Jurnal Riset Kesehatan, 14 (2), 2025, 191 - 199

DOI: 10.31983/jrk.v14i2.13995

Jurnal Riset Kesehatan

http://ejournal.poltekkes-smg.ac.id/ojs/index.php/jrk

CASE-CONTROL STUDY: RISK FACTORS FOR ADENOMYOSIS IN WOMEN OF REPRODUCTIVE AGE IN RELATION TO BLOOD PRESSURE AND BODY MASS INDEX

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Abstract

Adenomyosis is a benign uterine condition characterized by the presence of endometrial tissue within the myometrium. This study aimed to analyze the association between blood pressure and body mass index with the incidence of adenomyosis. This study employed a case control design, in which the case group comprised patients diagnosed with adenomyosis, while the control group consisted of patients with uterine leiomyoma. The research was conducted at PKU Muhammadiyah Hospital Surakarta. A total of 221 medical record samples were collected using purposive sampling from 2020 to 2024, consisting of 130 cases of adenomyosis and 91 controls of uterine leiomyoma. Clinical variables including blood pressure, body mass index, age, parity, and residence were assessed. Data analysis was performed using Chi-Square tests. The results showed a significant association between blood pressure and the incidence of adenomyosis, with hypertensive women having a 2.7-fold higher risk of adenomyosis compared to normotensive women. In contrast, there was no significant association between body mass index and adenomyosis. In conclusion, the findings suggest that hypertension is a more prominent risk factor than obesity in the development of adenomyosis. Future studies involving to enhance preventive strategies and optimize clinical management.

Keywords: *Adenomyosis; Blood Pressure; Body Mass Index; Hypertension; Risk Factor*

1. Introduction

Adenomyosis is a benign uterine disorder characterized by the presence of endometrial glands and stroma within the myometrium (Schrager and Yogendran, 2022). Clinically, adenomyosis is associated with a range of gynecological symptoms including menorrhagia, dysmenorrhea, chronic pelvic pain, uterine enlargement, and infertility (Zhai et al., 2020). The condition is most frequently diagnosed in women in their fourth and fifth decades of life (Shinohara et al., 2020). Beyond its gynecological manifestations, adenomyosis has profound effects on women's overall well-being, impairing physical, emotional, sexual, and professional quality of life (Benetti-Pinto et al., 2017). Despite its substantial burden, the true incidence and prevalence of adenomyosis remain poorly defined, partly due to variations in

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DOI: 10.31983/jrk.v14i2.13995

diagnostic criteria and differences in populations studied.

Epidemiological data show that adenomyosis has a wide range of reported prevalence. A large-scale Italian study involving 1.22 million women aged 15–50 years estimated a cumulative incidence of 0.027% (Upson and Missmer, 2020). Similarly, population-based research in the United States between 2006 and 2015 reported an incidence of 1.03%, corresponding to 28.9 cases per 10,000 women annually (Yu et al., 2020). In Indonesia, hospital-based data suggest relatively high rates of adenomyosis. At RSUD Cengkareng, West Jakarta, 37 cases were identified between 2017–2019, representing 24.2% of uterine pathology diagnoses (Alfarizan and Marindawati, 2020). At Dr. Hasan Sadikin Hospital, Bandung, 116 cases of adenomyosis were studied from 2015–2016, with 70.7% occurring in women above 35 years of age (Fitrina et al., 2018). At RSUP Prof. R. D. Kandou, Manado, adenomyosis accounted for 24.2% of 33 endometriosis cases diagnosed between 2011–2015 (Pangemanan et al., 2015). These findings highlight geographic variation and suggest that adenomyosis may be more common in Southeast Asian populations than previously reported in Western countries. Given these relatively high local rates, understanding modifiable risk factors, particulary vascular and metabolic parameters, becomes increasingly important to support early detection and prevention strategies in indonesian populations.

The precise etiology and pathophysiology of adenomyosis remain incompletely understood and continue to be the subject of ongoing research (Pados et al., 2023). The most widely accepted theory involves disruption of the junctional zone of the myometrium, possibly due to repetitive uterine contractions and microtrauma during reproductive life. This tissue injury and repair (TIAR) process is hypothesized to promote aberrant endometrial invagination into the myometrium, facilitated by local inflammatory responses and increased estrogen synthesis (Zhai et al., 2020). Established risk factors include multiparity, advanced reproductive age, and prior cesarean section or uterine surgery (Vannuccini and Petraglia, 2019; Pados et al., 2023). However, emerging evidence points toward potential systemic contributors, including vascular and metabolic factors, that may influence the risk of adenomyosis.

One area of growing interest is the relationship between blood pressure and adenomyosis. Hypertension has been reported with increased frequency among women with adenomyosis, though the nature of this association remains unclear. A retrospective population-based cohort study by Jung et al. (2024) involving over 1.2 million nulliparous women in South Korea demonstrated that adenomyosis was associated with higher rates of gestational hypertension and preeclampsia, both before and during pregnancy. Similarly, Chen et al. (2024), in a study of 1,208 pregnant women in China, found that the incidence of gestational hypertension was significantly higher in the adenomyosis group compared to controls ($p=0.004$). These findings suggest that adenomyosis may predispose to hypertensive disorders through abnormal placental development, spiral artery dysfunction, and intrauterine oxidative stress. In line with these observations, Gizzo et al. (2016) reported in an Italian case-control study that 89.2% of women with adenomyosis had a history of hypertension compared to 52% in the non-adenomyosis group, supporting the hypothesis that vascular dysregulation is a key pathogenic factor.

In addition to hypertension, body mass index (BMI) has been investigated as a possible determinant of adenomyosis. Adipose tissue is known to play a critical role in estrogen metabolism, and hyperestrogenemia is a recognized driver of adenomyosis pathophysiology (Cunningham et al., 2018). Several studies have shown that women with obesity (BMI ≥30 kg/m²) are at higher risk of developing adenomyosis, with risk estimates ranging from 1.4 to 3.8 compared with women of normal BMI (Upson and Missmer, 2020; Struble et al., 2016). However, conflicting evidence exists. Puente et al. (2016) reported that adenomyosis was found in women with lower BMI, with a mean BMI of 20.9 kg/m² compared to 21.8 kg/m² in controls. Similarly, Genc et al. (2015) observed adenomyosis prevalence among women with BMI <25 kg/m² in a Turkish cohort. These discrepancies may reflect differences in study populations, diagnostic methodologies, or the limitations of BMI as a proxy for fat distribution.

These inconsistencies underscore important gaps in the literature. While hypertension and obesity have been identified as risk factors in some studies, their precise contributions to the pathogenesis of adenomyosis remain controversial. Moreover, few studies have examined these factors simultaneously in

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DOI: 10.31983/jrk.v14i2.13995

the same population, and even fewer have explored them in Southeast Asian settings, where genetic, environmental, and lifestyle factors may differ from Western populations. Therefore, further investigation is needed to clarify whether blood pressure and BMI act as independent or interacting risk factors for adenomyosis.

The present study seeks to address these gaps by analyzing the association between blood pressure and BMI with adenomyosis incidence among women whose diagnoses were confirmed histopathologically at PKU Muhammadiyah Hospital Surakarta. By focusing on these two systemic factors, this study aims to contribute novel insights into the interplay between cardiovascular and metabolic health and uterine pathology. The innovative value of this research lies in its attempt to integrate vascular and metabolic perspectives into the study of adenomyosis, which has traditionally been investigated primarily from hormonal and surgical standpoints. The findings may have important implications for risk stratification, early detection, and prevention strategies, particularly in clinical settings where adenomyosis remains underdiagnosed. To our knowledge, no study in indonesia has simultaneously examined the combined role of blood pressure and BMI in adenomyosis using histopathological confirmation, making this investigation an important contribution to the existing literature.

2. Method

Research Design

This study employed an observational analytic retrospective hospital based case control design, in which adenomyosis cases were compared with leiomyoma uteri controls. This design was selected to identify potential association between blood pressure and BMI with the occurrence of adenomyosis. No matching was performed between cases and controls.

Population

The target population of this study consisted of all histopathology records of uterine tumors archived at the Pathology Anatomy Laboratory of PKU Muhammadiyah Hospital Surakarta. From this population, the actual population was determined as histopathology records that had been diagnosed with adenomyosis within the study period.

Sampling Technique and Sample Size Determination

The sample used in this study was derived from histopathology records with a diagnosis of adenomyosis between 2020 and 2024. A non-probability purposive sampling technique was applied, meaning that every subject meeting the inclusion criteria was selected until the required number was achieved. The study analyzed a total of 221 samples that met the eligibility criteria, comprising 130 cases of adenomyosis and 91 control of uterine leiomyoma.

Restriction Criteria

The inclusion criteria of this study were histopathology records with conclusions consistent with adenomyosis, patients within the age range of 25 to 50 years, and medical records with complete identity information. Conversely, the exclusion criteria included records with histopathology diagnoses other than adenomyosis, patients younger than 25 years or older than 50 years, incomplete medical record data, histopathology findings indicating malignancy, and patients with a history of tamoxifen therapy.

Measurement

The type of data used in this study was primary data obtained from histopathological medical record at the Department of Anatomical Pathological, PKU Muhammadiyah Surakarta Hospital. The independent variables analyzed include blood pressure and body mass index (BMI). Blood pressure was categorized as normal if <140/90 mmHg, and as hypertensive if ≥140/90 mmHg. Meanwhile, BMI was

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DOI: 10.31983/jrk.v14i2.13995

calculated by dividing body weight in kilograms by the square of height in meters. BMI values were then classified as obese if >25 kg/m^2 and non-obese if ≤ 25 kg/m^2.

Statistical Analysis

Data analysis was conducted in three stages. First, univariate analysis was carried out to describe the distribution of adenomyosis cases according to blood pressure and BMI. Second, bivariate analysis was performed using the Chi-square test to examine the relationship between the independent variables and the dependent variable.

Ethical Clearance

The researchers obtained a research permit from the Faculty of Medicine, Universitas Muhammadiyah Surakarta under the reference number 1314/C.4-III/FK/VIII/2025. Ethical approval was also granted by the Health Research and Development Ethics Committee (KEPK) of PKU Muhammadiyah Surakarta Hospital, with: approval No.07/KEPK/RS.PKU/IX/2025.

3. Result and Discussion

This study analyzed the association between body mass index (BMI) and blood pressure in cases of adenomyosis confirmed through histopathological examination. The research was conducted at the Laboratory of Anatomical Pathology, PKU Muhammadiyah Hospital Surakarta. Based on histopathology medical records, a total of 221 samples were included, collected using a purposive sampling technique from 2020 to 2024. These samples were divided into two groups: 130 adenomyosis samples as the case group and 91 leiomyoma uteri samples as the control group. The primary data examined included BMI, age, parity, residence, and blood pressure. Subsequently, the data were analyzed using SPSS version 26.0 for Windows. The results of the data analysis are presented as follows:

Table 1. Distribution of Clinical and Demographic Characteristics Among Adenomyosis Cases and Leiomyoma Controls

Variable	Category	Adenomyosis n (%)	Leiomyoma n (%)
Body Mass Index (BMI)	Obese (>25.0 kg/m^2)	53 (40.8)	37 (40.7)
	Normal (18.5–25.0 kg/m^2)	77 (59.2)	54 (59.3)
Blood Pressure	Hypertension (≥140/90 mmHg)	48 (36.9)	16 (17.6)
	Normotensive (<140/90 mmHg)	82 (63.1)	75 (82.4)
Age	At risk (25–50 years)	111 (85.4)	86 (94.5)
	Not at risk (>50 years)	19 (14.6)	5 (5.5)
Parity	Nulliparous	22 (16.9)	26 (28.6)
	Primiparous & multiparous	108 (83.1)	65 (71.4)
Residence	Urban	118 (90.8)	84 (92.3)
	Rural	12 (9.2)	7 (7.7)

(Primary Data, 2025)

Table 1 present the distribution of clinical and demographic characteristic among adenomyosis cases and leiomyoma controls. In the adenomyosis group, most respondents had a normal BMI (59.2%) and were normotensive (63.1%). A similar pattern was observed in the control group, where the majority

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DOI: 10.31983/jrk.v14i2.13995

also had a normal BMI (59.3%) and normal blood pressure (82.4%). Most respondents in both groups were within the reproductive age range of 25-50 years and were predominantly primiparous or multiparous. Additionally, most participants in both groups resided in urban areas. overall, the distribution of characteristic between cases and controls appeared comparable, except for blood pressure, wich showed a higher proportion of hypertension among adenomyosis cases.

Table 2. Bivariate Analysis of Blood Pressure and BMI with the Incidence of Adenomyosis

Variable	Category	Adenomyosis n (%)	Leiomyoma n (%)	OR	95% CI (Lower–Upper)	p-value
Blood Pressure	Hypertension (≥140/90 mmHg)	82 **(63.1)**	16 (17.6)	2.744	1.437–5.239	0.002
	Normotensive (<140/90 mmHg)	48 (36.9)	75 **(82.4)**			
Body Mass Index (BMI)	Obese (>25 kg/m²)	53 (40.8)	37 (40.7)	1.005	0.582-1.733	0.987
	Non-obese (≤25 kg/m²)	77 **(59.2)**	54 **(59.3)**			

(Primary Data, 2025)

The bivariat analysis presented in Table 2 shows a significant association between blood pressure and the incidence of adenomyosis, with a p-value of 0.002 ($p<0.05$). Most adenomyosis cases occurred among hypertensive women (63.1%), while the majority of leiomyoma controls were normotensive (82.4%). These findings indicate that the women with hypertension have approximately 2.7 times higher odds of developing adenomyosis compared to normotensive women. In contrast, the relationship between BMI and adenomyosis was not statistically significant, with a p-value of 0.987 ($p > 0.05$). Both adenomyosis and leiomyoma groups showed similar distribution of BMI, with the majority classified as non-obese. This suggest that obesity was not independent risk factor for adenomyosis in this population. Overall, these result imply that blood pressure particularly hypertnesion plays a more dominant role than body mass index in influencing the risk of adenomyosis among women of reproductive age.

The Relationship Between Blood Pressure and the Incidence of Adenomyosis

The findings of this study indicate that the majority of respondents with adenomyosis presented with elevated blood pressure (hypertension), amounting to 82 individuals (63.1%). In contrast, within the uterine leiomyoma group, most respondents exhibited normal blood pressure, accounting for 75 individuals (82.4%), while only 16 respondents (17.6%) were hypertensive. Bivariate analysis demonstrated a statistically significant association between blood pressure and the incidence of adenomyosis, with an odds ratio (OR) of 2.744. This suggests that women with hypertension are approximately 2.7 times more likely to develop adenomyosis compared to normotensive women.

These results are consistent with the study conducted by Jung et al. (2024) in South Korea, which employed a nationwide population-based retrospective cohort design involving 1,226,475 nulliparous women from 2017 to 2022. The researchers found that adenomyosis was associated with an increased incidence of gestational hypertension and preeclampsia, both prior to and during pregnancy. They emphasized that adenomyosis may impair placental development due to abnormalities in the spiral arteries and intrauterine oxidative stress, thereby increasing the risk of hypertension.

Similarly, a study by Chen et al. (2024) conducted at the Maternity and Child Hospital in China between July 2016 and December 2020 analyzed 1,208 medical records of pregnant women aged ≥18 years. The study reported that the incidence of gestational hypertension was significantly higher in the adenomyosis group compared to the control group, with adenomyosis being more prevalent among respondents who developed gestational hypertension (5.69%). The authors concluded that adenomyosis is associated with myometrial inflammatory activation and uterine vascular system impairment, which can affect systemic blood pressure regulation.

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DOI: 10.31983/jrk.v14i2.13995

Comparable findings were reported by Gizzo et al. (2016) in a retrospective case-control study involving 289 Italian women undergoing hysterectomy for benign uterine conditions. This study demonstrated a significant relationship between blood pressure and adenomyosis, revealing that 89.2% of women with adenomyosis had a history of hypertension compared to 52% in the non-adenomyosis group, reinforcing the notion that hypertension may serve as a risk factor for adenomyosis.

The significant association between blood pressure and adenomyosis observed in the present study may be explained by the high proportion of respondents with blood pressure ≥140/90 mmHg (hypertension), particularly within the adenomyosis group. Moreover, the majority of respondents fell into the borderline hypertension category, which physiologically already exerts detrimental effects on the uterine vascular system. This condition may progress to clinical hypertension and trigger systemic inflammatory activation that facilitates the pathogenesis of adenomyosis.

The primary mechanism underlying adenomyosis involves the Tissue Injury and Repair (TIAR) process, in which microtrauma from uterine contractions stimulates local estrogen synthesis through chronic inflammatory pathways, promoting endometrial invagination into the myometrium (Vannuccini and Petraglia, 2019; Zhai et al., 2020). According to the TIAR theory, estradiol (E2) has been shown to enhance peristaltic activity in the subendometrial myometrium. Furthermore, local endometrial E2 stimulates uterine peristalsis via activation of estrogen receptor-α (ERα) and oxytocin, leading to excessive mechanical stress on myometrial cells in the fundo-cornual region (Kurniati et al., 2024; Zhai et al., 2020).

Chronic inflammation is hypothesized to contribute to systemic blood pressure elevation. Persistent localized inflammation may disrupt vascular structure and endothelial function, thereby predisposing to preeclampsia and gestational hypertension (Martire et al., 2025). Elevated blood pressure can compromise tissue oxygenation and trigger oxidative stress, further accelerating chronic inflammatory processes (Yusuf et al., 2024). Chronic uterine inflammation induces activation of interleukin-1 (IL-1) and production of prostaglandin E2 (PGE2), which upregulates aromatase and Steroidogenic Acute Regulatory (STAR) enzyme expression, leading to increased local estrogen levels. This excess estrogen promotes endometrial invagination and supports the formation of adenomyotic lesions (Zhai et al., 2020).

Moreover, these processes can result in hyperplasia of endometrial spiral arteries and defective placentation, which serve as the biological basis for gestational hypertension (Jung et al., 2024). Consequently, adenomyosis may create a suboptimal endometrial environment for embryo implantation, thereby increasing the risk of miscarriage, abnormal placentation, and preterm birth (Vannuccini and Petraglia, 2019; Harada, Taniguchi, and Harada, 2022).

The Relationship Between BMI and the Incidence of Adenomyosis

The results of this study demonstrated that the incidence of adenomyosis was more frequently observed among respondents with a normal BMI, accounting for 77 individuals (59.2%). In contrast, within the uterine leiomyoma group, adenomyosis was more frequently identified among obese respondents, totaling 42 individuals (64.6%). Statistical analysis using the Chi-Square test revealed no significant association between BMI and the incidence of adenomyosis. This indicates that obesity is not a significant risk factor for adenomyosis in this cohort.

These findings are consistent with a study conducted by Puente et al. (2016) in Spain, carried out between 2009 and 2013, which similarly demonstrated that obesity was not associated with adenomyosis. Their analysis revealed that adenomyosis was identified in women with a lower mean BMI (20.9 kg/m²), compared to a mean BMI of 21.8 kg/m² in the non-adenomyosis group. The study included 1,015 women assessed using 3D ultrasound and histopathological examination. Similarly, a study conducted at a Turkish hospital reported that adenomyosis was predominantly found among women with normal body weight (BMI <25.0 kg/m²). This study examined 327 parous women diagnosed with adenomyosis confirmed by histopathological evaluation (Genc et al., 2015).

In contrast, the present findings are inconsistent with several other studies that demonstrated a significant association between obesity and adenomyosis. For instance, Stanekova et al. (2018) reported

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that patients with adenomyosis had a higher mean BMI of 27.6 kg/m² compared with 25.6 kg/m² in the non-adenomyosis group, both within the overweight category. This retrospective cohort study involved 34 patients diagnosed with adenomyosis, with a mean age of 37 years, the majority of whom were nulliparous women.

The high degree of homogeneity in respondent characteristics in this study may partially explain the lack of significant association between BMI and adenomyosis. Most participants were women aged 25–50 years, with either primiparous or multiparous status, and predominantly resided in urban areas. Moreover, the nonsignificant findings may also be attributed to the limitations of BMI as a proxy for fat distribution. BMI does not account for the specific localization of adipose tissue, such as visceral or pelvic subcutaneous fat, which may be more relevant to the pathogenesis of adenomyosis. Even in individuals with a normal BMI, excessive local fat accumulation may still occur, contributing to increased estrogen levels via hyperestrogenemia. One study demonstrated that subcutaneous fat thickness is a more reliable predictor of adenomyosis risk compared to overall BMI values (Kadıyoran, 2019).

Theoretically, obesity is believed to influence the risk of adenomyosis through hormonal mechanisms, particularly hyperestrogenemia. Adipose tissue is known to increase the conversion of androgens into estrogens via aromatase activity, thereby contributing to elevated circulating estrogen levels. Excess estrogen stimulates the proliferation of endometrial tissue and promotes invagination of the endometrium into the myometrium (Cunningham et al., 2018; Zhai et al., 2020). In addition, repeated and excessive uterine contractions induced by estrogen may cause trauma to the uterine junctional zone (JZ). This microtrauma initiates inflammatory responses, increasing IL-1β levels, which subsequently upregulate prostaglandin E2 (PGE2) and cyclooxygenase-2 (COX-2). This process ultimately enhances estradiol (E2) production and estrogen receptor beta (ERβ) expression, both of which are hypothesized to facilitate adenomyotic lesion development (d'Otreppe et al., 2024).

4. Conclusion and Suggestion

This study demonstrated a significant association between hypertension and the incidence of adenomyosis, with an odds ratio (OR) of 2.744. Women with high blood pressure were found to have a 2.7 times greater of risk developing adenomyosis compared to those with normal blood pressure. Meanwhile, body mass index (BMI) did not show a significant relationship with adenomyosis, as most cases occurred in women with normal BMI. Future research should be conducted with larger and more diverse populations, and include additional variables such as the duration of hypertension and detailed body fat distribution profiles. These approaches may help to provide a deeper understanding of the complex pathophysiology of adenomyosis and support the development of more effective prevention, risk stratification, and clinical management strategies for women at risk.

5. Acknowledgement

The authors wish to extend their sincere gratitude to the Department of Pathology Anatomy, Faculty of Medicine, University of Muhammadiyah Surakarta, for providing the necessary facilities and support throughout the course of this research. Appreciation is also conveyed to PKU Muhammadiyah Surakarta Hospital for granting permission to carry out the study within its premises.

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