



Risk Factors Determining to Uterine Myoma among Women in Semarang: A Case- Control Study

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ABSTRACT:

Uterine myoma is a benign monoclonal tumor originating from myometrium smooth muscle cells; it is the most common gynecological disease in reproductive-age women. There are many risk factors contributing to the occurrence of uterine myoma, including age, race, hormonal status, obesity, hypertension, diabetes mellitus, family history, contraceptive use, lifestyle, and diet. The incidence of uterine myoma in Semarang has significantly increased in recent years, necessitating research to identify the factors associated with this condition. This study aims to analyze the relationship between age, menarche, parity, family history, obesity, hypertension, diabetes mellitus, contraceptive use, lifestyle, diet, and the occurrence of uterine myoma in Semarang. The study employed an observational analytical approach with a case-control design, with 44 respondents in each group. Data were collected through medical records and interviews with patients diagnosed with uterine myoma at Dr. Kariadi General Hospital Semarang. Statistical analysis was conducted to determine the relationship between risk factors and the occurrence of uterine myoma. The results showed that age, parity status, family history of uterine myoma, and hypertension had a significant association with the uterine myoma incidence ($p < 0,05$). Additionally, a high-fat and low-fiber diet, exposure to stress, and a sedentary lifestyle contributed to an increased risk. In conclusion, various risk factors such as hormonal and metabolic factors play a role in the occurrence of uterine myoma. Therefore, prevention strategies should focus on weight management, blood pressure control, healthy diet, and regular physical activity. Although the results of this study show the influence of several risk factors on the development of fibroids, further research is necessary to understand all the risk factors contributing to the growth of myomas and how exactly these risk factors influence the pathogenesis of myomas.

1. Introduction

Uterine myoma is a benign tumor originating from smooth muscle cells of the myometrium and found to be the most common pelvic tumor in reproductive women.^{1,2} The results of microscopic examination of uterine fibroids show an extracellular matrix consisting of type I and type III collagen arranged abnormally, resembling keloid formation, fibronectin, and proteoglycans.¹ Globally, the incidence of uterine myoma reaches 70%, especially in people with darker skin. The incidence of uterine fibroids detected through sonographic examination in women ≥ 35 years old from the African-American race reaches 60%, increasing to 80% at the age of 50. The incidence of uterine myoma in Caucasian women at the age of 35 is 40% and increasing to 70% at the age of 50.³ Uterine myoma also has a significant economic impact, with annual healthcare costs in the United States estimated at \$34 billion. In Indonesia, the prevalence of uterine myoma ranges from 2.39% to 11.70% of all gynecological disorders and is among the top ten most common gynecological diseases in various hospitals.^{4,5}

Several epidemiological factors contribute to the development of uterine myoma, including age, race, hormonal status, obesity, hypertension, diabetes mellitus, and family history, as well as diet and lifestyle.⁶ Obesity, metabolic syndrome, and essential hypertension increase the risk of uterine myoma, particularly in younger women.⁷ Alcohol consumption has also been linked to the pathogenesis of myoma through molecular mechanisms involving steroid hormones, growth factors, and cytokines.⁸ Chromosomal abnormalities are found in about 40% of uterine myomas, including translocation between chromosomes 12 and 14, deletion of chromosome 7, and trisomy of chromosome 12.¹ The risk of uterine myoma is 2.5 times higher in women with a family history of first-degree relatives with this type of tumor.⁹

Considering the high incidence and substantial healthcare burden associated with uterine fibroids, this study aims to analyze the relationship between various risk factors and the prevalence of uterine fibroids in Semarang City. All the factors examined included age, menarche, pre-menopausal status, parity, family history



of uterine fibroids, obesity, hypertension, diabetes mellitus, contraceptive use, lifestyle, and diet. This study is expected to provide deeper insights into the risk factors for uterine fibroids and serve as a foundation for developing more effective prevention and management strategies in the future.

2. METHOD

This was an observational-quantitative approach with a case-control study design focusing on factors associated with the incidence of uterine myoma. The research was conducted at RSUP dr. Kariadi Semarang from October 2024 to March 2025; data were collected retrospectively through medical records and questionnaire surveys.

Inclusion criteria for the case group require patients to have complete medical records related to the studied variables. Exclusion criteria include pregnancy, deceased patients, or those residing outside Semarang. The control group comprises healthy individuals without a diagnosis of uterine myoma, having normal menstrual cycles and who do not experience menstrual pain. A consecutive sampling technique was employed, where all eligible patients were included until the required sample size was reached. The sample size was determined using the Slovin formula, with a minimum of 44 patients.

This study was conducted following ethical guidelines and received approval from the Medical Research Ethics Commission of Diponegoro University and RSUP dr. Kariadi Semarang. The confidentiality of subject identities was strictly maintained, and all research costs were covered by the researcher.

Data Analysis

The collected data were analyzed using SPSS version 27. Descriptive analysis was conducted to present data in tables and percentages. Bivariate analysis was performed using the chi-square test or an alternative test, such as Kolmogorov-Smirnov. Multivariate analysis was carried out using logistic regression to determine the relationship between risk factors and the incidence of uterine myoma, with statistical significance set at $p < 0.05$.

3. RESULT AND DISCUSSION

Table 1. Summary of Chi-Square Test Results of the Relationship between Risk Factors and Uterine Myoma

Variable	Category	Uterine Myoma (n = 44)	Healthy Subject (n = 44)	OR (95% CI)	P-value
Age	≥ 40 years old	34 (77.3%)	22 (50%)	3.4	0.008

	< 40 years old	10 (22.7%)	22 (50%)	(1.35-8.53)	
	Total	44 (100%)	44 (100%)		
Menarche	Early Menarche	3 (6.8%)	1 (2.3%)	3.146 (0.314 - 31.484)	0.306
	Not Early Menarche	41 (93.2%)	43 (97.7%)		
	Total	44 (100%)	44 (100%)		
Parity Status	Nulliparous	10 (22.7%)	3 (6.8%)	4.02 (1.02-15.79)	0.035
	Non-Nulliparous (Primiparous or Multiparous)	34 (77.3%)	41 (93.2%)		
	Total	44 (100%)	44 (100%)		
Family History of Uterine Myoma	Family History Present	14 (31.8%)	0 (0%)	20.07 (1.872 - 3.250)	0.000
	No Family History	30 (68.2%)	44 (100%)		
	Total	44 (100%)	44 (100%)		
Obesity	Obese	10 (22.7%)	4 (9.1%)	2.941 (0.846 - 10.229)	0.08
	Not Obese	34 (77.3%)	40 (90.9%)		
	Total	44 (100%)	44 (100%)		
Hypertension	Hypertensive	15 (34.1%)	6 (13.6%)	3.28 (1.13-9.48)	0.024
	Non-Hypertensive	29 (65.9%)	38 (86.4%)		
	Total	44 (100%)	44 (100%)		
Diabetic		1	0	2.023	0.315



Diabetes Mellitus		(2.3%)	(0%)	(1.636 - 2.502)	
	Non-Diabetic	43 (97.7%)	44 (100%)		
	Total	44 (100%)	44 (100%)		
Contraceptive Use	Using Hormonal Contraceptives	13 (29.5%)	6 (13.6%)		
	Using Non Hormonal Contraceptives	8 (18.2%)	4 (9.1%)	2.656 (0.904 - 7.800)	0.070
	Not Using Contraceptives	23 (52.3%)	34 (77.3%)		
	Total	44 (100%)	44 (100%)		
	Physical Activity Level	Light (<600 METs)	12 (27.3%)	31 (70.5%)	
	Moderate (600-1499 METs)	25 (56.8%)	13 (29.5%)	6.36 (2.52-16.07)	0.000
	High (≥1500 METs)	7 (15.9%)	0 (0%)		
	Total	44 (100%)	44 (100%)		
Stress Levels	No Stress	23 (52.3%)	40 (90.9%)		
	Mild Stress	13 (29.5%)	3 (6.8%)		
	Moderate Stress	7 (15.9%)	1 (2.3%)	9.13 (2.79-29.89)	0.001
	Severe Stress	1 (2.3%)	0 (0%)		
	Total	44 (100%)	44 (100%)		

Smoking Exposure	Passive Smoker	22 (50.0%)	23 (52.3%)		
	No Smoking Exposure	22 (50.0%)	21 (47.7%)	0.91 (0.39-2.11)	0.831
	Total	44 (100%)	44 (100%)		
Dietary Habits	Frequent Intake of Unhealthy Foods	16 (36.4%)	4 (9.1%)		
	Rare Intake of Unhealthy Foods	28 (63.6%)	40 (90.9%)	5.71 (1.73-18.92)	0.002
	Total	44 (100%)	44 (100%)		

The collected data were analyzed using SPSS version 27. Descriptive analysis was conducted to present data in tables and percentages. Bivariate analysis was performed using the chi-square test or an alternative test, such as Kolmogorov-Smirnov. Multivariate analysis was carried out using logistic regression to determine the relationship between risk factors and the incidence of uterine myoma, with statistical significance set at $p < 0.05$. Age shows a significant relationship with the incidence of uterine myoma (p -value = 0.008). The odds ratio of 3.400 (95% CI: 1.35-8.531) indicates that women aged ≥ 40 years old have a 3.4 times greater risk of uterine myoma incidence compared to those aged < 40 years old. This result is statistically significant and consistent with the literature; fibroids are more common in reproductive age. These findings are similar to those of Lilyani et al.,¹⁰ Nadila and Zulala also concluded that ages between 30 and 50 years old are significantly associated with the occurrence of uterine fibroids, with a risk increase of 3.279 times compared to ages < 30 years or > 50 years.¹¹ The increase in age raises the incidence and number of uterine fibroids.² The advancement of age is associated with the continuous stimulation of estrogen hormones, which triggers the formation and development of layered uterine fibroids resembling an onion.¹² Decreasing estrogen levels in postmenopausal women, resulting in smaller fibroid sizes and a lower number of fibroids.^{13, 14}



Menarche does not show a significant relationship with the incidence of uterine myoma (p -value = 0.306). This result is similar to Fatahillah¹⁵ and Manalu et al.¹⁶; menarche is not related to the incidence of uterine fibroids. Contrary to the findings of Lilyani et al.¹⁰ stating that menarche is associated with the occurrence of uterine fibroids. Early menarche is linked to tissue sensitivity to hormones or feedback control suppression of steroid production¹⁷, while menarche above the age of 16 is considered a protective factor against the occurrence of uterine fibroids.¹⁸

Parity status shows a significant relationship with the occurrence of uterine fibroids (p -value = 0.035). An odds ratio of 4.02 (95% CI: 1.02-15.79) indicates that nulliparous women have a 4 times higher risk of uterine fibroid incidence compared to non-nulliparous women. This result is similar to Nadila and Zulala; parity status is significantly related to the incidence of uterine myoma; nulliparous and primiparous women may increase the risk of uterine fibroid.¹¹ The risk of uterine fibroids decreases by 20-50% with one childbirth.¹⁹ Giving birth between 25 and 29 years old is considered to provide the greatest protection against the development of fibroids.¹

Family history of uterine fibroids has a highly significant association with the incidence of uterine fibroids (p -value = 0.000). This result is similar to the research by Nadila and Zulala; a family history of uterine fibroids is significantly associated with the uterine fibroid incidence; women with a family history of uterine fibroids will increase the risk of developing uterine fibroids by 7.517 times compared to women without a family history of uterine fibroids.¹¹ The risk of uterine fibroids is known to be 2.5 times higher in women with a history of first-degree relatives with this type of tumor.⁹

Obesity does not show a significant relationship with the incidence of uterine fibroids (p -value = 0.08). The research results regarding body mass index (BMI) and the uterine fibroid incidence are inconsistent. Fatahillah concluded that BMI is not associated with the incidence of uterine fibroids.¹⁵ Umar et al. concluded that obesity is not a risk factor for the occurrence of uterine fibroids.²⁰ Conversely, Manalu et al. concluded that BMI is associated with the incidence of uterine fibroids.¹⁶ Nadila and Zulala also concluded that BMI is significantly related to the incidence of uterine fibroids; a BMI in the overweight and obese categories increases the risk of developing uterine fibroids by 5.625 times compared to individuals with a normal or underweight BMI.¹¹

Hypertension shows a significant association with the incidence of uterine myoma (p -value = 0.024). An odds ratio of 3.28 (95% CI: 1.13-9.48) indicates that women

with hypertension have a 3.3 times greater risk of developing uterine fibroids compared to women without hypertension. The results support the existence of a relationship between high blood pressure and the development of uterine fibroids; women with hypertension have a 5 times greater risk of uterine myoma compared to women with normal blood pressure.²¹ There is a relationship between hypertension and the occurrence of uterine fibroids;²² an increase in diastolic blood pressure is associated with a higher risk of developing uterine fibroids.²³

Diabetes mellitus did not show a significant relationship with the occurrence of uterine fibroids (p -value = 0.315). The results of the research regarding the relationship between diabetes mellitus and the uterine fibroid incidence are inconsistent. Baird et al. state that diabetic conditions are inversely related to the incidence of uterine fibroids.²⁴ However, a study by Alashqar et al. reported that women with cases of uterine fibroids are more likely to experience diabetes mellitus.⁷

The use of hormonal contraceptives does not show a significant relationship with the incidence of uterine fibroids (p -value = 0.070). This result is consistent with the research by Fatahillah¹⁵, Umar et al.²⁰, and Nadia and Zulala¹¹, which states that the use of hormonal contraception is not related to the occurrence of uterine fibroids. The use of hormonal contraception containing progesterone and progestin is considered to suppress the growth of uterine fibroids.²⁵

Physical activity shows a very significant relationship with the occurrence of uterine fibroids (p -value= 0.000). An odds ratio of 6.36 (95% CI: 2.52-16.07) indicates that women with heavy physical activity have a 6.4 times greater risk of uterine fibroid incidence. This result contradicts several previous studies and requires further research. The literature suggests exercise is a protective factor against the occurrence of uterine fibroids by reducing circulating sex hormones, insulin levels, and the bioavailability of circulating estrogen with SHBG.^{2,4,26}

Stress levels show a significant relationship with the occurrence of uterine fibroids (p -value = 0.001). An odds ratio of 9.13 (95% CI: 2.79-29.89) indicates that women with stress conditions have a 9.1 times greater risk of developing uterine fibroids. This result indicates the psychological role in the uterine myoma pathogenesis. Based on literature, stress is one of the risk factors for the occurrence of uterine fibroids due to the release of cortisol and the stimulation of the hypothalamic-pituitary-adrenal gland axis, which leads to increased levels of estrogen and progesterone, causing the formation of uterine fibroids.²⁷⁻²⁹ Chronic psychological



stress increases the risk of uterine fibroid incidence by up to 24%, especially in non-Hispanic Black women.³⁰

Smoking exposure does not show a significant relationship with the uterine fibroid incidence (p-value = 0.831). The relationship between smoking exposure and the uterine fibroid incidence is inconsistent. Smoking is considered to have an anti-estrogenic effect with a decrease in serum estrogen and estradiol levels in smokers; it disrupts estrogen metabolism in the liver, leading to reduced levels of activated estrogen in circulation.³¹ Smoking is associated with a decreased risk of uterine fibroid incidence.³² Contrary results were obtained in a study by Bidgoli et al., where smoking habits were associated with an increased risk of uterine fibroids;³³ possibly due to components in cigarette smoke that affect cell proliferation in the uterus.³¹

Dietary habits show a significant relationship with the incidence of uterine myoma (p-value= 0.002). An odds ratio of 5.71 (95% CI: 1.73-18.92) indicates that a diet with a high glycemic index poses a 5.7 times greater risk of uterine fibroid incidence compared to a healthy diet. This result underscores the importance of a healthy diet in the prevention of uterine fibroids. High glycemic index and glycemic load in the diet are associated with an increased risk of uterine fibroids, as they stimulate tumorigenesis by enhancing the bioavailability of estradiol or endogenous IGF-1 concentrations, which trigger the proliferation of fibroid cells and increase the expression of the IGF-1 gene and protein synthesis.³⁴ One type of food with a high glycemic index that is frequently consumed by respondents is fried food. Fried foods are suspected to be linked to the occurrence of uterine fibroids due to the frying process involving hot oil, which results in high levels of estrogen, saturated fat, and trans fats. Processed meat such as sausages, ham, bacon, corned beef, and meatballs contains artificial preservatives, as well as saturated fats and LDL cholesterol. Some preservatives in processed meats, like sodium nitrate, are carcinogenic substances. However, further research on processed meats is needed. Typically, women with uterine fibroids consume more processed meats than those women without uterine fibroids.¹

4. CONCLUSIONS

Our results of this study led to these conclusions: age, parity status, family history of uterine myoma, and hypertension had a significant association with the uterine myoma incidence. Additionally, a high-fat and low-fiber diet, exposure to stress, and a sedentary lifestyle contributed to an increased risk. Therefore, prevention strategies should focus on weight management, blood pressure control, healthy diet, and

regular physical activity. Although the results of this study show the influence of several risk factors on the development of fibroids, further research with a bigger sample size that controls numerous potential confounders and considers different food content, environmental exposures, and ethnicities is necessary to understand all the risk factors contributing to the growth of myomas and understanding of myoma biology and pathophysiology.

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