrome. It may occur because the pathophysiology and criteria for metabolic syndrome refer to cardiovascular disease, resulting in the metabolic disorder known as metabolic syndrome.[4]

Globally, the incidence of metabolic syndrome is increasing rapidly. Epidemiological data show a prevalence of 20-25%. The total population with metabolic syndrome in Indonesia is 23.34%, with the prevalence being 26.2% in men and 21.4% in women [5] Adults with metabolic syndrome are twice as likely to die and three times as likely to have a heart attack or stroke.[6] The NCEP ATP-III, a standard criterion often used to determine metabolic syndrome, is characterized by its simplicity and reliability. 5 These criteria include: 1) Waist circumference >90 cm in men and >88 cm in women; 2) HDL <40 mg/dl in men and <50 mg/dl in women; 3) Triglycerides ≥150 mg/dl; 4) Blood pressure ≥130/85 mmHg; and 5) Fasting blood glucose (FBS) ≥110 mg/dl.[7]

Metabolic syndrome is associated with endothelial dysfunction due to the oxidative stress it causes, which plays a significant role in the pathophysiology of metabolic syndrome.[8] Endothelial dysfunction is a condition characterized by an imbalance of relaxing and contractile factors produced by endothelial cells. Endothelial damage caused by inflammation results in endothelial leakage, leading to increased vascular permeability. This condition also leads to increased expression of the adhesion molecule VCAM-1.[9] VCAM-1-1 is a marker for detecting endothelial dysfunction in cardiovascular disease. Circulating VCAM-1 reflects endothelial dysfunction and the inflammatory state of the blood vessels.[10] To date, no research has examined the relationship between VCAM-1 levels in patients with metabolic syndrome, despite the rapid increase in the incidence of metabolic syndrome. It allows the prevalence of metabolic syndrome in Cimahi City, especially in Cibeber Village, which is the area under the guidance of FK Unjani, to increase quite high and based on the profile data of the local health center, RW 01 is the area with the highest number of hypertension sufferers among other RW in Cibeber, so this study aims to determine the relationship between metabolic syndrome components and VCAM-1 levels in metabolic syndrome patients.

METHOD

This study used a descriptive analytical method with a cross-sectional design. The sample size was determined using the 2-proportion difference test formula, and a minimum sample size of 28 was required. Sampling was conducted using a consecutive sampling technique. The sample was selected according to the following inclusion criteria: subjects residing in the Cibeber area, RW 01 Cimahi, aged 17 years or older, and diagnosed with metabolic syndrome.

Data collection began with obtaining informed consent from subjects with metabolic syndrome to determine whether they had a history of cardiovascular disease, such as heart disease and stroke, which were exclusion criteria for this study. Next, metabolic syndrome components were assessed based on the NCEP-ATP III criteria, including blood pressure and waist circumference. Additionally, laboratory tests included serum triglyceride levels, fasting blood glucose levels, and HDL cholesterol levels, which were determined using the Trinder PEG precipitation method. A quantitative enzyme immunoassay was used to assess VCAM-1 levels in subjects who met the criteria for metabolic syndrome. Blood samples were drawn intravenously with the assistance of qualified laboratory personnel.

RESULT AND DISCUSSION

Characteristics of Research Subjects Based on Age and Gender in Residents of RW 01, Cibeber Village, Cimahi

This study was conducted on 44 subjects, with the majority aged 56-65 years (26 individuals, 59.1%). The results showed that those aged 56-65 years had the highest incidence of metabolic syndrome across all five components of metabolic syndrome. Of the five components of metabolic syndrome, the majority of subjects had high FBG levels (80.8%), stage I hypertension (61.5%), high triglycerides (53.8%), low HDL levels in women (66.7%) and men (62.5%), and increased waist circumference in women (77.8%) and men (25%). According to the American Medical Association, the prevalence of metabolic syndrome increases significantly with age.11 The age and gender distribution is shown in Table 1 below:

Table 1. Frequency distribution of respondent characteristics

Variable	N=44	
	n	Percentage (%)
Age		
26 – 35 tahun	1	2.3
36 – 45 tahun	0	0
46 – 55 tahun	7	15.9
56 – 65 tahun	7	15.9
>65 tahun	26	59.1
Gender		
Male	14	31.8
Female	30	68.2

Table 2. Characteristics of Research Subjects in RW 01, Cibeber Village, Cimahi Based on Metabolic Syndrome Components and Age

Variable	17-25 years		36-45 years		46-55 years		56-65 years		>65 years	
	n	Percentage (%)	n	Percentage (%)	n	Percentage (%)	n	Percentage (%)	n	Percentage (%)
Blood Pressure										
Pre-Hipertention	0	0	1	14.3	0	0	3	11.5	0	0
Hypertension Stage I	1	100	1	14.3	2	28.6	16	61.5	1	33.3
Hypertension Stage II	0	0	5	71.4	5	61.5	7	26.9	2	66.7
Fasting Blood Sugar Levels										
≥ 110 mg/dl	1	100	7	100	4	57.1	21	80.8	3	100
< 110 mg/dl	0	0	0	0	3	42.9	5	19.2	0	0
Triglyceride Levels										
≥ 150 mg/dl	0	0	6	85.7	1	14.3	14	53.8	3	100
< 150 mg/dl	1	100	1	14.3	6	85.7	12	46.2	0	0
Waist size										
Male										
< 90 cm	0	0	1	50	0	0	6	75	0	0
≥ 90 cm	1	100	1	50	1	100	2	25	2	100
Female										
< 80 cm	0	0	0	0	0	0	4	22.2	0	0
≥ 80 cm	0	0	5	100	6	100	14	77.8	1	100
HDL Levels										
Male										
≥ 40 mg/dl	1	100	0	0	0	0	3	37.5	1	50
< 40 mg/dl	0	0	2	100	1	100	5	62.5	1	50
Female										
≥ 50 mg/dl	0	0	1	20	1	16.7	6	33.3	0	0
< 50 mg/dl	0	0	4	80	5	83.3	12	66.7	1	100

Table 3. Characteristics of Research Subjects in RW 01, Cibeber Village, Cimahi, Based on Metabolic Syndrome Components and Gender

Variable	Male		Female	
	n	%	n	%
Blood Pressure				
Pre-Hipertention	2	14.3	2	6.7
Hypertension Stage I	8	57.1	13	43.3
Hypertension Stage II	4	28.6	15	50
Fasting Blood Sugar Levels				
≥ 110 mg/dl	13	92.9	23	76.7
< 110 mg/dl	1	7.1	7	23.3
Triglyceride Levels				
≥ 150 mg/dl	8	57.1		53.3
< 150 mg/dl	6	42.9		46.7
Waist size				
Male				
< 90 cm	7	50	0	0
≥ 90 cm	7	50	0	0
Female				
< 80 cm	0	0	8	26.7
≥ 80 cm	0	0	22	73.3
HDL Levels				
Male				
≥ 40 mg/dl	5	35.7	0	0
< 40 mg/dl	9	64.3	0	0
Female				
≥ 50 mg/dl	0	0	5	13.3
< 50 mg/dl	0	0	26	86.7

The study's results showed that the prevalence of metabolic syndrome was high. The majority of respondents in this study were women (n = 30, 68.2%) and men (n = 14, 31.8%). Based on gender, the highest prevalence of metabolic syndrome was low HDL levels in women (76.7%), increased waist circumference in women (73.3%), and high triglycerides (52.3%), and the highest prevalence of stage II hypertension in women (50%). This study aligns with Soewondo P, et al. (2010), who stated that, based on gender, using the NCEP-ATP III criteria, it was most common in women.[12]

Metabolic Syndrome Components in Patients with Metabolic Syndrome in Neighborhood Unit 01, Cibeber Village, Cimahi The number of metabolic syndrome components in patients with metabolic syndrome in Neighborhood Unit 01, Cibeber Village, Cimahi can be seen in the following table:

Table 4. Number of metabolic syndrome components in metabolic syndrome sufferers in RW 01, Cibeber Village, Cimahi

Number of SM Components	Number	Percentage (%)
3	22	50.0
4	8	18.2
5	14	31.8
Total	44	100.0

According to the NCEP ATP-III criteria, a person is considered to have metabolic syndrome if at least three of the five components are present. 13 The number of metabolic syndrome components found in metabolic syndrome patients

in RW 01, Cibeber Village, Cimahi, was 22 (50%). Of these, 14 (31.8%) had all components, and 8 (18.2%) had four of the five components.

Table 5. Characteristics of research subjects based on metabolic syndrome components in RW 01 Cibeber Village, Cimahi

Variable	Number	Percentage (%)
Blood Pressure		
Pre-Hipertention	4	9,1
Hypertension Stage I	21	47.7
Hypertension Stage II	19	43.2
Fasting Blood Sugar Levels		
≥ 110 mg/dl	36	81.8
< 110 mg/dl	8	18.2
Triglyceride Levels		
≥ 150 mg/dl	24	54.5
< 150 mg/dl	20	45.5
Waist size		
Male		
< 90 cm	7	50.0
≥ 90 cm	7	50.0
Female		
< 80 cm	8	26.7
≥ 80 cm	22	73.3
HDL Levels		
Male		
≥ 40 mg/dl	5	35.7
< 40 mg/dl	9	64.3
Female		
≥ 50 mg/dl	5	13.3
< 50 mg/dl	26	86.7

Based on Table 5, the characteristics of the study subjects based on metabolic syndrome components were: 36 (81.8%) had high FBG levels, or ≥ 110 mg/dl; 24 (54.5%) had triglyceride levels above normal, or ≥ 150 mg/dl; 7 (50%) had waist circumferences >90 cm in men and >80 cm in women; 22 (73.3%) had waist circumferences >80 cm in women; and 9 (64.3%) had low HDL levels, or <40 mg/dl in men and <50 mg/dl in women; 26 (86.7%) had waist circumferences >80 cm in women. The components of metabolic syndrome are associated with cardiovascular disease because metabolic syndrome is a cluster of cardiovascular disease risk factors, such as insulin resistance, central obesity, dyslipidemia, and hypertension.[8]

Description of VCAM-1 Levels in Metabolic Syndrome Patients in Residents of RW 01, Cibeber Village, Cimahi

After measuring VCAM-1 levels in metabolic syndrome patients in RW 01, Cibeber Village, Cimahi, the following data were obtained:

Table 6. Description of VCAM-1 levels in metabolic syndrome sufferers in RW 01, Cibeber Village

VCAM-1 Levels	Number	Percentage (%)
395-714	16	36.4
> 714	28	63.6
Total	44	100.0

Table 6 shows that more than half of the study subjects (28 individuals, 63.6%) had elevated VCAM-1 levels >714, while 16 subjects

(36.4%) had normal VCAM-1 levels (395-714). A previous study by Varona et al. (2019) also found elevated VCAM-1 levels in individuals with metabolic syndrome.[14] Another study by A. Basu et al. (2010) reported decreased VCAM-1 levels in subjects with metabolic syndrome after consuming strawberries.[15] All five components of metabolic syndrome can disrupt pro-inflammatory pathways and oxidative stress by increasing ROS. which leads to decreased endothelial function due to an imbalance between endothelial vasodilation and vasoconstriction. Individuals with endothelial dysfunction will experience decreased NO production and trigger pro-inflammatory activation in endothelial cells. During an inflammatory response. endothelial cell surface molecules, known as vascular adhesion molecules (ICAM and VCAM), function as adhesion molecules for leukocytes. VCAM-1 is a cellular adhesion molecule that attracts and accumulates inflammatory cells and regulates transendothelial migration. Furthermore, VCAM-1 is a soluble form of an adhesion molecule found in the circulation, which can indicate vascular inflammation and endothelial dysfunction.[9,10,16,17]

Relationship between Metabolic Syndrome Components and VCAM-1 Levels in Metabolic Syndrome Patients

Table 7 shows a significant relationship between fasting blood sugar levels and VCAM-1 levels, with a strong correlation ($p = 0.000$; $r = 0.570$), and between triglyceride levels and VCAM-1 levels, with a moderate correlation ($p = 0.001$; $r = 0.501$).

Table 7. Relationship between metabolic syndrome components and VCAM-1 levels in residents of RW 01, Cibeber Village, Cimahi

Variable	VCAM-1		
	R	R^2	P-Value
Waist Size	0.066	0.004	0.670
Systolic Blood Pressure	0.008	0.000	0.958
Diastolic Blood Pressure	0.027	0.001	0.864
Fasting Blood Sugar	0.570	0.325	0.000*
HDL Cholesterol	0.260	0.068	0.088
Triglyceride Levels	0.501	0.251	0.001*

The results of this study indicate no relationship between waist circumference and VCAM-1 levels. This research aligns with the findings of Charles et al. (2005), who also found no relationship between waist circumference and VCAM-1 levels.[18] However, research by Susan et al. (2009) found a relationship between waist circumference and VCAM-1 levels. [18] Increased visceral fat in the body causes increased oxidative stress and changes in the profile of pro-inflammatory adipokines. Furthermore, surrounding adipocytes stimulate the expression of increased adhesion molecules and endothelial cell apoptosis, leading to higher VCAM-1

levels.[19] The results of this study regarding the relationship between blood pressure and VCAM-1 levels are inconsistent with research conducted by Santina et al. (2009).[20] This is supported by research by Rodrigo, et al 2007, namely disruption of endothelial function due to hemodynamic stress, exposure to inflammatory cytokines and oxidative stress is characterized by an increase in various adhesion molecules, namely VCAM-1.[21] The results of further research stated that there was no relationship between HDL levels in the blood and VCAM-1 levels in this study. It differs from research conducted by Varona et al. (2019), which found a relationship between blood HDL levels and VCAM-1 levels.[22] High lipid levels cause damage and disruption of vascular tissue, which causes a decrease in NO activity, resulting in disruption of blood vessel vasodilation [19]

Elevated fasting blood sugar levels cause hyperglycemia, which disrupts insulin signaling and thus impairs NP production, resulting in vasodilation in resistance arteries.[19] This study's findings on the relationship between fasting blood sugar and VCAM-1 levels align with previous research by Giannella et al. (2017), which found increased VCAM-1 levels in patients with hyperglycemia.[8] Further research on the relationship between triglyceride levels and VCAM-1 levels aligns with research by Varona et al. (2019), which found a relationship between elevated blood triglyceride levels and elevated VCAM-1 levels. High blood triglyceride levels cause oxidative stress, which impairs vascular tissue function and leads to damage. Furthermore, continuous exposure of the endothelium to lipids leads to lipid accumulation in the endothelial layer, triggering interactions between leukocytes and the endothelial surface, ultimately resulting in impaired endothelial function and increased expression of adhesion molecules and leukocyte activation.[9]

CONSLUSION

Based on the research results, it can be concluded that, according to the NCEP ATP-III criteria, 22 individuals (50%) experienced three or more of the five components of metabolic syndrome in RW 01, Cibeber Village, Cimahi. VCAM-1 levels in RW 01, Cibeber Village, Cimahi, were mostly elevated (>714), with 26 individuals (63.6%). Fasting blood glucose and triglycerides were significantly associated with increased VCAM-1, highlighting their role in endothelial dysfunction among metabolic syndrome patients.

CONFLICT OF INTEREST

The author hereby declares that there is no conflict of interest in the scientific article written.

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