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THE EFFECT OF DYSLIPIDEMIA ON THE INCIDENCE OF CORONARY HEART DISEASE IN WOMEN

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Kata Kunci:
Dislipidemia; Penyakit Jantung Koroner; Wanita

Abstrak
Penyakit Jantung Koroner (PJK) merupakan salah satu penyakit tidak menular yang menyebabkan kematian tertinggi di dunia. Dislipidemia merupakan faktor risiko penting untuk PJK. Penelitian ini bertujuan untuk mengetahui hubungan dislipidemia secara detail meliputi peningkatan kolesterol, peningkatan trigliserida, peningkatan kolesterol LDL dan penurunan kolesterol HDL terhadap kejadian PJK pada wanita di RS PKU Muhammadiyah Yogyakarta. Metode Penelitian ini menggunakan desain kasus-kontrol yang melibatkan 58 wanita sebagai subjek penelitian. Kelompok kasus terdiri dari 29 wanita yang didiagnosis dengan PJK dan kelompok kontrol terdiri dari 29 wanita yang didiagnosis sebagai pasien non-PJK, termasuk penyakit paru kronis, pneumonia, gagal jantung, dispepsia dan keganasan. Penelusuran data melalui rekam medis dilakukan pada bulan Maret-September 2019. Hasil penelitian ini rentang usia pada kelompok kasus adalah 45-84 tahun dan pada kelompok kontrol adalah 42-90 tahun. Berdasarkan uji Chi-Square, terdapat hubungan bermakna antara dislipidemia (RO=7.04 (1.73-28.6), p=0.003), kadar kolesterol total tinggi (RO=5.14 (1.54-17,2), p=0,012), kadar kolesterol LDL tinggi (RO=9,286 (2,29-37,6), p=0,001) terhadap kejadian PJK pada wanita. Dari uji Chi-Square tidak terdapat hubungan bermakna antara kadar trigliserida tinggi (OR=2.16 (CI:0.62-7.49), p=0.358), kadar kolesterol HDL rendah (RO=2.554 (0.83-7.84), p=0.167) terhadap kejadian PJK pada wanita. Kesimpulan penelitian ini terdapat pengaruh dislipidemia meliputi peningkatan kolesterol dan kolesterol LDL terhadap kejadian PJK pada wanita di RS PKU Muhammadiyah Yogyakarta.

Keywords :
Dyslipidemia; Corona Heart Disease; Women

Abstract
Coronary heart disease (CHD) is one of the non-communicable diseases that causes the highest mortality in the world. Dyslipidemia is an important risk factor for CHD. This study aims to determine the relationship of dyslipidemia in detail including increased cholesterol, increased triglycerides, increased LDL cholesterol, and decreased HDL cholesterol on the incidence of CHD in women at PKU Muhammadiyah Hospital Yogyakarta.

This study used a case-control design involving 58 women as research subjects. The case group consisted of 29 women diagnosed with CHD and the control group consisted of 29 women diagnosed as non-CHD patients, including chronic lung disease, pneumonia, heart failure, dyspepsia, and malignancy. Data tracing through medical records was carried out in March-September 2019. The results of this study the age range in the case group was 45-84 years and in the control group was 42-90 years. Based on the Chi-Square test, there was a significant relationship between dyslipidemia (RO = 7.04 (1.73-28.6), p = 0.003), high total cholesterol levels (RO = 5.14 (1.54-17.2), p = 0.012), high LDL cholesterol levels (RO = 9.286 (2.29-37.6), p = 0.001) and the incidence of CHD in women. From the Chi-Square test, there was no significant relationship between high triglyceride levels (OR=2.16 (CI:0.62-7.49), p=0.358), low HDL cholesterol levels (RO=2,554 (0.83-7.84), p=0.167) and CHD incidence in women. The conclusion of this study is the effect of dyslipidemia including increased cholesterol and LDL cholesterol on the incidence of CHD in women at PKU Muhammadiyah Hospital Yogyakarta.

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INTRODUCTION

The main cause of hospitalization in developed countries is coronary heart disease (CHD), as well as the cause of death and health care costs worldwide (Farquhar et al., 2018). According to the World Health Organization (WHO) in 2018, in South East Asian Region (SEAR) countries in 2008, 7.9 million people died from Non-Communicable Diseases and 3.6 million of them were cardiovascular diseases. In Indonesia, one-third of the most common causes of death are dominated by heart disease, such as stroke and CHD, which occupy the top rankings (Hussain et al., 2016).

Dyslipidemia is a major risk factor for cardiovascular disease, especially in the formation of atherosclerosis due to increased levels of triglycerides (TG) and LDL cholesterol and decreased levels of High-Density Lipoprotein (HDL) cholesterol (Cabezas et al., 2018). Ages over 44 years old experienced a significant increase of 1.1% from the previous age category, with the highest age category being above 75 years, namely 4.7%, a 1% difference from the age category 65-74 years. According to data from Basic Health Research (2018), based on gender, the prevalence of CHD is higher in women concerning a doctor's diagnosis, which is 1.6% (Kurniawan et al., 2022). In Arabic, there have been studies on the incidence of coronary heart disease caused by dyslipidemia. The results show that the incidence is more common in women than men (Al-Zakwani et al., 2018) (Găman et al., 2020). The absence of research on the incidence of dyslipidemia that affects the incidence of CHD in women in Indonesia encourages researchers to determine the effect of dyslipidemia on the incidence of CHD in women.

Research conducted by Odden et,al (2011) on "The Impact of the Aging Population on Coronary Heart Disease in the United States" found a study result that In 2010, an estimated 156 million adults 35 to 84 years of age will be living in the US. This population is expected to increase by 28% to 200 million in 2040. The 65- to 84-year-old population is expected to increase by 89% percent over this period because of the aging of baby boomers and their longer life expectancy. The increase in coronary heart disease will reflect this population growth: incidence, prevalence, mortality, and cost are all expected to increase monotonically over the next 30 (Odden et al.,

2011). The difference in this study lies in the object of research carried out. This research could help identify and understand the extent to which dyslipidemia may be a risk factor in the development of coronary heart disease in women.

This study aimed to investigate the effect of dyslipidemia on the incidence of coronary heart disease in women. By conducting this study, researchers were able to determine whether the severity of dyslipidemia had a significant correlation with the risk of coronary heart disease in women. This can provide more information about how influential it is.

RESEARCH METHOD

This study was an analytic observational study with a case-control design that aims to assess the relationship between lipid profiles including total cholesterol, triglycerides, LDL cholesterol, and HDL cholesterol on the incidence of CHD in women at PKU Muhammadiyah Hospital, Yogyakarta. In this study, the selection of subjects based on observations of the medical records of patients with CHD as a case group and subjects of patients who were treated with a history of chest pain not due to CHD were the control group. Data were collected using a purposive sampling method according to the inclusion and exclusion criteria in this study. Determination of CHD and non-CHD is based on the diagnosis of an Internal Medicine Specialist.

Data collection was carried out for 6 months, from March 2019 to September 2019. From medical records for the period 2010 to 2019, there were 29 cases and 29 controls, so the total number of subjects was 58 subjects. Lipid profile data obtained from medical records. The lipid profile laboratory examination was carried out at the Clinical Laboratory of PKU Muhammadiyah Hospital Yogyakarta. For laboratory examination of lipid profile, internal and external quality control has been carried out.

The collected data was analyzed using the SPSS program version 20. Data analysis included bivariate analysis. Bivariate analysis is a statistical method that tests the relationship between two variables First, the data will be tested for normality using a normality test. The normality test is a technique used to determine whether a data set is from a normal distribution or not. Furthermore, to determine the relationship between case and control variables, data analysis was carried out using the chi-square test. Chi-square is a non-parametric test used to test the relationship or effect of two nominal variables.

RESULT AND DISCUSSION

The subjects of this study involved 58 people, consisting of 29 female patients with coronary heart disease and 29 female patients with non-coronary heart disease at PKU Muhammadiyah Yogyakarta Hospital according to the inclusion and exclusion criteria.

Table 1. Distribution of subjects by age group

Age (years)	CHD		Non-CHD	
	n	%	n	%
<51	4	13.8	4	13.8
51-60	3	10.3	6	20.7
>60	22	75.9	19	65.5
Total	29	100	29	100

Seen from Table 1, the distribution of subjects by age group, in the case group as many as 4 people (13.8%) aged <51 years, 3 people (10.3%) aged between 51-60 years, and 22 people (75.9 %) aged >60 years. In the control group, it was found that the distribution of subjects by age group in the control group was mostly at the age of >60 years, namely 19 people (65.5%), followed by ages between 51-60 years as many as 6 people (20.7%), and age < 51 years as many as 4 people (13,8%).

Table 2. The disease diagnosis of subjects control

Disease Diagnosis	Non-CHD	
	n	%
Asthma	1	3.4
Bronchitis	4	13.8
Bronchopneumonia	1	3.4
CHF	1	3.4
COPD	15	51.7
Dyspepsia	2	6.9
Malignant Neoplasm	1	3.4
Pneumonia	4	13.8
Total	29	100

Table 2 shows that patients in the control group were dominated by patients with a diagnosis of COPD (Chronic Obstructive Pulmonary Disease) which amounted to 15 people with a percentage of 51.7%, followed by bronchitis and pneumonia with 4 people each (13.8%), dyspepsia as many as 2 people (6.9%), and diseases such as asthma, bronchopneumonia, CHF, and malignant neoplasms as many as 1 people each (3.4%).

There were 26 women (90%) with CHD who experienced dyslipidemia, while 3 people (10%). The control group with dyslipidemia was 16 people (55%) while the normal group had 13 people (45%). Based on the Chi-Square test, OR = 7.04 (CI: 1.73-28.6), p-value = 0.003 ($p < 0.05$). There is a significant relationship between dyslipidemia and the incidence of CHD in women.

There were 15 women (51.7%) with CHD who had elevated total cholesterol levels, while 14 people (48.3%) had normal cholesterol levels. The mean total cholesterol level was 194.9 mg/dl (78.0-270.0 mg/dl). The control group that had an increase in total cholesterol was 5 people (17%) while the normal group was 24 people (83%). The average total cholesterol level was 171.4 mg/dl (119.0-270.0 mg/dl). From the results of the Chi-Square test, OR = 5.14 (CI:1.54 -17.2), p-value = 0.012 ($p < 0.05$). There is a significant relationship between increased total cholesterol levels and the incidence of CHD in women.

Women with CHD who had elevated triglyceride levels were 9 (31%) while the normal 20 people (69%). The mean triglyceride was 138.3 mg/dl (60.0-359.0 mg/dl). The control group who had increased triglyceride levels was 5 people (17.2%) while the normal group was 24 people (82.8%). The mean triglyceride level was 109.2 mg/dl (34.0-411.0 mg/dl). Based on the Chi-Square test, OR = 2.16 (CI: 0.62-7.49), p-value = 0.358 ($p > 0.05$). Although the proportion of elevated triglyceride levels was greater in cases than in controls, there was no significant relationship between elevated triglyceride levels and the incidence of CHD in women.

Women with CHD who have increased LDL cholesterol levels are 15 people (52%) while those who are normal are 14 people (48%). The mean LDL cholesterol level is 127.65 mg/dl (9-197mg/dl). The control group had an increase in LDL cholesterol in as many as 3 people (10%) while the normal group had 26 people (90%). The mean LDL cholesterol level is 99 mg/dl (47-163mg/dl). From the Chi-square test, OR = 9.286 (CI: 2.29-37.6), p-value = 0.001 ($p < 0.05$). There is a significant relationship between increased LDL cholesterol levels and the incidence of CHD in women.

Women with CHD who have decreased HDL cholesterol are 13 people (45%), while the normal ones are 16 people (55%). The mean HDL level is 42 mg/dL (2-72 mg/dL). The control group had a decrease in HDL cholesterol levels in as many as 7 people (24%) while the normal group was 22 people (76%). The mean HDL cholesterol is 48 mg/dL (10-80 mg/dL). From the Chi-Square test, OR = 2.554 (CI: 0.83-7.84), p-value = 0.167 ($p > 0.05$). Although the proportion of decreased HDL cholesterol was greater in cases than in controls, there was no significant relationship between decreased HDL cholesterol levels and the incidence of CHD in women.

Discussion

In the study, most CHD patients were in the age range of 60 years and over with a percentage of 79.3%. This is by research conducted by Odden, et al. (2011) which states that the greatest frequency of CHD occurs at the age of 65 years and will increase twice at an older age (Odden et al., 2011). The aging process is an independent factor in triggering atherosclerosis and will increase the risk factors for cardiovascular disease if influenced by other modifiable risk factors (Head et al., 2017).

This study found that the case population with 48 CHD events was dominated by age >60 years (75.9%) by the theory of Cholesterol reduction to prevent CAD by Sorrentino MJ, namely the risk of CHD occurring in women aged 45 years when menopause onset was normal (Kannel & Vasan, 2009). Endogenous estrogen has protective properties in women, Estrogen has a positive effect on the inner lining of the artery walls, and it helps keep blood vessels elastic. After entering the menopause period, women will experience a decrease in estrogen which will increase the risk factors for the disease.

According to the study of Taqueti et al, women referred for angiography had a significantly lower incidence of coronary artery disease than men, but not with cardiovascular events. According to the Basic Health Research (Riskesdas) in 2018, based on a doctor's diagnosis, women suffer from heart disease. CHD is the leading cause of death in post-menopausal women living in industrial areas. The female hormone estrogen protects the coronary arteries. Thus, postmenopausal women have a higher prevalence of CHD than premenopausal women (Taqueti et al., 2017).

According to Robert H and Nelson, dyslipidemia is a disorder of lipid metabolism in the form of increased levels of total cholesterol, triglycerides (TG), low-density lipoprotein (LDL), and decreased levels of high-density lipoprotein (HDL), which are the main risk factors for cardiovascular disease and the most modifiable (Kaplan & Manuck, 2017). In this study, it was found that there was an effect of dyslipidemia on the incidence of CHD. The relationship between CHD and dyslipidemia lies in the process of atherosclerosis. If there is atherosclerosis, which is an abnormality in the lipid profile such as an increase in LDL cholesterol levels, the cholesterol transported by LDL cholesterol will settle in the coronary arteries and atherosclerosis occurs (Pedram et al., 2018). Dyslipidemia can cause CHD because in this situation there is a decrease in the concentration of HDL cholesterol which has anti-atherogenic, anti-inflammatory, and antioxidant properties where the whole process can reduce natural anti-oxidant reserves (Ma'rufi, 2012).

In this study, there was a relationship between total cholesterol levels and the incidence of coronary heart disease in women at PKU Muhammadiyah Yogyakarta Hospital with an odds ratio of 5.14. The results of this study are in line with research conducted by Kamilla, Laila and Salim, Maulidiyah in 2018 which stated that there was a relationship between total cholesterol levels and the incidence of CHD as evidenced by data analysis using the Chi-square statistical test and obtained p value = 0.024 (smaller than 0,05) and research by Oemiati, Ratih, and Rustika (2015) which states that menopause is a risk factor that greatly influences the incidence of CHD in women with a 1.5 times higher risk when compared to women who are not menopausal (Oppedisano et al., 2020) (Kamila & Salim, 2018). This is by what we know that age >45 years is a transition period from premenopause to perimenopause, so it is important to take a gender-specific approach that discusses risk factors for CHD (Oemiyati & Rustika, 2015).

The results of this study indicate that there is no relationship between triglyceride levels and the incidence of coronary heart disease in women. This is supported by Herman's research in 2012, namely in a study of 68 patients with the percentage of high triglyceride levels in CHD patients was 73.3% with a p-value> 0.05 (Rosano et al., 2017). However, in other studies, different results were obtained, namely, there was a significant relationship between triglyceride levels and the incidence of coronary heart disease (Herman et al., 2015). This difference in results may be because triglyceride levels are not the sole factor that causes CHD. The main fat in food is triglycerides, after arriving in the intestine, triglycerides will be converted in the form of chylomicrons and undergo hydrolysis by the lipoprotein lipase enzyme into free fatty acids which are then carried to the liver to become hepatic triglycerides. Triglycerides and liver cholesterol

will be converted through the process of synthesis into VLDL and then carried into the bloodstream. VLDL is transformed into IDL which then becomes LDL. LDL is what underlies the process of atherosclerosis in coronary heart disease (Shabana et al., 2020). Epidemiological studies have shown that the relationship between hypertriglyceridemia and CHD differs depending on the level of total or LDL cholesterol. That is, the strongest relationship between triglycerides and CHD is in lower cholesterol levels. The relationship between triglycerides and CHD is not entirely dependent on cholesterol, but cholesterol modifies the effect of the association of triglycerides with CHD (Ference et al., 2019). Increased low-density lipoprotein cholesterol (LDL-C) has a strong position as a major predictor of the risk of coronary heart disease (Ala-Korpela, 2019).

This study also found that high triglyceride levels had a 2-fold risk (OR = 2.160 (95% CI; 0.623 – 7.493)) of coronary heart disease. This result is supported by Brian's research in 2019 which showed that for every 10 mg/dL decrease in the concentration of ApoB-containing lipoprotein, triglyceride levels also decreased, but LDL cholesterol levels continued to increase. This is a risk factor for coronary heart disease because LDL cholesterol is an independent risk factor for coronary heart disease. Apo B is an acceptor for neutral lipid donors that must be available with microsomal triglyceride transfer protein (MTP) for the formation of lipoprotein-rich triglycerides in the intestine (Liou & Kaptoge, 2020).

In this study, it is known that there is a relationship between LDL cholesterol levels and the incidence of CHD in children. In line with research conducted by Wang et al in 2017, high levels of cholesterol biosynthesis in the liver will result in an increase in VLDL secretion in plasma, this makes an increase in the concentration of LDL cholesterol in the body which is one of the risk factors for heart disease in humans. as well as animals (Giammanco et al., 2015). LDL cholesterol plays an important role in the transportation of cholesterol from the liver to peripheral tissues and then storage occurs in the intima layer of the coronary arteries so that the process of atherosclerosis can occur which is the beginning of the occurrence of CHD (Wang et al., 2018).

In this study, the odds ratio (OR) was 9.286, which means that high LDL cholesterol has a 9x greater risk of CHD in women compared to patients with normal LDL cholesterol levels. These results are supported by Xiang, Q (2019) that an increase in LDL cholesterol levels is an independent risk factor as a cause of CHD (Félix-Redondo et al., 2013). According to Higashioka's research (2019), there was a twofold increase in the risk of CHD in patients with LDL cholesterol levels > 120 mg/dl and serum small dense LDL > 33 mg/dl (Xiang et al., 2020). o the high LDL level can be used as a reference to see the risk of CHD although sometimes it is found that low LDL cholesterol levels can still be a high risk of CHD if there is a small dense LDL serum level > 34 mg/dl because it is more sensitive and more specific to the incidence CHD. LDL cholesterol can be affected by the age of the patient. Due to the aging process, a woman has an increased risk of LDL cholesterol levels. In this study, it was found that the age of the most female patients who experienced the incidence of CHD was >60 years. As supported by Exam research (2015) the older a person is, the metabolic process, especially fat, will be which results in the accumulation of excess fat in the body and leads to obesity. In addition to fat accumulation, in women there is also a decrease in muscle mass which causes many components to be converted into fat and a decrease in the production of the hormone estrogen (Higashioka et al., 2020). The decrease in the hormone estrogen occurs due to the aging process or the menopause phase in women. According to research by Felix-Redondo et al. (2013), high cholesterol levels that cause a woman to develop CHD were overall found in patients aged >65 years which supports the results of this study

Female gender also affects high LDL cholesterol levels compared to men. This statement is supported by the research results of Russo et al (2015) that women have less optimal LDL cholesterol levels (<100mg/dl) than men. However, LDL cholesterol levels of 130 mg/dl are more common in women than men (Russo et al., 2015). This is because in women, the menopause phase. This menopausal phase causes changes in serum lipoprotein concentrations (Ujani, 2015). Like the research of Karvinen, S et al (2019) which examined the relationship between menopause and the risk of CHD events, it was found that menopause was independently associated with

increased levels of LDL cholesterol and total cholesterol. Karvinen's research also states that the menopausal transition apart from aging factors will encourage an increase in LDL cholesterol levels. During menopause, there will be changes in lipid metabolism resulting in the development of metabolic syndrome and the risk of CHD which can be prevented if women are still producing the hormone estrogen optimally, but due to changes in lipid metabolism, there is a decrease in estrogen hormone production as evidenced by the administration of estrogen. orally with the result of lowering LDL cholesterol levels (Lee et al., 2015).

In this study, there was no significant relationship between HDL cholesterol levels and the incidence of coronary heart disease. This is supported by a previous study by Iskandar & Alfridsyah (2017) at the Meuraxa General Hospital Banda Aceh with the results for HDL cholesterol levels that P value > 0.05 so there was no difference in the mean HDL cholesterol levels between subjects with CHD and subjects with CHD. not suffering from CHD (Karvinen et al., 2019). The meta-analysis research conducted by Huxley et al. (2011) also showed that in the Asia-Pacific region, there was no relationship between HDL cholesterol levels and the incidence of CHD (Iskandar et al., 2017).

Individuals with a high ratio of total cholesterol/HDL cholesterol or LDL cholesterol/HDL cholesterol have a higher risk of cardiovascular disease due to imbalanced levels of atherogenic cholesterol and protective (antiatherosclerotic) lipoproteins. The ratio of total cholesterol and HDL cholesterol is also known as atherogenic or Castelli Index. When total cholesterol, HDL cholesterol, and the ratio of total cholesterol and HDL cholesterol were compared between the healthy population and the CHD population, the ratio of total cholesterol and HDL cholesterol was higher in the CHD population (Favari et al., 2018). Although in this study 27.6% of CHD patients had normal HDL cholesterol levels, it would still be a risk if the total cholesterol levels of CHD patients increased significantly. For example, total cholesterol levels of 150 mg/dl and HDL cholesterol of 50 mg/dl would have a ratio of 3 which indicates low risk. On the other hand, an increased total cholesterol level, 250 mg/dl, and with the same HDL level will have a higher ratio of 5 which indicates an atherogenic risk. This study also found a small odds ratio (OR) value of 2.5, which means that patients with low HDL cholesterol levels have a 2 times greater risk of coronary heart disease than patients with normal HDL cholesterol levels. This is to the results of research conducted by Zhou et.al (2020), namely the risk of HDL cholesterol was positively and significantly associated with the risk of CHD (p for trend = 0.0038) (Zhou et al., 2020).

CONCLUSION

In conclusion, this study investigated the relationship between lipid profiles and the incidence of coronary heart disease (CHD) in women. The research involved 58 female participants, divided into those with CHD and those without. The majority of CHD cases were observed in women aged 60 and above. Dyslipidemia was prevalent among CHD patients, with a significant association between dyslipidemia and CHD incidence. Elevated total cholesterol levels were also significantly associated with CHD. Furthermore, increased levels of low-density lipoprotein (LDL) cholesterol exhibited a substantial relationship with CHD, indicating a ninefold greater risk in women with CHD compared to those with normal LDL levels. However, no significant relationship was found between elevated triglyceride levels and CHD. Additionally, decreased high-density lipoprotein (HDL) cholesterol levels were more common in CHD cases, although the association did not reach statistical significance. The study suggests that dyslipidemia, particularly elevated total cholesterol and LDL cholesterol, plays a crucial role in the development of CHD in women. The findings emphasize the importance of lipid profile management in preventing and managing coronary heart disease in this population. The results contribute valuable insights to the existing literature on the subject and underscore the significance of age, hormonal changes, and lipid metabolism in understanding CHD risk factors in women.

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