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Prevalence of Adenomyosis in Hysterectomy Specimens from Patients with Benign Gynecological Conditions

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Abstract

Background: Adenomyosis is defined by the ectopic presence of endometrial tissue within the myometrium. The reported histopathological prevalence in hysterectomy specimens varies substantially (8.8–61.5%), and associated risk factors remain a subject of debate.

Objectives: This study aimed to determine the prevalence of adenomyosis in hysterectomy specimens obtained for benign gynecological indications and to evaluate its association with key demographic and clinical variables.

Methods: This cross-sectional investigation (2023–2025) consecutively enrolled 99 women who underwent hysterectomy for benign conditions at hospitals affiliated with Mashhad Medical Sciences, Islamic Azad University. Patients with gynecological malignancies or incomplete medical records were excluded. Demographic and obstetric data, including age, body mass index (BMI), educational attainment, gravidity, parity, mode of delivery, and history of abortion, were systematically recorded. Adenomyosis was diagnosed through histopathological examination. Following assessment of normality using the Shapiro–Wilk test, continuous variables were compared using the independent-samples t-test, and categorical variables were analyzed using the chi-square test (statistical significance set at $p < 0.05$).

Results: Adenomyosis was histologically confirmed in 36 women (36.4%). The mean age of the cohort was 55.3 ± 10.4 years, and the mean BMI was 27.7 ± 3.7 kg/m². Women diagnosed with adenomyosis exhibited a significantly higher mean BMI compared to those without the condition (30.1 ± 3.0 vs. 26.3 ± 3.4 kg/m²; $p < 0.001$). In the categorical analysis, adenomyosis was absent in all participants with a normal BMI (<25 kg/m²) but was identified in 38.3% of overweight women and 58.1% of obese women ($p < 0.001$). No statistically significant associations were observed between adenomyosis and age, gravidity, parity, mode of delivery, history of abortion, or educational level.

Conclusion: Adenomyosis was present in over one-third of hysterectomy specimens obtained for benign indications. Elevated BMI emerged as the sole significant risk factor associated with the condition, highlighting overweight and obesity as potentially modifiable contributors to adenomyosis pathogenesis.

Keywords: Adenomyosis; Body Mass Index; Hysterectomy; Benign Gynecologic Diseases; Risk Factors

1. Background

The uterus is a complex anatomical organ comprising three histologically and anatomically distinct layers: the endometrium, myometrium, and perimetrium (1). Adenomyosis is a common, yet etiologically elusive, gynecological disorder characterized by the ectopic proliferation of endometrial glands and stroma deep within the myometrium, typically accompanied by adjacent smooth muscle hyperplasia and hypertrophy (2). Although the precise pathogenesis remains incompletely understood, the condition is widely believed to originate from a disruption of the endometrial–myometrial

interface, facilitating the aberrant invasion of endometrial tissue into the myometrial layer, along with associated neoangiogenesis and myocyte proliferation (3). Notably, a significant correlation has been established between KRAS gene mutations within the endometrial epithelium and the development of adenomyosis (4).

The reported prevalence of adenomyosis in hysterectomy specimens ranges widely, from 8.8% to 61.5%. This considerable variation is primarily attributed to the lack of universally standardized histopathological diagnostic criteria and inconsistencies in the extent of tissue sampling and analysis (5). Proposed risk factors for adenomyosis include advancing age, multiparity, prior uterine surgery, cigarette smoking, a history of ectopic pregnancy, antidepressant use, and tamoxifen therapy (6). While no single symptom is pathognomonic, the clinical presentation is frequently characterized by a constellation of symptoms including pelvic pain (dysmenorrhea, dyspareunia, and chronic pelvic pain), abnormal uterine bleeding (AUB), subfertility, and a sensation of pelvic pressure or fullness (7). Histopathological assessment of hysterectomy specimens remains the gold standard for definitive diagnosis (8). Although advances in imaging modalities, particularly transvaginal ultrasound, have facilitated earlier detection, the diagnosis is still frequently established only postoperatively (9). Therapeutic strategies are tailored according to symptom severity, patient age, fertility preservation goals, and the extent of disease, and are broadly categorized into medical and surgical interventions (10).

Adenomyosis frequently coexists with other benign uterine pathologies, and its diagnosis remains challenging due to the substantial overlap in clinical presentation and imaging findings with conditions such as uterine leiomyomas and endometriosis. Given its strong association with chronic pelvic pain, heavy menstrual bleeding, dyspareunia, and impaired fertility—factors that profoundly diminish quality of life and escalate healthcare utilization—a rigorous evaluation of its prevalence and associated risk factors is of considerable clinical relevance. Accordingly, the present study was designed to ascertain the histopathological prevalence of adenomyosis in hysterectomy specimens obtained for benign gynecological indications and to assess its relationship with key demographic and obstetric parameters.

2. Methods

2.1. Study Design and Population

This cross-sectional study was conducted between 2023 and 2025 on a consecutive series of patients who underwent hysterectomy for benign gynecologic indications. The study protocol received approval from the Research Ethics Committee of Mashhad Medical Sciences, Islamic Azad University (Approval Code: IR.IAU.MSHD.REC.1402.190). The study population encompassed all women undergoing hysterectomy at university-affiliated hospitals in Mashhad for various benign indications. The primary presenting symptoms were categorized into four groups: abnormal uterine bleeding (AUB), symptomatic pelvic organ prolapse (POP), chronic pelvic pain, and a combination of symptoms (Table 1). Inclusion criteria specified women undergoing hysterectomy for benign disease. Exclusion criteria comprised incomplete medical records or histopathological evidence of malignancy.

2.2. Data Collection and Variables

Demographic variables, including age, body mass index (BMI), and educational attainment, were abstracted from medical

records. Each participant was interviewed to ascertain a comprehensive obstetric and gynecologic history, including gravidity, parity, mode of previous deliveries, and history of spontaneous or induced abortion. Histopathological findings from the hysterectomy specimens were collected and assessed for all enrolled patients.

2.3. Sample Size Calculation

Sample size estimation was based on a previously reported prevalence of adenomyosis among hysterectomy patients by Parazzini et al. (11). Using the standard formula for cross-sectional study sample size calculation, assuming a prevalence (P) of 0.282, a margin of error (d) equivalent to 10% of P (d = 0.1 × P), a confidence level of 95% (α = 0.05), and a corresponding Z-score ($Z_{1-\alpha/2}$) of 1.96, the minimum required sample size was calculated as follows: $N = (Z_{1-\alpha/2})^2 \times P \times (1 - P) / d^2$. Substituting the values yielded $N = (1.96)^2 \times 0.282 \times (1 - 0.282) / (0.1 \times 0.282)^2 \approx 97.8$. Thus, a minimum of 98 patients was required for the study.

2.4. Statistical Analysis

All statistical analyses were performed using SPSS software, version 26 (IBM Corp., Armonk, NY, USA). The Shapiro–Wilk test was employed to assess the normality of distribution for continuous variables. Normally distributed data are presented as mean ± standard deviation (SD), while non-normally distributed data are reported as median and interquartile range (IQR). Given the total sample size of 99 participants and subgroup sizes exceeding 30, the independent-samples t-test was used for comparisons of continuous variables between groups, a robust approach under the central limit theorem. Categorical variables were compared using the chi-square test, with Fisher's exact test applied in cases of low expected cell frequencies. A p-value < 0.05 was considered statistically significant for all analyses.

3. Result

A total of 99 women who underwent hysterectomy for benign gynecologic lesions between 2023 and 2025 were included in the analysis. As detailed in Table 1, the most frequent primary indication for hysterectomy was AUB (31.3%), followed by symptomatic POP (28.3%) and chronic pelvic pain (26.3%). Histopathological examination confirmed the presence of adenomyosis in 36 patients, yielding a prevalence of 36.4%.

The mean age of the study cohort was 55.3 ± 10.4 years, and the mean BMI was 27.7 ± 3.7 kg/m². The mean number of pregnancies was 3.7 ± 1.4, mean parity was 2.9 ± 1.6, and the mean number of abortions was 0.8 ± 1.0. A substantial majority of participants (78.8%) were classified as overweight or obese. Furthermore, 83.8% of women had experienced more than two pregnancies, and 43.4% had attained an educational level of a high school diploma or less (Table 1).

A comparative analysis of continuous variables between women with and without adenomyosis is presented in Table 2. Women with adenomyosis had a significantly higher mean BMI than those without the condition (30.1 ± 3.0 vs. 26.3 ± 3.4 kg/m²; p < 0.001). No statistically significant differences were detected between the two groups regarding age, gravidity, parity, or number of abortions.

Table 1. Baseline demographic and clinical characteristics of the study population.

Variable	Subgroups	N (%)
Age (years)	≤50 >50	32 (32.3%) 67 (67.7%)
BMI (kg/m²)	Normal Overweight Obese	21 (21.2%) 47 (47.5%) 31 (31.3%)
Gravidity	≤2 >2	16 (16.2%) 83 (83.8%)
Parity	≤2 >2	49 (49.5%) 50 (50.5%)
Educational level	Diploma or below Bachelor's Master's/Doctorate	43 (43.4%) 31 (31.3%) 25 (25.3%)
History of abortion	No Yes	49 (49.5%) 50 (50.5%)
History of C-Section	No Yes	59 (59.6%) 40 (40.4%)
History of NVD	No Yes	15 (15.2%) 84 (84.8%)
Major Symptom	AUB Prolapse* Pelvic pain Combined symptoms**	31 (31.3%) 28 (28.3%) 26 (26.3%) 14 (14.1%)
Adenomyosis	Present	36 (36.4%)

**Includes patients presenting with vaginal bulging and/or urinary incontinence.*

*** includes patients presenting with both abnormal uterine bleeding (AUB) and pelvic pain as co-dominant symptoms.*

Table 2. Comparison of continuous variables between women with and without adenomyosis.

Variable	Adenomyosis present (n=36)*	Adenomyosis absent (n=63)*	95% Confidence Interval		Statistic	p-value
			Lower	Upper		
Age (years)	53 [48–55]	55 [48–66]	53.194	57.351	1.5509	0.124
BMI (kg/m²)	30.13 (2.96)	26.34 (3.40)	26.980	28.464	-5.5892	**<0.001**
Gravidity	3 [3–4]	4 [3–5]	3.426	3.968	1.5631	0.121
Parity	2 [2–3]	3 [2–4]	2.596	3.242	1.4377	0.154
Number of NVD	1 [1–2]	2 [1–3]	1.591	2.207	1.4114	0.161
Number of CS	1 [0–2]	0 [0–1]	0.692	1.349	0.0918	0.927
Number of abortions	1 [0–1]	0 [0–1]	0.603	0.993	-0.0579	0.954

***Note:** Values represent median [interquartile range] or mean (SD), depending on the Shapiro-Wilk normality test.

Analysis of categorical variables, summarized in Table 3, revealed that adenomyosis was absent in all women classified as normal weight (BMI < 25 kg/m²). In contrast, the condition was identified in 38.3% of overweight women and 58.1% of obese women ($p < 0.001$). Other categorical variables, including educational level, history of abortion, history of cesarean section, and history of vaginal delivery, showed no statistically significant association with the presence of adenomyosis.

Table 3. Comparison of categorical variables between women with and without adenomyosis

Variable	Subgroups	Adenomyosis present(n=36)*	Adenomyosis absent(n=63)*	p-value
BMI (kg/m²)	Normal	0 (0.0%)	21 (33.3%)	**<0.001**
	Overweight	18 (50.0%)	29 (46.0%)	
	Obese	18 (50.0%)	13 (20.6%)	
	Diploma or below	18 (50.0%)	25 (39.7%)	
Educational level	Bachelor's	10 (27.8%)	21 (33.3%)	0.609
	Master's/Doctorate	8 (22.2%)	17 (27.0%)	
History of abortion	No	17 (47.2%)	32 (50.8%)	0.732
	Yes	19 (52.8%)	31 (49.2%)	
History of CS	No	23 (63.9%)	36 (57.1%)	0.511
	Yes	13 (36.1%)	27 (42.9%)	
History of NVD	No	7 (19.4%)	8 (12.7%)	0.398
	Yes	29 (80.6%)	55 (87.3%)	

***Note:** Values represent number (percentage)

Adenomyosis was diagnosed in over one-third of the hysterectomy specimens examined. An elevated BMI—whether analyzed as a continuous or categorical variable—was the sole significant risk factor associated with the presence of adenomyosis in this cohort.

4. Discussion

The present study identified a notable prevalence of adenomyosis (36.4%) among hysterectomy specimens obtained for benign gynecologic indications. While no significant associations were observed between adenomyosis and factors such as age, gravidity, parity, mode of delivery, history of abortion, or educational level, a robust and statistically significant relationship was demonstrated between adenomyosis and elevated BMI. This finding underscores a higher disease burden among patients with increased adiposity.

The pathophysiological link between obesity and adenomyosis is biologically plausible and multifactorial. Obesity promotes a state of chronic low-grade systemic inflammation and is associated with elevated levels of prostaglandin F2α, which can enhance uterine contractility and exacerbate pain symptomatology. Furthermore, the hormonal milieu of excess adipose tissue, characterized by altered estrogen metabolism and increased

peripheral aromatization of androgens to estrone, fosters a hyperestrogenic environment conducive to the aberrant growth and persistence of ectopic endometrial tissue within the myometrium. These mechanistic pathways provide a robust framework for understanding the significant positive correlation observed between obesity and adenomyosis severity (12).

The prevalence rate of 36.4% reported in this study aligns closely with findings from several large-scale investigations employing comparable histopathological diagnostic standards. In a retrospective evaluation of 2,544 hysterectomy specimens, Zaid et al. (2017) reported an adenomyosis prevalence of 31.2% (13). Similarly, Giorgi et al. (2024) documented a 39.4% prevalence among women undergoing hysterectomy for postpartum hemorrhage (14). The consistency of these prevalence estimates, derived from diverse clinical indications but utilizing the gold standard of post-hysterectomy histopathological evaluation, reinforces the reliability and generalizability of our findings.

Our observed prevalence of 36.4% falls within the range reported by Krentel et al. (2022) (42.0% in 307 cases) and Goti et al. (2025) (25.0% in 600 cases), both of which also relied on histopathological evaluation of hysterectomy specimens (15, 16). The variations among these studies can reasonably be attributed to differences in sample size, population demographics, and specific inclusion and exclusion criteria. Notably, the stringent exclusion of malignant pathologies in our analysis may have contributed to a relative increase in diagnostic specificity. Despite a modest sample size, the prevalence identified in our cohort closely mirrors that of larger studies, attesting to the robustness of the data. Future multicenter investigations with harmonized exclusion criteria and standardized histopathological confirmation protocols are warranted to further delineate the true prevalence and diagnostic landscape of adenomyosis.

In contrast to our findings, Bai et al. (2025), in a cross-sectional study of 171 women aged 18–45 years presenting with AUB, reported an adenomyosis prevalence of only 10.5% and found no significant association with BMI (17). Similarly, a systematic review by Mishra et al. (2023) estimated a pooled prevalence of 10% based on para-clinical diagnostic methods (18). The discrepancy between these findings and our own higher prevalence and strong association with BMI is likely attributable to two principal factors. First, the mean age of our cohort was significantly older, aligning with the established understanding that adenomyosis is more frequently diagnosed in perimenopausal and postmenopausal women. Second, our reliance on histopathological assessment of hysterectomy specimens offers the most definitive diagnostic confirmation, in contrast to the lower sensitivity of imaging-based or clinical diagnoses. Intriguingly, factors such as age, mode of delivery, and education were non-significant in both our study and that of Bai et al., suggesting shared demographic patterns despite methodological and population differences. This underscores the profound impact of diagnostic methodology and population characteristics on reported prevalence rates.

Further supporting the link between adenomyosis and elevated BMI, a retrospective cohort study by Li et al. (2024) involving 154 infertile women, half of whom were diagnosed with adenomyosis via MRI and confirmed by hysteroscopy and endometrial biopsy, demonstrated a significant association with higher BMI ($p = 0.007$) (12). While the prevalence reported in their focused infertility cohort was higher (50%), the concordant finding regarding BMI as a potential risk factor strengthens the evidence base established by our data.

This study possesses several notable

strengths and limitations. A key strength is the diagnosis of adenomyosis using the gold standard method: histopathological evaluation of multiple sections from hysterectomy specimens, ensuring superior diagnostic accuracy compared to non-invasive techniques such as ultrasound or endometrial biopsy. However, several limitations warrant consideration. The relatively modest sample size may have limited the statistical power to detect weaker associations and could affect the generalizability of the findings. The single-center design may introduce selection bias and limit demographic heterogeneity. Additionally, incomplete documentation of medication histories relevant to adenomyosis pathogenesis, such as tamoxifen, antidepressants, or GnRH agonist therapy, may have precluded the identification of other significant associations. Given the incomplete understanding of adenomyosis pathogenesis, future studies should rigorously examine patients' medication histories to better inform prevention and monitoring strategies. Finally, the retrospective design and data availability precluded a detailed correlative analysis between specific symptom profiles and histopathological subtypes. Large-scale, prospective multicenter studies with diverse populations are warranted to validate and extend these findings.

5. Conclusion

This investigation revealed no statistically significant associations between adenomyosis and age, gravidity, parity, mode of delivery, history of abortion, or educational level. In contrast, a BMI of ≥25 kg/m² was strongly and independently associated with an increased prevalence of adenomyosis. These findings position excess body weight as a potentially modifiable risk factor for adenomyosis in this population, warranting further investigation into the role of metabolic and inflammatory pathways in disease pathogenesis.

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manuscript and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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