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Potential Screening Relationship Between Lipid Profil and Preeclampsia

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ABSTRACT

Per-eclampsia and eclampsia are among the leading causes of maternal perinatal mortality and morbidity worldwide. Lipid Profile examination screening is one of the potential screening relationships between the incidence of pre-eclampsia in pregnant women. This study aims to determine the difference in average lipid profile (total cholesterol, LDL cholesterol, HDL cholesterol, and triglycerides) between per-eclamptia pregnant women and normal pregnant women. The research method used an observational study design with a case-control study approach. The population is all pregnant women with pre-eclampsia and normal pregnant women who seek outpatient treatment and have been hospitalized at RSUZA Banda Aceh from May to November 2024. The sample in this study consisted of 2 unpaired groups, so the number of samples of each group was 11 people. Data collection was carried out by clinical laboratory examination. Data analysis used is descriptive analysis and inferential analysis using independent t-test and chi-square test. The results showed there was a difference in average total cholesterol (p=0.000) and LDL cholesterol (p=0.006) between the pre-eclampsia pregnant women group and normal pregnant women, and there is no difference in the average levels of HDL cholesterol (p=0.102) and triglycerides (p=0.679). It is recommended that pregnant women conduct routine lipid profile checks to detect the risk of pre-eclampsia in pregnancy.

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1. Introduction

Hypertensive disorders of pregnancy affect approximately 10% of all pregnant women worldwide and are the cause of 76,000 maternal deaths and 500,000 infant deaths annually. This group includes pre-eclampsia and eclampsia. These conditions stand out for their impact on maternal and newborn health, being one of the leading causes of maternal perinatal mortality and morbidity worldwide. The pathogenesis of pre-eclampsia is only partially understood. Other uncertainties such as diagnosis, screening, and management of pre-eclampsia remain controversial. Maternal mortality is still a problem in many parts of the world, including Indonesia. Based on the latest survey data, Indonesia's maternal mortality rate (MMR) is 305/100,000 live births (BPS, 2016). The most common causes of maternal mortality in Indonesia occur due to hypertension/pre-eclampsia/eclampsia, bleeding, and infection. Hypertension in pregnancy ranks as the first cause of death in Indonesia at 33% (Hamsah & Budiman, 2024).

Persistent diastolic pressure > 90 mm Hg and proteinuria (>0.3 g/24 hours) as criteria for identifying pre-eclampsia, becomes evident in the second trimester of pregnancy occurring in approximately 2%-8% of all pregnancies overall and is classified as severe when any of the following conditions occur: severe hypertension, severe proteinuria or substantial maternal organ dysfunction. Earlier onset (before 32-34 weeks of pregnancy). Several factors related to preeclampsia in pregnant women such as history of hypertension, history of preeclampsia, age, BMI, parity, stress, knowledge, completeness of ANC, diet and exposure to cigarette smoke (Rahmawati et al., 2022). Obesity and nulliparity are other risk factors associated with preeclampsia in pregnant women (Yang et al., 2021).

Some preeclampsia disorders can be avoided with effective care to prevent and treat preeclampsia by screening for preeclampsia which is easy to do in the first and second trimesters. Screening Lipid Profile examination is one of the potential links between the incidence of preeclampsia. Results of the study Maternal lipid profile and risk of preeclampsia in African pregnant women: A systematic review and meta-analysis on 15 observational studies, the mean values of triglycerides (TG), total cholesterol (TC), low-density lipoprotein-cholesterol (LDL-c) and low-density lipoprotein-cholesterol (VLDL-c), were significantly higher in pre-eclamptic women compared to normotensive pregnant women (Tesfa et al., 2020).

Lipid profile, which includes total cholesterol, LDL cholesterol, HDL cholesterol, and triglycerides, has been associated with the risk of pre-eclampsia in pregnant women. Several recent studies have been conducted to evaluate the relationship between lipid profile and pre-eclampsia. One study showed that higher total cholesterol and triglycerides in early pregnancy were associated with an increased risk of pre-eclampsia. The study included 1,773 pregnant women and showed that women with higher total cholesterol and triglycerides had a higher risk of pre-eclampsia (Tesfa et al., 2020).
This study was conducted to determine the differences in lipid profile levels (total cholesterol, LDL cholesterol, HDL cholesterol, and triglycerides) in pregnant women with pre-eclampsia and normal pregnant women, and to identify the relationship between lipid profile levels and the incidence of pre-eclampsia in pregnant women.

2. Methods

Research Design

This study uses an observational study design with a case-control study approach, which is carried out by comparing individuals who have a certain disease or condition (case group of pre-eclampsia pregnant women) with individuals who do not have the same disease or condition (control group of normal pregnant women). This study uses a case-control design because preeclampsia is a reasonably specific pregnancy complication condition, so this condition does not occur very often. In addition, this research design was used because the researcher wanted to compare lipid factors with the incidence of preeclampsia in normal pregnant women and preeclamptic pregnant women.

Population and Sample

The population in this study were all pregnant women with pre-eclampsia who received outpatient treatment at Dr. Zainoel Abidin Hospital (RSUDZA) the main referral center hospital in Aceh Province from May to November 2024.

The sample in this study consisted of a case group which was pregnant women who experienced pre-eclampsia, did not have other diseases, and were not in the pre-eclampsia treatment period), while the control group was normal pregnant women without any complications. The sampling technique uses a minimum sample size with the formula for the size of the research sample for 2 unpaired groups. The results of these calculations obtained the number of each group, namely 11 people. Non-probability sampling technique using Purposive sampling method.

Data Collection Procedure

The data collected included subject characteristics such as age, history of disease, and measurement of lipid profile levels (total cholesterol, triglycerides, HDL, and LDL) by conducting clinical laboratory examinations to help diagnose the risk of cardiovascular disease with the colorimetric

method, with the procedure of examining blood samples taken from a vein in the arm using a syringe conducted in a clinical laboratory.

The results of the examination of blood samples for each lipid profile level were also categorized based on the Plasma Lipid Level Guidelines according to the Guidelines for the Management of Dyslipidemia in Indonesia. Total cholesterol is categorized into 3 categories: low risk (if the test result is <200 gr/dl), moderate risk (if the test result is 200 - 239 gr/dl), and high risk (if the test result is ≥240 gr/dl). LDL cholesterol can be categorized into 5 categories, namely optimal (if the test result is <100 mg/dl), near-optimal (if the test result is 100-129 mg/dl), borderline (if the test result is 130-259 mg/dl), high (if the test result is 160-189 mg/dl) and very high (if the test result is ≥190 mg/dl). HDL cholesterol can be categorized into 2 categories: low risk (if the test result is <40 gr/dl) and high risk (if the test result is ≥60 gr/dl). Triglycerides are categorized into 4 categories: normal (if the test result is <150 gr/dl), borderline (if the test result is 150-199 gr/dl), high (if the test result is 200-499 gr/dl) and very high (if the test result is ≥500 gr/dl) (Perkeni, 2021).

Data analysis

The data used are descriptive analysis and inferential analysis using the independent t-test (for knowledge of the difference in mean lipid profiles between pre-eclampsia pregnant women and normal pregnant women) and the chi-square test (to determine the relationship between lipid profiles and the incidence of pre-eclampsia in pregnant women).

Research Ethical Considerations

This study took into account the ethical principles in research, including anonymity, confidentiality, and benefits. This research has also received approval from RSUZA and consent from respondents. The study and ethical approval were also obtained from the Ethics Committee of the Zainoel Abidin Hospital with 190/ETIK-RSUDZA/2024.

3. Results and Discussion

The results of the normality test showed that all variables including age, gestational age, total cholesterol, LDL cholesterol, HDL cholesterol, and triglycerides were normally distributed, so to determine the difference in the mean of each variable between pre-eclampsia pregnant women and normal pregnant women can use an independent t-test.

Table 1.
Characteristics of respondents

No.	Characteristics	Group	Mean	SD	Minimum	Maximum	p-value
1	Age	Case	31,36	6,68	21,00	40,00	0,548
		Control	32,90	5,06	23,00	41,00	
2	Pregnancy Age	Case	30,00	2,72	25,00	33,00	0,846
		Control	30,27	3,69	24,00	35,00	

Based on Table 1. shows the average age of respondents in pregnant women who experience pre-eclampsia (case group) is 31.36 years with a standard deviation of 6.68, while in the group of normal pregnant women (control group) is 32.90 years with a standard deviation of 5.06. The statistical test results showed no difference in the average age of mothers between the pre-eclampsia pregnant women group and normal pregnant women (p=0.548).

The average gestational age of respondents in pregnant women who experienced pre-eclampsia (case group) was 30.00 weeks with a standard deviation of 2.72, while in the group of normal pregnant women (control group) was 30.27 weeks with a standard deviation of 3.69. The statistical test results showed no difference in the average gestational age of mothers between the pre-eclampsia pregnant women group and normal pregnant women (p=0.846).

Table 2.
Mean difference in lipid profile levels between pre-eclamptic pregnant women (Case) and normal pregnant women (Control)

No.	Lipid Profile	Group	Mean	SD	Min - Max	ΔMean	p-value
1	Total Cholesterol	Case	315,63	79,67	158,00 - 429,00	199,18	0,000
		Control	196,45	34,00	135,00 - 239,00		
2	LDL Cholesterol	Case	194,63	76,94	39,00 - 357,00	76,63	0,006
		Control	118,00	30,97	49,00 - 152,00		
3	HDL Cholesterol	Case	45,18	11,67	25,00 - 69,00	-8,09	0,102
		Control	53,27	10,42	41,00 - 78,00		
4	Triglycerides	Case	195,81	50,46	85,00 - 246,00	10,81	0,679
		Control	185,00	68,98	72,00 - 313,00		

Based on Table 2. shows the average total cholesterol level in the pre-eclampsia pregnant women group (average = 315.63 mg/dL, SD = 79.67) is higher than the normal pregnant women group (average = 196.45 mg/dL, SD = 34.00). The statistical test results showed there was a difference in the average total cholesterol levels between the pre-eclampsia pregnant women group and normal pregnant women (p=0.000).

The average LDL cholesterol level in the pre-eclampsia pregnant women group (average = 194.63 mg/dL, SD = 79.94) was higher than the normal pregnant women group (average = 118.00 mg/dL, SD = 30.97). Statistical test results showed there was a difference in the average LDL cholesterol levels between the pre-eclampsia pregnant women group and normal pregnant women (p=0.006).

The average HDL cholesterol level in the pre-eclampsia pregnant women group (average = 45.18 mg/dL, SD = 11.67) was lower than the normal pregnant women group (average = 53.27 mg/dL, SD = 10.42). The statistical test results showed no difference in the average HDL cholesterol levels between the pre-eclampsia pregnant women group and normal pregnant women (p=0.102).

The average triglyceride level in the pre-eclampsia pregnant women group (average = 195.81 mg/dL, SD = 50.46) was higher than the normal pregnant women group (average = 185.00 mg/dL, SD = 68.98). Statistical test results showed no difference in the average triglyceride levels between the pre-eclampsia pregnant women group and normal pregnant women (p=0.679).

Table 3.
Relationship between Lipid Profile and Pre-Eclampsia in Pregnant Women

No.	Lipid Profile		Group				p-value
			Case		Control		
			f	%	f	%	
1	Total cholesterol	High	10	90,9	0	0,0	0,000
		Borderline	0	0,0	6	54,5	
		Normal	1	9,1	5	45,5	
2	LDL cholesterol	Very High	5	45,5	0	0,0	0,003
		High	4	36,4	0	0,0	
		Borderline	1	9,1	4	36,4	
		Approaching Optimal	0	0,0	5	45,5	
		Optimal	1	9,1	2	18,2	
3	HDL cholesterol	High Risk	3	27,3	2	18,2	1,000
		Low Risk	8	72,7	9	81,8	
4	Triglycerides	High	7	63,6	5	45,5	0,693
		Borderline	2	18,2	3	27,3	
		Normal	2	18,2	3	27,3	

Based on Table 3. shows that mothers who have high total cholesterol are more dominant in pre-eclampsia pregnant women (90.9%) compared to normal pregnant women (0%). Conversely, mothers who have total cholesterol in the normal category are higher in normal pregnant women

(45.5%) compared to pregnant women with pre-eclampsia (9.1%). The statistical test results showed that there was a relationship between total cholesterol and pre-eclampsia in pregnant women (0.000).

Mothers who had high LDL cholesterol were more dominant in pre-eclampsia pregnant women (45.5%) compared to normal pregnant women (0%). Conversely, mothers who have LDL cholesterol in the near-optimal category are more dominant in normal pregnant women (45.5%) compared to pregnant women with pre-eclampsia (0%). The statistical test results showed that there was an association between LDL cholesterol and pre-eclampsia in pregnant women (p=0.003).

Mothers who have HDL cholesterol in the high-risk category are more dominant in pre-eclampsia pregnant women (27.3%) compared to normal pregnant women (18.2%). Conversely, mothers who had HDL cholesterol in the low-risk category were more dominant in normal pregnant women (72.7%) compared to pregnant women with pre-eclampsia (81.8%). Statistical test results showed no association between HDL cholesterol and pre-eclampsia in pregnant women (p = 0.000).

Mothers who had high triglycerides were more dominant in pre-eclampsia pregnant women (63.6%) compared to normal pregnant women (45.5%). Conversely, mothers who had triglycerides in the normal category were more dominant in normal pregnant women (27.3%) compared to pregnant women with pre-eclampsia (18.2%). The statistical test results showed no association between triglycerides and pre-eclampsia in pregnant women (p=0.693).

Analysis

Relationship between Respondent Characteristics and Pre-eclampsia in Pregnant Women

The results showed no difference in age and gestational age between pre-eclampsia pregnant women and normal pregnant women. These results are in line with previous research conducted by Harun, et al (2019) which shows there is a relationship between age and the incidence of pre-eclampsia (p>0.05) (Harun et al., 2019). Likewise, research conducted by Wardhana et al., (2021) showed no difference in age and gestational age between pregnant women who experienced pre-eclampsia and normal pregnant women at the East Java Government Referral Hospital.

In contrast, some studies show that there is an association between age and gestational age with pre-eclampsia in pregnant women (Fatkhiyah et al., 2018; Marniati et al., 2019; Nabella, 2021; Rahmawati & Fauziah, 2019). According to a literature review, the age of pregnant women at risk of pre-eclampsia is <20 years old or >35 years old. (Tendean & Wagey, 2021). Mothers who become pregnant at the age of <20 years are more at risk of experiencing high complications than those aged 20-35 years. This is because the age of <20 years known as adolescence is a crucial period characterized by significant development in physical, mental, and intellectual aspects (Rima Wirenviona et al., 2020). When pregnancy occurs in adolescence, it can have various consequences, not only in terms of the health of the mother and baby but also have an impact on social and economic aspects (Tendean & Wagey, 2021) . In addition, at the age of under 20 years, reproductive organs such as the uterus are still in the growth stage and have not yet reached the ideal size for pregnancy. This condition can increase the risk of preeclampsia (Pasaeono et al., 2023).

On the other hand, women who become pregnant over the age of 35 also face risks. At this age, there is an aging (degenerative) process that affects the peripheral blood vessels, resulting in structural and functional changes that impact blood pressure. As a result, women over 35 years of age have a higher susceptibility to preeclampsia compared to women who become pregnant at the ideal age of 20-35 years of age (Tendean & Wagey, 2021).

This study is also not in line with the research of Sitohang et al., (2023) which shows there is an association between gestational age and severe preeclampsia with a risk of occurring at >34 weeks of gestation by 0.244 times compared to <34 weeks of gestation. High blood pressure at 20 weeks gestation is an early indication of preeclampsia. If not treated immediately it can endanger the mother and baby (Marbun & Irnawati, 2023).

Pre-eclampsia is a complex condition with multiple risk factors, not just limited to age and gestational age. The causes of pre-eclampsia are multifactorial, involving interactions between genetic, immunologic, and environmental factors (Mol et al., 2016). Maternal age and gestational age are not directly risk factors for pre-eclampsia but can be predisposing factors. Researchers assume there is no

difference between age and gestational age between pre-eclamptic pregnant women and normal pregnant women due to the possibility that the sample in the study has more homogeneous characteristics.

The mean difference in lipid profile levels between pre-eclampsia pregnant women (Case) and normal pregnant women (Control)

The results of the t-test showed that there were significant differences in the average levels of total cholesterol and LDL cholesterol between the pre-eclampsia pregnant women and normal pregnant women, where the pre-eclampsia group had higher levels of total cholesterol and LDL cholesterol. If the results of total cholesterol are categorized, the results of statistical tests show that total cholesterol in the high category is more dominant in pregnant women who experience pre-eclampsia compared to normal pregnant women and is statistically significant. Likewise, the LDL level data were categorized, which showed that pregnant women with very high and high LDL cholesterol categories were higher in pregnant women who experienced pre-eclampsia compared to normal pregnant women, and were statistically significant.

These results are supported by previous studies that showed the average total cholesterol and LDL cholesterol was significantly higher in preeclamptic pregnant women compared to normal pregnant women (Tesfa et al., 2020). Likewise, Siringoringo, et al (2016) showed that there was a difference in the average LDL cholesterol levels in the preeclampsia and normal pregnancy groups, but there was no difference in the average total cholesterol levels in the preeclampsia and normal pregnancy groups (Siringoringo et al., 2016).

The cause of preeclampsia has not been well elucidated. However, reduced uteroplacental perfusion due to abnormal spiral artery remodeling may contribute to preeclampsia (Tesfa et al., 2020). According to Cunningham et al., (2018), elevated total and LDL cholesterol levels during pregnancy can lead to endothelial dysfunction and inflammation, which play a role in the pathogenesis of pre-eclampsia. High LDL cholesterol can increase oxidative stress and cause endothelial cell damage (Vahratian et al., 2010).

The results of this study also showed no significant difference in the average HDL cholesterol and triglyceride levels between the two groups. HDL cholesterol in the high-risk category was higher in pregnant women with pre-eclampsia compared to normal pregnant women, but not significant. Likewise, triglyceride levels in the high category were higher in pregnant women with pre-eclampsia compared to normal pregnant women but were not significant.

These results are in line with the research of Siringoringo et al., (2016) which showed no difference in the average triglyceride levels in the preeclampsia group and normal pregnancy. Physiologically, changes in lipid profiles in normal pregnancy as an adaptation to meet the needs of fetal growth. Increased lipid levels during normal pregnancy are a response to increased estrogen and insulin resistance that occurs naturally (Wild & Feingold, 2023). According to Chen et al., (2023), adaptations in lipid metabolism are essential to meet the physiological demands of pregnancy and any deviations may result in adverse outcomes for the mother and her offspring. The results of a longitudinal study identified lipid signatures associated with cardiometabolic risk traits with potential implications in both pregnancy and postpartum life.

The results of this study are supported by a study conducted by Akter et al., (2022) who also found no significant difference in HDL and triglyceride levels between normal pregnant women and pre-eclampsia in the second trimester of pregnancy. Changes in lipid profile may be more related to disease progression rather than as an initial risk factor. The pattern of lipid changes during pregnancy is more important in predicting the risk of pre-eclampsia than the absolute values at one particular time point (Spracklen et al., 2014).

The association of lipid profiles with pre-eclampsia suggests that the endothelial dysfunction that occurs in pre-eclampsia is not always reflected in changes in HDL and triglyceride levels. HDL quality and function may be more important than its quantity in the pathogenesis of pre-eclampsia (Wang et al., 2009). In addition, changes in specific lipid subclasses and lipid modifications may be more relevant in the development of pre-eclampsia than total lipid levels (Chappell et al., 2021).

Researchers assume that dyslipidemia in pre-eclamptic pregnant women may be a risk factor for endothelial dysfunction and inflammation, thus contributing to the onset of pre-eclampsia. In addition, there was no difference between HDL cholesterol and triglyceride levels between the two groups due to several reasons, firstly because the timing of blood sampling may have affected the results, given that lipid profiles change dynamically during pregnancy. Secondly, factors such as diet, physical activity, and body mass index before pregnancy may have more influence on lipid profile than pre-eclampsia status itself (Lambert et al., 2014). Third, the pathophysiologic mechanisms of pre-eclampsia may be more related to changes in endothelial function and oxidative stress rather than direct changes in lipid profiles (Cornelius, 2018).

4. Conclusion

The conclusion is that there is a difference in the average levels of total cholesterol (p=0.000) and LDL cholesterol (p=0.006) between the group of pre-eclampsia pregnant women and normal pregnant women. If the data of lipid profile examination results are categorized, it also shows that there is a relationship between total cholesterol (p=0.000) and LDL cholesterol (p=0.003) with pre-eclampsia in pregnant women. In addition, there was no difference in the average levels of HDL cholesterol (p=0.102) and triglycerides (p=0.679) between the pre-eclampsia pregnant women group and normal pregnant women.

It is expected for pregnant women to routinely check lipid profiles during pregnancy, especially total cholesterol and LDL, and implement a healthy lifestyle by eating balanced nutritious foods and regular physical activity. In addition, health workers conduct lipid profile screening in pregnant women, especially those at risk of pre-eclampsia, as well as provide education and counseling on the importance of maintaining an optimal lipid profile during pregnancy and collaborate with nutritionists to provide appropriate dietary interventions for pregnant women with abnormal lipid profiles. And than, standard guidelines for lipid profile monitoring during pregnancy, cost-effective screening strategies, and evaluation of the impact of early intervention on maternal and fetal health outcomes need to be developed.

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