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ASSOCIATION BETWEEN METABOLIC SYNDROME AND CORONARY HEART DISEASE IN WOMEN PATIENTS AT DR. MOHAMMAD HOESIN HOSPITAL PALEMBANG

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ABSTRACT

Metabolic syndrome is still a risk factor for coronary heart disease. This study aims to analyze the association between metabolic syndrome and coronary heart disease in women. This study is an observational analytic study using a cross-sectional design on 138 samples selected using consecutive sampling method and data were collected through observation of the medical records of patients at dr. Mohammad Hoesin Palembang. The results showed that the highest proportion of metabolic syndrome components in the sample of this study was hypertension (54.3%), while the lowest was hyperglycemia (26.8%). This study found a significant relationship between metabolic syndrome and coronary heart disease in female patients (p = 0.047). Female patients with metabolic syndrome had a 2.218 times greater risk of developing coronary heart disease (PR 2.218 95% CI = 1.072 - 4.587).

Keywords: *metabolic syndrome, coronary heart disease, women*

1. INTRODUCTION

Coronary heart disease (CHD) is a cardiovascular disease caused by narrowing of the coronary arteries. CHD is also commonly referred to as coronary artery disease and ischemic heart disease. When the coronary arteries are narrowed, the blood and oxygen that reaches the heart muscle is reduced causing ischemia conditions.[4] Although narrowing can be caused by blood clots or coronary artery constriction, the most common cause is plaque buildup, which is called atherosclerosis.[14]

According to the NHANES database from 2013 to 2016 an estimated 18.2 million Americans over the age of 20 experience CHD with a total prevalence of 6.7%.[5] According to the Riskesdas report on 2018, the prevalence of heart disease based on doctor's diagnosis at all ages in Indonesia is 1.5%.[27] According to the WHO mortality data on 2016, CHD is the number 1 cause of death in the world. The results of the data show that there are 9 million deaths caused by CHD in the world.[32]

Metabolic syndrome consists of several physiological, biochemical, clinical, and metabolic factors that are interrelated that increase the risk of cardiovascular disease and type 2 diabetes mellitus.[12] The main components of the metabolic syndrome are central obesity, hypertriglyceridemia, low HDL levels, hyperglycemia, and hypertension.[15]

It is estimated that 12 - 37% of the Asian population and 12 - 26% of the European population have metabolic syndrome.[30] National-scale research in Indonesia using data from the fourth *Indonesian Family Life Survey* (IFLS) 2007/2008 states that the prevalence of metabolic syndrome in Indonesia is 21.66%

which corresponds to the estimated prevalence of global metabolic syndrome (20-25%) by the *International Diabetes Federation.* The research also states that the prevalence of metabolic syndrome in South Sumatra is 19.78%.[13]

One study stated that a study conducted by the *WISE Study* in women who underwent angiography of suspected CHD, that metabolic syndrome exacerbates the prognosis of CHD in women by about 5 times greater. This research also said that women with metabolic syndrome with diabetes have a higher chance of experiencing cardiovascular disease, especially CHD than men.[26] Other research also states that the interacting metabolic components that cause metabolic syndrome and diabetes increase the risk of cardiovascular disease more in women, especially older women than men.[25] It is estimated that the prevalence of metabolic syndrome among patients with CHD is 50% and the prevalence is higher in women.[15]

Previous research on the relationship between metabolic syndrome and the incidence of coronary heart disease in women showed a significant relationship. The results of research conducted by Kasai *et al*. (2008) showed a significant relationship between metabolic syndrome and metabolic syndrome in women. Female patients who have metabolic syndrome have a 2.32 times risk of developing coronary heart disease.[19]

2. METHOD

Research Design

This study is an observational analytic study with cross sectional design with the dependent variable is the incidence of coronary heart disease and the independent variable is metabolic syndrome that fulfills 3 of the 4 components that being studied, namely: blood pressure, HDL levels, triglyceride levels, fasting blood sugar levels and also age as an influencing factor in this study. These variables are taken by observing the patient's medical record. The study was conducted in November 2020.

Population and Sample

The population in this study were the medical records of all female patients diagnosed with coronary heart disease and non-coronary heart disease at dr. Mohammad Hoesin Palembang public hospital for the period of January 1, 2019 - December 31, 2019. Meanwhile, the sample taken was the medical records of female patients diagnosed with coronary heart disease and non-coronary heart disease with a complete history of the metabolic syndrome components recorded. The number of samples in this study were 138 samples that were taken using *consecutive sampling* technique.

Data Analysis

Data analysis used in this study was univariate analysis to describe each variable and bivariate analysis to see the relationship between metabolic syndrome and coronary heart disease incidence using *chi-square* test.

3. RESULT

The results of this study found 69 female patients with coronary heart disease and 69 female patients with non-coronary heart disease. The distribution of the metabolic syndrome is higher in female patients with coronary heart disease by 42.0%, whereas in female patients with non-coronary heart disease was 24.6%. The distribution of blood pressure variables with hypertension was higher in female patients without coronary heart disease compared to female patients with coronary heart disease (60.9% vs. 47.8%). Variable distribution of triglyceride levels with hypertriglyceridemia is higher in female patients with coronary heart disease compared to female patients without coronary heart disease (42.0% vs. 21.7%). Variable distribution of HDL levels who have low HDL is higher in female patients

with coronary heart disease compared to female patients without coronary heart disease (56.5% vs. 43.5%). The distribution of fasting blood sugar levels with hyperglycemia is higher in female patients with coronary heart disease compared to female patients without coronary heart disease (33.3% vs. 20.3%). In the age distribution, female patients with coronary heart disease were higher in the age over 50 years old (76.8%) and female patients with non-coronary heart disease were also higher in over 50 years old (65.2%). More details can be seen in table 1.

Table 1. Data Distribution of Metabolic Syndrome Variable, Blood Pressure, Triglyceride Levels, HDL Levels, Fasting Blood Sugar Levels, and Age

Variables	CHD (+)	CHD (-)
Metabolic Syndrome	29 (42.0%)	17 (24.6%)
Hypertension	33 (47.8%)	42 (60.9%)
Hypertriglyceridemia	29 (42.0%)	15 (21.7%)
Low HDL	39 (56.5%)	30 (43,5%)
Hyperglycemia	23 (33.3%)	14 (20.3%)
Age over 50 years	53 (76.8%)	45 (65.2%)

The results of the bivariate analysis between metabolic syndrome and the incidence of coronary heart disease shows significant association (p = 0.047) with an increased risk of 2.218 times (PR 2.218 95% CI = 1.072 - 4.587). More details can be seen in Table 2.

Table 2. Relationship Events Metabolic Syndrome with Coronary Heart Disease in Women Patients

Variable	Prevalence Ratio (95% CI)	p Value
Metabolic Syndrome	2.218 (1.072 to 4.587)	0.047

4. DISCUSSION

In the blood pressure data distribution, obtained more female patients suffering from hypertension (54.3%) and it is the highest proportion compared with other components of the metabolic syndrome. The results of this study are in line with research conducted by Marroquin *et al.* (2004) with the results that the proportion of hypertension (79%) was the highest compared to other components of the metabolic syndrome in female patients with coronary heart disease.[21]

The increased risk of hypertension in women is associated with age specifically due to hormonal influences at menopause.[1]

The association of increased blood pressure with cardiovascular disease does not appear to have a certain threshold. However, the risk of developing cardiovascular disease continues to increase with progressively high-pressure numbers. *Circumferential strains* cyclic, increased in high pressure arteries, can support smooth muscle cells to produce proteoglycans that

bind and retain LDL particles, increase their accumulation in the intima and accelerate the oxidative modification of LDL.[18] In the metabolic syndrome it can be associated with visceral adipose tissue which increases leptin secretion and decreases adiponectin secretion. Adiponectin is a protective factor against hypertension. Obesity and insulin resistance are also associated with an increase in angiotensin II.[28] A study on visceral obesity showed that *lipidomes*, such as *dihydroceramide,* diacylglycerols, triacylglycerols (triglycerides) increased while *phosphatidylcholines* decreased in people with central obesity.[20] The first study examining the relationship of *lipidome* in hypertension showed that *phosphatidylcholines* and *ether phosphatidylethanolamines were* reduced in people with hypertension compared with people with normotension.[11]

In the data distribution of triglyceride levels, it was found that more female patients had normal triglyceride levels (68.1%). These results may be influenced by hormonal factors in women, seeing that the subjects in this study were mostly women aged 51 and over. In a study conducted on patients with myocardial infarction, it was found that triglyceride levels were higher in the elderly female population.[31] A meta-analysis found that triglyceride levels were significantly elevated in post-menopausal women compared with pre-menopausal women. However, according to this study too, although age is a key predictor of differences in lipid levels between pre-menopausal and post-menopausal women, there are other possible genetic and environmental factors that may explain the mixed results of many studies.[2]

Hypertriglyceridemia along with low HDL levels are associated with uncontrolled type 2 diabetes where type 2 diabetes is a risk factor for coronary heart disease.[18] One study found that high triglyceride levels were significantly associated with elevated lipids and reduced component *fibrous plaque* after evaluation with an integrated backscatter intravascular ultrasound in women, but this was not found in men. Triglycerides in the blood vessels are transported by *very low-density lipoprotein* (VLDL) and chylomicrons. VLDL and chylomicrons are both large, therefore triglycerides cannot penetrate artery walls. Increased triglyceride levels can increase triglyceride-rich lipoproteins such as VLDL and chylomicrons. Remnants of lipoproteins can accumulate in the artery walls because their clearance is disturbed and contribute to the accumulation of lipids in the vessel walls. The debris can also promote an inflammatory response in the vascular wall. Thus, the accumulation of triglyceride-rich lipoproteins and their residues promotes the formation of atherosclerotic plaques.[33]

In the distribution of HDL levels, it was found that the distribution in female patients between low and normal levels was the same. The lipid profile (triglycerides, HDL, LDL) in women is influenced by hormonal factors. One study showed an increase in HDL levels until menopause and then decreased.[6] However, a study conducted in China showed no significant difference in HDL levels among different menopausal status groups.[35]

The theory suggests that HDL is associated with protection against atherosclerosis. It is stated that HDL can transport cholesterol from peripheral tissues to the liver for disposal, a process called *reverse cholesterol transport*. Therefore, a decrease in HDL levels can be a risk factor for cardiovascular disease.[10]

In the distribution of fasting blood sugar levels, it was found that patients with hyperglycemia were less (26.8%) and had the least proportion of other components. These results are in line with research conducted by Marroquin *et al.* (2004) where the proportion of hyperglycemia (40%) was the least compared to other metabolic

syndrome components in female patients with coronary heart disease.[21]

Research suggests that women with diabetes can suffer from more severe coronary heart disease than men with diabetes.[23] Several studies have also reported that the impact of diabetes on the risk of cardiovascular events is greater in women than in men. Research states that the cardioprotective effect on estrogen is weakened by diabetes which can inhibit the work of *ovarian aromatase inhibitors*.[16]

In the age distribution, it was found that the highest distribution on age is patients over 50 years old (71%). Research conducted by Samil (1994) and Palacios *et al.* (2010) found that the average age of menopause for women in Indonesia is 51 years. In this study, age as a risk factor is directly related to hormonal changes in women, particularly menopausal status.[24] This theory is supported by Agrinier *et al*. (2010) who found that the risk factors for CHD in that study (total cholesterol and LDL levels) were higher in the group of post-menopausal women.[3] Another study conducted by Carr (2003) found that all components of the metabolic syndrome as a risk factor for the occurrence of cardiovascular disease began to occur frequently with decreased estrogen in menopausal women.[7]

In healthy blood vessels, estrogen is involved in relaxation and expansion of blood vessels, aiding in the accommodation of blood flow. Estrogen affects the bioavailability of endothelium-derived nitric oxide (NO) and through NO mediation, increases *guanosine monophosphate*, leading to relaxation of vascular smooth muscle cells. As a result, decreased estrogen levels cause blood vessels to become stiffer.[22] Plus the loss of ovarian function due to menopause is associated with activation of the renin angiotensin-aldosterone system (RAAS), which leads to endothelial dysfunction, inflammation, and immune dysfunction.[35]

In this study, more female patients suffering from metabolic syndrome were coronary heart disease patients (42.0%) than non-coronary heart disease patients (24.6%). The results of this study are in line with the research conducted by Chen *et al.* (2008) with results showing that there were more metabolic syndrome sufferers in the group with coronary heart disease (48.7%) compared to the non-coronary heart disease group (23.4%).[8]

The results of the bivariate analysis between metabolic syndrome and coronary heart disease in female patients in this study indicated that there was a significant relationship between the two ($p = 0.047$). The results of this study are supported by the results of research conducted by Chen *et al.* (2008) which states that there is a significant relationship between metabolic syndrome and the incidence of coronary heart disease with a p value <0.01.[8] This result is also in line with research conducted by Marroquin *et al.* (2004) who stated that there was a significant relationship between female coronary heart disease patients with metabolic syndrome and female coronary heart disease patients with normal metabolic status with a value of $p = 0.03$.[21]

The results of this study are in line with the theory that metabolic syndrome is a risk factor for coronary heart disease. This can be seen from the *prevalence rate* in this study of 2.218 (PR> 1). These results imply that women with metabolic syndrome have a 2.218 times greater risk of coronary heart disease. These results are in line with research conducted by Kasai *et al.* (2008) that showed an odds ratio of 2.32 (95% CI = 1.11-4.86) which indicated that metabolic syndrome is a risk factor for coronary heart disease in women and has a risk of 2.32 times. In a study conducted by Lee *et al.* (2020) the presence of metabolic syndrome was independently associated with coronary heart disease incidence in women even after controlling for potential confounders with an *odds ratio* of 1.92 (95% CI = 1.31-2.81).[19]

In this study, the incidence of coronary heart disease and metabolic syndrome was more prevalent in women aged 51 and over. These results support the theories of the relationship between metabolic syndrome and coronary heart disease in women, which is largely influenced by hormonal factors. Estrogens have both physiological and biological effects on cardiovascular risk and insulin resistance. Estrogen has anti-inflammatory and antioxidant effects and protects cells from apoptosis. Estrogens also decrease hepatic glucose production and increase muscle glucose transport to improve insulin sensitivity which can promote lipolysis and prevent central obesity. Estrogen also has a vasodilator effect on the coronary arteries and maintains myocardial blood flow.[16] In addition, women showed lower salt sensitivity in blood pressure regulation before menopause and increased sensitivity to salt after menopause. Natriuresis pressure, renal hemodynamics, and tubular response to salt are affected by sex hormones and the renin angiotensin system (RAS). The RAS system may be regulated differently in men and women, with endogenous estrogens suppressing angiotensin receptor type-1 receptor expression and angiotensinogen synthesis.[26] Leptin, adiponectin, resistin, and TNF-α secreted from the accumulated fat mass are associated with insulin resistance, increasing the incidence of metabolic syndrome and its comorbidities and the risk of cardiovascular events.[16] In older women, the amount of visceral fat mass increases due to reduced effects of estrogen.[9]

Endothelial dysfunction is the most rapidly detectable functional disorder in the history of atherosclerosis and a strong predictor of cardiovascular events. Endothelial dysfunction is a pathological condition characterized by an imbalance of endogenous vasodilator and vasoconstrictor substances. In addition to insulin resistance and inflammation, central obesity may be a possible mechanism of effect on endothelial function. The metabolic syndrome can lead to a higher degree of endothelial dysfunction than the traditional multiple cardiovascular risk factors. Factors such as systemic inflammation and central obesity can cause endothelial dysfunction in the metabolic syndrome.[17]

5. CONCLUSION

Metabolic syndrome with coronary heart disease incidence in female patients at dr. Mohammad Hoesin Palembang has a meaningful relationship. Female patients with metabolic syndrome have a risk of developing coronary heart disease by 2.218 times. This is closely related to hormonal changes in women, especially menopausal status. This study has limitations, namely the medical record data does not have complete data on menopausal status and body mass index. Therefore, further research on the association of metabolic syndrome with coronary heart disease in women is recommended to add these two variables.

The results of this study support the theory of age as a risk factor for metabolic syndrome and coronary heart disease. However, age in women has a strong relationship with menopausal status. Therefore, future studies examining the relationship between metabolic syndrome and coronary heart disease should add a menopausal status variable so that it can be studied more accurately.

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