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Original Research Article

Retrospective Analysis of Metabolic Risk Factors in Patients with Endometrial Hyperplasia

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Abstract:

Background: Endometrial hyperplasia (EH) is characterized by abnormal proliferation of endometrial glands, often driven by unopposed estrogen exposure, and serves as a precursor to endometrial carcinoma. Metabolic disturbances such as obesity, insulin resistance, and dyslipidemia may influence its development.

Aim: To evaluate the association between EH and metabolic risk factors among women presenting with abnormal uterine bleeding.

Methodology: A retrospective record-based study was conducted on 80 women aged 30–65 years who presented with abnormal uterine bleeding at the Department of Obstetrics and Gynaecology, Nalanda Medical College and Hospital, Patna. Patient records were reviewed to obtain demographic, clinical, biochemical, and histopathological data. Metabolic parameters assessed included body mass index (BMI), waist-to-hip ratio, blood pressure, fasting blood glucose, and lipid profile. Endometrial evaluation was based on transvaginal ultrasonography findings and histopathological examination of endometrial biopsy specimens. Statistical analysis was performed using t-test, chi-square test, and logistic regression to determine the association between metabolic risk factors and EH.

Results: EH was significantly associated with older age (48.6 ± 7.5 vs. 45.2 ± 6.8 years, $p = 0.03$), higher BMI (27.4 ± 3.2 vs. 24.8 ± 2.9 kg/m², $p = 0.01$), waist-to-hip ratio, hypertension, hyperglycemia, and dyslipidemia (all $p < 0.01$). Histopathology revealed 25% simple and 25% atypical hyperplasia. Logistic regression identified BMI ≥25, waist-to-hip ratio ≥0.85, and dyslipidemia as strong independent predictors.

Conclusion: Metabolic dysfunction plays a pivotal role in EH. Early detection and management of metabolic risk factors are essential to prevent progression to malignancy.

Keywords: Endometrial hyperplasia, metabolic syndrome, obesity, dyslipidemia, insulin resistance, atypical hyperplasia.

Introduction

Endometrial hyperplasia (EH) is a disease process that involves the excessive growth of the endometrial glands in comparison with the stroma leading to thickening of the endometrial layer [1]. This is a peculiar condition because it can be the fore predecessor of endometrial carcinoma, particularly in case of any atypical cellular alterations. The pathophysiology of EH is mainly caused by the protracted unopposed estrogen stimulation that could be the result of the lack of sufficient progesterone-mediated opposition. Endometrial glandular proliferation is triggered by estrogen exposure (both endogenous and exogenous) and secretory differentiation and regulated shedding of the endometrial lining are provoked by progesterone. In turn, the disproportion in this hormone balance including constant exposure to estrogen without the compensatory progesterone predetermines hyperplastic endometrial changes. This hormonal imbalance is caused by a number of factors, which are obesity, polycystic ovary syndrome (PCOS), anovulation and exogenous estrogen therapy [2].

Obesity is one of the key public health issues, which over time have been attributed to an elevated risk of endometrial hyperplasia [3]. The adipose tissue is an extragonadal source of estrogen, which aromatizes the androgens into estrone and increases the levels of estrogen in circulation. It is further aggravated by the insulin resistance and hyperinsulinemia that has been attributed to obesity, and that known to impacts gonadotropin secretion and increase the production

of ovarian androgens. Moreover, hyperinsulinemia can have direct mitogenic action on endometrial tissue that interacts with insulin-like growth factor (IGF) receptors and additionally stimulates cell proliferation [4]. A number of epidemiological studies have found a dose-dependent connection of the body mass index (BMI) on the risk of endometrial hyperplasia, where metabolic dysregulation is central among the risk factors of this disease.

Another important metabolic factor that causes EH is polycystic ovary syndrome, a frequent endocrine disease in women of reproductive age [5]. The PCOS women tend to have chronic anovulation with resultant continuous exposure to estrogen without opposition, and as such, endometrial proliferation. In addition, PCOS is often linked with insulin resistance, dyslipidemia and central obesity which form a metabolic environment that predisposes women to hyperplastic endometrial changes further [6]. The metabolic syndrome characterizes insulin resistance that supports hyperandrogenism and leads to the aggravation of anovulatory cycles and causes endometrial instability. Also, the inflammatory condition seen in the metabolic syndrome can result into cytokine and growth factor production which can favour abnormal endometrial growth implying that systemic metabolic imbalances have both direct and indirect influences on endometrial pathology.

The development of endometrial hyperplasia has been linked to multiple metabolic risk factors which include type 2 diabetes mellitus and hypertension and dyslipidemia according to [7]. The combination of chronic diabetes hyperglycemia with hyperinsulinemia leads to endometrial growth through the IGF-1 pathway while the disease decreases normal cell death which results in continuous existence of damaged cells. The combination of hypertension with dyslipidemia leads to endothelial dysfunction, which causes systemic inflammation that creates conditions for abnormal endometrial development. The metabolic syndrome, which causes multiple metabolic abnormalities to group together, increases the possibility of developing both endometrial hyperplasia and endometrial carcinoma according to the research which shows how body metabolic health interacts with endometrial disease.

Endometrial hyperplasia shows different clinical presentations which do not provide specific diagnosis because patients most commonly experience abnormal uterine bleeding. The symptomatology becomes especially dangerous for women who experience perimenopause and postmenopause because they should receive complete medical assessment for any unusual bleeding patterns which increase their chances of developing cancer [8] .The diagnostic process begins with transvaginal ultrasonography to measure endometrial thickness, which doctors use to determine the need for endometrial biopsy or curettage as the next step in obtaining definitive diagnosis through histopathological assessment. The histological classification of EH, based on glandular complexity and the presence or absence of atypia, guides clinical management and prognostication, with atypical hyperplasia carrying a markedly higher risk of progression to endometrial carcinoma.

The management strategies for EH use multiple approaches to achieve three goals which include reversing hyperplasia and preventing cancer development and treating the underlying metabolic risk factors. Progestin therapy serves as the main method of medical treatment which doctors can administer through three delivery methods: oral agents and intrauterine devices and injectable formulations. Hysterectomy and other surgical procedures only become necessary when patients experience atypical hyperplasia or their medical treatments do not succeed or they choose that option. The medical field has begun to recognize weight loss and insulin sensitivity improvement and lifestyle changes as necessary elements for complete patient treatment. The metabolic dysfunction which underlies EH requires gynecologists and endocrinologists and primary care doctors to work together in an interdisciplinary approach.

Endometrial hyperplasia manifests as an endometrial tissue growth that occurs because of hormonal stimulation and metabolic and endocrine system control. The combination of obesity with insulin resistance and PCOS and metabolic syndrome creates conditions which enable unopposed estrogen to drive endometrial growth, thus raising the likelihood of hyperplasia development and subsequent cancer risk. The process of early detection together with histopathological assessment and specific treatment methods which include metabolic risk factor management serves as a critical requirement for reducing negative health effects and enhancing both reproductive and overall well-being. The development of successful prevention and treatment methods requires researchers to comprehend how metabolic risk factors impact endometrial hyperplasia development in communities where metabolic disorders occur frequently.

Methodology

Study Design: This study was designed as a retrospective observational study aimed at evaluating endometrial hyperplasia and its association with metabolic risk factors among women presenting to the gynecology department. The design allowed for systematic collection of clinical, biochemical, and histopathological data to explore potential correlations between metabolic parameters and endometrial pathology.

Study Area: The study was conducted in the Department of Obstetrics and Gynaecology, Nalanda Medical College and Hospital, Patna, Bihar, India.

Study Duration: The study was carried out over a period of one year from January 2024 to December 2024.

Study Participants

Inclusion Criteria:

- Women aged 30–65 years presenting with abnormal uterine bleeding or suspected endometrial pathology.
- Patients undergoing endometrial biopsy or hysteroscopy for diagnostic purposes.
- Patients providing informed written consent for participation in the study.
- Willingness to undergo metabolic evaluations, including glucose, lipid, and blood pressure assessment.

Exclusion Criteria:

- Patients with known malignancy at other sites or evidence of metastatic disease.
- Women on hormone therapy (including oral contraceptives or menopausal hormone replacement).
- Patients taking antihypertensive or hypoglycemic medications that could interfere with metabolic assessments.
- Individuals with thyroid disorders, chronic liver disease, or renal insufficiency affecting metabolic parameters.
- Patients with incomplete laboratory or histopathology data or poor compliance with follow-up protocols.

Sample Size: A total of 80 participants were enrolled in the study, based on sample size calculations using expected prevalence rates of metabolic risk factors in women with endometrial hyperplasia and a 95% confidence interval, allowing adequate power to detect statistically significant associations.

Procedure: All participants underwent a detailed clinical evaluation, including history taking and physical examination, with special attention to menstrual patterns, body mass index (BMI), and waist-to-hip ratio. Blood pressure measurements were recorded, and metabolic risk factors including fasting blood glucose, lipid profile (total cholesterol, LDL, HDL, triglycerides), and insulin resistance were assessed.

Patients underwent transvaginal ultrasonography to assess endometrial thickness, followed by hysteroscopic-directed endometrial biopsy for histopathological evaluation. Biopsy specimens were preserved in formalin and analyzed by experienced pathologists, classifying endometrium as simple hyperplasia, atypical hyperplasia, or normal. Participants were then categorized into case and control groups based on histopathological results.

Metabolic syndrome was defined according to WHO criteria, considering the presence of diabetes or impaired glucose tolerance plus at least two of the following: obesity (BMI $\geq$ 25), hypertension (BP $\geq$ 140/90 mmHg), and dyslipidemia (triglycerides $\geq$ 1.7 mmol/L or HDL < 1.0 mmol/L). Additional cut-offs for total cholesterol ($\geq$ 240 mg/dL) and LDL ($\geq$ 160 mg/dL) were applied based on ATP III guidelines.

Statistical Analysis: Data were entered into SPSS version 27.0 for analysis. Continuous variables were assessed for normality using the Shapiro-Wilk test and expressed as mean ± standard deviation or median (IQR) as appropriate. Independent samples t-test was used for comparison of continuous variables between groups, while chi-square (χ^2) test was applied for categorical variables. Logistic regression analysis, both univariate and multivariate, was performed to determine the odds ratios (ORs) with 95% confidence intervals (CIs), estimating associations between metabolic risk factors and endometrial hyperplasia. A p-value < 0.05 was considered statistically significant, and all tests were two-tailed".

Result

Table 1 summarizes the demographic characteristics of the 80 study participants, divided equally into the endometrial hyperplasia and control groups. The mean age of participants with endometrial hyperplasia was 48.6 ± 7.5 years, which was significantly higher than the control group at 45.2 ± 6.8 years (p = 0.03). Similarly, the mean BMI was significantly greater in the hyperplasia group (27.4 ± 3.2 kg/m²) compared to controls (24.8 ± 2.9 kg/m², p = 0.01), and the waist-to-hip ratio was also elevated (0.88 ± 0.05 vs. 0.82 ± 0.04, p < 0.01). Parity was comparable between groups, with a median of 2 in both (p = 0.47). Regarding menopausal status, 60% of the hyperplasia group were premenopausal versus 70% in controls, while postmenopausal women comprised 40% and 30%, respectively (p = 0.31), indicating no significant difference in menopausal distribution. Overall, age, BMI, and waist-to-hip ratio were significantly higher in the endometrial hyperplasia group, whereas parity and menopausal status did not differ significantly.

Table 1: Demographic Characteristics of Participants (n = 80)			
Characteristic	**Endometrial Hyperplasia (n=40)**	**Control (Normal/Polyp, n=40)**	**p-value**
Age (years, mean ± SD)	48.6 ± 7.5	45.2 ± 6.8	0.03
BMI (kg/m², mean ± SD)	27.4 ± 3.2	24.8 ± 2.9	0.01
Waist-to-hip ratio (mean ± SD)	0.88 ± 0.05	0.82 ± 0.04	<0.01
Parity (median, range)	2 (0–4)	2 (0–3)	0.47
Menopausal status (n, %)			
- Premenopausal	24 (60%)	28 (70%)	0.31
- Postmenopausal	16 (40%)	12 (30%)	

Table 2 shows a comparison of clinical and biochemical parameters between patients with endometrial hyperplasia (n=40) and healthy controls (n=40). Patients with endometrial hyperplasia had significantly higher mean systolic blood pressure (138 ± 12 mmHg vs. 125 ± 10 mmHg, p<0.01) and diastolic blood pressure (88 ± 8 mmHg vs. 80 ± 7 mmHg, p<0.01) compared to controls. Similarly, fasting glucose levels were elevated in the hyperplasia group (112 ± 15 mg/dL) relative to controls (98 ± 12 mg/dL, p<0.01). Lipid profile analysis revealed significantly higher total cholesterol (220 ± 28 mg/dL vs. 195 ± 25 mg/dL, p<0.01), LDL cholesterol (145 ± 20 mg/dL vs. 125 ± 18 mg/dL, p<0.01), and triglycerides (180 ± 35 mg/dL vs. 145 ± 30 mg/dL, p<0.01) in patients, whereas HDL cholesterol was significantly lower (42 ± 6 mg/dL vs. 50 ± 5 mg/dL, p<0.01). Overall, these findings indicate that endometrial hyperplasia is associated with adverse metabolic and cardiovascular parameters compared to healthy individuals.

Table 2: Clinical and Biochemical Parameters			
Parameter	**Endometrial Hyperplasia (n=40)**	**Control (n=40)**	**p-value**
Systolic BP (mmHg, mean ± SD)	138 ± 12	125 ± 10	<0.01
Diastolic BP (mmHg, mean ± SD)	88 ± 8	80 ± 7	<0.01
Fasting glucose (mg/dL, mean ± SD)	112 ± 15	98 ± 12	<0.01
Total cholesterol (mg/dL, mean ± SD)	220 ± 28	195 ± 25	<0.01
LDL cholesterol (mg/dL, mean ± SD)	145 ± 20	125 ± 18	<0.01
HDL cholesterol (mg/dL, mean ± SD)	42 ± 6	50 ± 5	<0.01
Triglycerides (mg/dL, mean ± SD)	180 ± 35	145 ± 30	<0.01

Table 3 presents the histopathological findings of the study participants (n = 80). Among them, half of the cases (50%) showed either normal endometrium or endometrial polyps, indicating no significant pathological changes. Simple hyperplasia and atypical hyperplasia were each observed in 20 participants, accounting for 25% of cases respectively. This distribution suggests that while a substantial portion of the participants had normal or benign endometrial findings, an equal proportion exhibited hyperplastic changes, with atypical hyperplasia highlighting a subgroup at higher risk for potential progression to malignancy.

Table 3: Histopathological Findings		
Histopathology Type	**Number (n)**	**Percentage (%)**
Simple hyperplasia	20	25%
Atypical hyperplasia	20	25%
Normal endometrium / Polyp	40	50%
Total	80	100%

Table 4 shows a significantly higher prevalence of metabolic syndrome components among patients with endometrial hyperplasia compared to controls. Obesity was observed in 70% of cases versus 30% in controls ($p < 0.01$), hypertension in 55% versus 25% ($p = 0.01$), dyslipidemia in 65% versus 30% ($p < 0.01$), and hyperglycemia in 60% versus 20% ($p < 0.01$). Overall, 45% of patients with endometrial hyperplasia had metabolic syndrome, defined as the presence of three or more components, compared to only 10% of controls ($p < 0.01$), indicating a strong association between metabolic abnormalities and endometrial hyperplasia".

Table 4: Prevalence of Metabolic Syndrome Components			
Component	**Endometrial Hyperplasia (n=40)**	**Control (n=40)**	**p-value**
Obesity (BMI ≥25)	28 (70%)	12 (30%)	<0.01
Hypertension (BP ≥140/90 mmHg)	22 (55%)	10 (25%)	0.01
Dyslipidemia (TG ≥150 or HDL <50 mg/dL)	26 (65%)	12 (30%)	<0.01
Hyperglycemia (Fasting glucose ≥100 mg/dL)	24 (60%)	8 (20%)	<0.01
Metabolic syndrome (≥3 components)	18 (45%)	4 (10%)	<0.01

Table 5 shows the results of logistic regression analysis assessing the association between metabolic risk factors and endometrial hyperplasia. The analysis indicates that women over 45 years had a significantly higher risk (OR = 1.8, 95% CI: 1.1–3.2, p = 0.04) of developing endometrial hyperplasia. Similarly, overweight or obese individuals with a BMI ≥25 had a markedly increased risk (OR = 3.5, 95% CI: 1.7–7.1, p < 0.01). Other significant metabolic risk factors included hypertension (OR = 2.2, 95% CI: 1.0–4.8, p = 0.04), dyslipidemia (OR = 3.0, 95% CI: 1.4–6.3, p < 0.01), hyperglycemia (OR = 2.8, 95% CI: 1.3–6.0, p = 0.01), and a waist-to-hip ratio ≥0.85 (OR = 3.2, 95% CI: 1.5–6.9, p < 0.01). Overall, these results suggest that multiple components of metabolic syndrome significantly increase the likelihood of endometrial hyperplasia, with BMI, waist-to-hip ratio, and dyslipidemia showing the strongest associations.

Table 5: Logistic Regression Analysis of Metabolic Risk Factors and Endometrial Hyperplasia		
Risk Factor	**OR (95% CI)**	**p-value**
Age > 45 years	1.8 (1.1–3.2)	0.04
BMI ≥25	3.5 (1.7–7.1)	<0.01
Hypertension	2.2 (1.0–4.8)	0.04
Dyslipidemia	3.0 (1.4–6.3)	<0.01
Hyperglycemia	2.8 (1.3–6.0)	0.01
Waist-to-hip ratio ≥0.85	3.2 (1.5–6.9)	<0.01

Discussion

The current research demonstrates that endometrial hyperplasia links with multiple metabolic and anthropometric risk factors, which strengthens the existing research that connects metabolic disorders to endometrial diseases. The study results show that women in the endometrial hyperplasia group of this cohort reached an average age of 48.6 years while their control group counterparts reached 45.2 years because advancing age leads to increased endometrial tissue growth. The researchers Sanderson et al. (2017) [9] reported that women above 45 years' experience a substantial increase in endometrial hyperplasia risk, which establishes age as an unchangeable risk factor for endometrial diseases. The study results showed that hyperplasia cases had higher BMI and waist-to-hip ratio values, which demonstrated that both total body fat and abdominal fat distribution serve as critical factors in endometrial tissue growth. The research by Arthur et al. (2019) [10] found that women with a BMI of 30 kg/m² or above faced a 2.4 times higher endometrial cancer risk and a 1.9 times higher atypical hyperplasia risk compared to women with normal BMI.

The study found that metabolic disorders which included high fasting glucose levels and hypertension and dyslipidemia occurred with greater frequency in the hyperplasia group. The metabolic syndrome criteria were fulfilled by almost half of the women with hyperplasia while only 10% of the control group met the same criteria. The observation supports the research results from Kitson et al. (2018) [11] which found that 45% of women with freshly diagnosed endometrial cancer showed metabolic syndrome symptoms while 12% of age-matched controls showed similar symptoms. The study by Raffone et al. (2020) [12] found that diabetes mellitus patients had higher chances to develop atypical hyperplasia or early endometrial carcinoma which resulted in odds ratios of 2.1 for hyperglycemia and 2.3 for insulin resistance that matched our findings of increased fasting glucose levels in the affected participants.

Obesity leads to endometrial hyperplasia because it increases estrogen production through androgen conversion and it reduces sex hormone-binding globulin (SHBG) levels while it creates chronic low-grade inflammation from adipose tissue (Deng et al., 2016) [13]. The study found that waist-to-hip ratio which measures central adiposity became the main factor that predicted hyperplasia because visceral fat produced a greater effect on endometrial growth than general obesity did. Ward et al. (2014) [14] showed that bariatric surgery patients who kept off their extra weight experienced a 71 to 81 percent drop in uterine cancer risk which shows how obesity directly causes endometrial disorders.

Our investigation discovered hyperglycemia as an essential risk factor. The fasting glucose levels of women with endometrial hyperplasia showed statistically significant higher results compared to previous research findings. Friberg et al. (2007) [15] conducted a meta-analysis which included 16 studies and found that diabetes led to a 2.1 relative risk (RR) of developing endometrial cancer. Insulin resistance together with hyperinsulinemia led to increased endometrial cell proliferation according to Lai and Sun (2018) [16]. Our research results support these mechanisms because logistic regression analysis showed that hyperglycemia functioned as an independent risk factor for endometrial hyperplasia.

The hyperplasia group showed a significant increase of dyslipidemia which involves high LDL cholesterol and triglycerides together with low HDL cholesterol levels. There has been less research on abnormal lipid metabolism than on obesity and diabetes but it has been found to play a role in endometrial carcinogenesis. Madak-Erdogan et al. (2019) [17] showed that obese women with high free fatty acid levels experience cancer cell growth through both estrogen receptor pathways and mTOR pathways. The research by Gibson et al. (2018) [18] showed that high serum cholesterol levels lead to increased endometrial cancer cell growth through estrogen receptor activation which supports our discovery that dyslipidemia functions as a major metabolic factor.

The study results showed no differences in menopausal status and parity between the case group and control group which conflicts with previous research that found nulliparity and postmenopausal status to increase endometrial cancer risk (Morice et al., 2016) [19]. The differences between our results and previous research findings exist because our study group had similar reproductive patterns while metabolic risk factors had greater effect on our cohort.

Our cohort demonstrated histopathological results with 25% of cases showing simple hyperplasia and 25% showing atypical hyperplasia which indicated that this group had a higher likelihood of developing cancer. The findings of the research are confirmed by Hutt et al. (2019) [20] which showed that atypical hyperplasia has a strong link to endometrial carcinoma that occurs at the same time or later in women who have metabolic syndrome. The results from the logistic regression analysis showed that age above 45 years and high BMI and central obesity and metabolic disorders functioned as separate risk factors which confirmed previous findings that metabolic disorders drive endometrial disease development.

The current results support previous research which shows that endometrial hyperplasia is strongly connected to age and obesity and hyperglycemia and dyslipidemia. The research establishes that healthcare professionals need to detect and treat all components of metabolic syndrome because these conditions lead to excessive endometrial growth which results in cancer development. The implementation of weight loss programs together with glucose management and lipid level control interventions will help decrease the impact of medical conditions. The need for active screening procedures to detect atypical hyperplasia in people with metabolic risk factors exists because these practices enable doctors to provide essential medical treatment at the right moments.

Conclusion

The research shows that endometrial hyperplasia develops through metabolic risk factors which link to increasing age and obesity and central fat distribution and high blood pressure and elevated blood sugar and abnormal lipid levels. The histopathological evaluation found that 25% of study participants displayed atypical hyperplasia which identified a group that faced increased risk of developing malignant tumors. The logistic regression analysis identified BMI and waist-to-hip ratio and dyslipidemia as the main independent predictors of endometrial pathology while metabolic dysfunction emerged as the primary cause. The results show that doctors need to conduct complete tests for metabolic disorders which affect women who experience unusual uterine bleeding. At-risk groups can achieve better reproductive and overall health results through early detection and appropriate lifestyle changes and continuous health supervision.

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