

# Clinicopathological study of endometrial polyps: experience from a tertiary care center

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## Abstract

**Introduction:** An endometrial polyp (EP) is an abnormal growth of the endometrium inside the uterine cavity. Histologically, the polyp contains glandular, stromal, vascular (thick-walled vessels), and connective tissue elements (fibrous stroma). The most common symptoms of patients with endometrial polyps are abnormal bleeding and infertility.

**Aim:** To assess cases of endometrial polyps received at the pathology department of a hospital by exploring the different presentations of the patients and the correlation with the clinico-pathological features.

**Materials and methods:** This retrospective, cross-sectional study used patient data from January 2018 to December 2022. It was conducted in the pathology department of a tertiary care center. It included 180 women with endometrial polyps. Data were collected from the hospital information system's medical records, and the Statistical Package for the Social Sciences (SPSS), version 26.0, was used to analyze the data.

**Results:** The patients' ages ranged from 29 to 88 years. About one-third of the patients were aged between 30 and 40 years. Patients with a single polyp were more than those with multiple polyps. Abnormal bleeding and infertility were the most prevalent symptoms. All the cases were histopathologically benign except for one who presented with malignancy. Age did not show significant association with recurrence. In more than 75% of patients, there was a consensus between the clinical assessments and pathology results.

**Conclusion:** Most endometrial polyps are benign and single with a good concordance between the clinical suspicion and the histopathological confirmation.

## Keywords

benign, bleeding, endometrium, polyp, infertility

## Introduction

Endometrial polyp (EP) is an abnormal growth of the endometrium into the uterine cavity. The condition is usually benign in the form of overgrowth of endometrial tissue that forms a localized projection into the endometrial cavity and is composed of a variable amount of glands and stroma.<sup>[1,2]</sup> Endometrial polyps can be single or multiple, small or large, and sessile or pedunculated.<sup>[3]</sup>

Histologically, the polyp contains glandular, stromal, vas-

cular (thick-walled vessels), and connective tissue elements (fibrous stroma).<sup>[1]</sup> The glands within the polyp might show cyst formation and glandular crowding.<sup>[2]</sup> Other variants include those polyps with atrophic glands, commonly seen in post-menopausal women. Secretory changes may also be seen within a polyp. Moreover, the polyp may show hybrid features of endometrial and endocervical type epithelium when arising from the lower uterine segment.<sup>[2]</sup> Despite the fact that most of the endometrial polyps are benign, there is a risk of malignant transformation in some cases.<sup>[1,2]</sup>

The pathogenesis beyond the evolution of endometrial polyps remains unclear, but several factors could contribute to their appearance. Some of these factors are family history, diabetes, hypertension, obesity, and some drugs like tamoxifen which is used for breast cancer.<sup>[5]</sup> Also, the concentration of estrogen and progesterone receptors is believed to play a role, as it was found that their concentration is higher in the polyp compared to the normal endometrium.<sup>[5]</sup> Therefore, patients with unopposed estrogen are more likely to develop EPs.<sup>[1,3]</sup> Abnormalities in chromosomes 6 and 12, such as translocation, could contribute to the evolution of endometrial polyps.<sup>[4]</sup> There are potential roles for Bcl-2 (an inhibitor of apoptosis), and Ki67 (marker for proliferation and cell mitotic activity) in the evolution of EP. Furthermore, the expression of p63, aromatase P450 (P450 arom) and steroidogenic factor-1 (SF-1) might also play a role in the formation of endometrial polyps.<sup>[4,5]</sup> Among the other conditions that could be associated with EP is hormone replacement therapy (HRT). Postmenopausal women on HRT have been found to have a higher chance of developing endometrial polyps. This may be due to the continuous estrogenic stimulation of the endometrium.<sup>[5]</sup>

The exact prevalence of endometrial polyp is not known with accuracy. This might be explained by the fact that many women with EPs are asymptomatic.<sup>[4]</sup> EPs could be identified in 2% and 23% of patients undergoing endometrial biopsy because of abnormal uterine bleeding.<sup>[1,2]</sup> Previous studies showed that about 6%–12% of asymptomatic premenopausal women might have EPs, whereas 11% of postmenopausal women do have them.<sup>[3,4,7]</sup> The percentage is getting higher for symptomatic women as up to 15 to 30% with those of AUB or infertility patients.<sup>[3,4]</sup>

Some risk factors increase the possibility of malignant transformation like age greater than 60, large-sized polyps, menopause status, symptomatic bleeding, and polycystic ovarian syndrome.<sup>[1]</sup>

The most common symptoms of patients with endometrial polyps are abnormal bleeding and infertility. Some studies show that 68% of pre- and post-menopausal patients complain of abnormal bleeding which involves irregular periods, amenorrhea, dysmenorrhea, and menorrhagia. The reason behind the abnormal bleeding could be the congestion of the stroma within the polyp.<sup>[5]</sup> According to some studies, 15% to 35% of EP patients experience infertility, whether primary (3.8%–38.5%) or secondary (1.8%–17%), but the relationship between infertility and the development of endometrial polyps remains unknown.<sup>[4,5]</sup> It could be because of recurrent implantation failure and increasing certain cytokines with reducing mediators like TNF-alpha and IGFBP-1 that contribute to cause infertility.<sup>[4]</sup> On the other hand, patients with EP could be asymptomatic or only have abdominal or pelvic pain.<sup>[1]</sup>

There are investigative tools to diagnose endometrial polyps such as ultrasound, endometrial biopsy, or hysteroscopy.<sup>[3]</sup> Saline-infusion sonography (SIS) is another method to evaluate the endometrial cavity by instilling warmed saline into the uterine cavity during the proliferative phase

of the menstrual cycle where polyps are better visualized with fluid outlining the mass.<sup>[1]</sup> Another investigation for diagnosing and treating EP is polypectomy by removing the polyps and leaving the adjacent endometrium intact.<sup>[6]</sup> The treatment of endometrial polyps depends on the history of the patients, associated symptoms, and the risk of malignant transformation.<sup>[4]</sup> Asymptomatic endometrial polyps or low-risk ones mostly do not need any treatment, as the polyp might resolve spontaneously.<sup>[5]</sup> Management of endometrial polyps by hormonal therapy cannot be recommended because there is limited support in the literature. Another management is hysteroscopic polypectomy which is considered the standard treatment for endometrial polyps.<sup>[1]</sup>

## AIM

This study examined cases of endometrial polyps received by the Pathology Department of our hospital from 2018 to 2022. We considered the correlation with the clinicopathological features and parameters of the patients.

## Materials and methods

### Study design

This retrospective cross-sectional study evaluated all endometrial polyp patients over a five-year period from January 2018 to December 2022 at Sultan Qaboos University Hospital (SQUH), which is affiliated with University Medical City (UMC).

### Subjects

A total of 180 women participated in this study. The study included all patients who were clinically suspected of having and/or histopathologically diagnosed with endometrial polyps. These patients were among the 3,668 individuals served by the Obstetrics and Gynecology Department during that period. However, cases identified solely as having benign endocervical polyps were excluded from the study. Patients with purely endocervical polyps were excluded based on clinical information and confirmed by histological findings—specifically, a polyp composed entirely of endocervical glands with columnar cells, basally located nuclei, and apical cytoplasmic mucin.

### Ethical approval and data collection

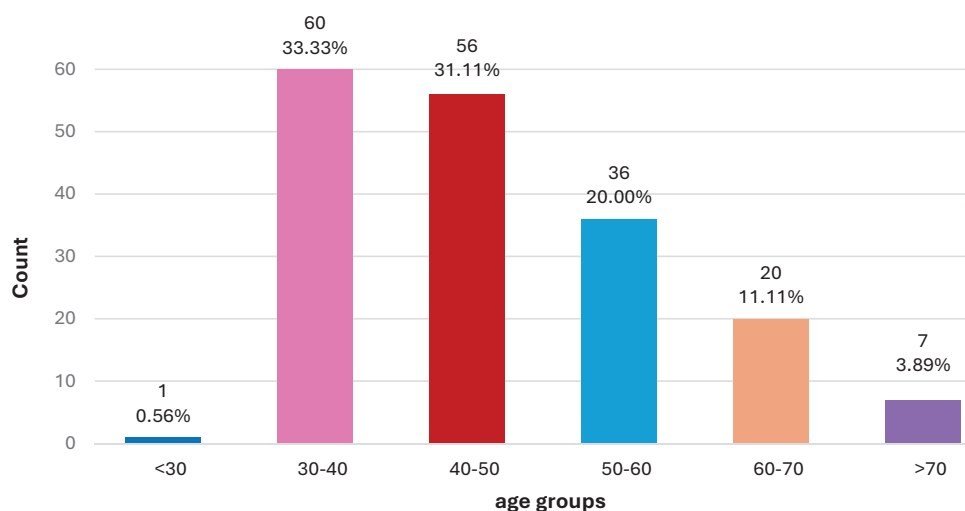
On May 4, 2023, the Medical Research Ethics Committee (MREC) of the College of Medicine and Health Sciences at Sultan Qaboos University granted ethical approval (MREC#3011) for the study. After receiving approval, data was collected from hospital information system medical records over the next ten months using weekly time slots.

## Statistical analysis

The statistical package of the social sciences (SPSS) software (version 26.0) was used to analyze the variables that were gathered. The chi-square test was applied to assess the relationship among different variables and a *p*-value less than 0.05 was considered significant. The categorized variables were also described and presented with appropriate graphs and tables to support the research findings.

## Results

The age range of the patients was 29 to 88 years old (mean 47.35 yrs, standard deviation 11.56). Most cases were presented during the reproductive age. The highest percentage was in the age group between 30 and 40 years, which accounted for 33.33% of cases, followed by 31.11% of cases that occurred in the age group from 40 to 50 years. The age group under 30 years old, however, had the lowest percentage (Fig. 1). The prevalence of endometrial polyps in this study was 4.9%.



**Figure 1.** Frequency of endometrial polyps in relation to age.

The clinical presentation of the polyps varied among patients. The most common symptoms were abnormal bleeding (105 cases, 58.33%) followed by infertility (39 cases, 21.67%). Abnormal bleeding forms included menorrhagia, irregular periods, spot bleeding, postmenopausal bleeding, and dysmenorrhea. Other symptoms accompanied by endometrial polyps were amenorrhea (18 cases, 10%), miscarriage (7 cases, 3.89%), and ectopic pregnancy (1 case, 0.56%), and premature ovarian failure (1 case, 0.56%). Some patients were asymptomatic and accidentally found that they had endometrial polyps during clinical evaluation of other non-gynecological complaints (9 cases, 5%).

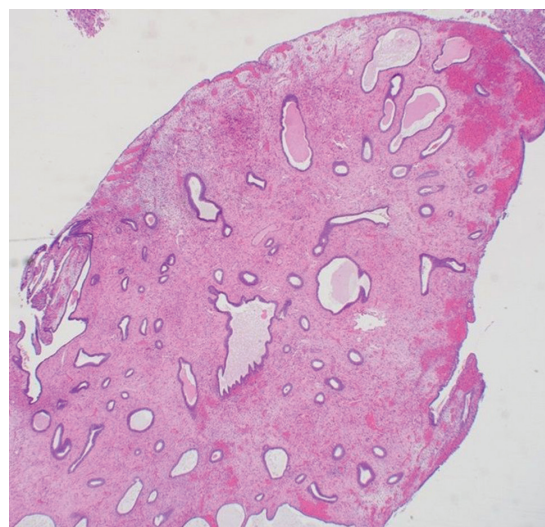
In terms of polyp count, the majority of cases (78.9%) featured a single polyp, while 21.1% of patients had multiple polyps. As regards the histopathological features of the

endometrial polyps, most cases were benign. Only one polyp was malignant showing adenocarcinoma. An example of histopathologically benign endometrial polyp is shown where the classic polyp consisted of endometrial-type glands set in a fibrotic stroma having thick-walled blood vessels (Fig. 2).

In terms of recurrence, endometrial polyps were more likely to recur in older patients. Recurrences were reported in approximately 23.81% of patients under 40 and 39.68% of patients over 50 (Table 1). However, the *p*-value equals 0.100 which is considered not significant but there is a trend between increasing age and recurrent risk.

The majority of the 180 cases studied (76.1%, 137 women) showed concordance between clinical and histopathological diagnoses, indicating that endometrial polyps were suspected clinically and confirmed pathologically. On the other hand, 11.1% of patients were clinically suspected but not microscopically confirmed. Conversely, only the histopathological examination detected the presence of EP in 12.8% of patients (*n*=23).

Correlation with other variables revealed that 51.1% (92 cases) give birth before receiving an endometrial polyp di-



**Figure 2.** Microscopic features of an endometrial polyp.

**Table 1.** Relationship between the patients' ages and risk of recurrence of endometrial polyps

		Recurrence		
			No	Yes
Age groups	≤40 yrs	Count	46	15
		% within recurrence	39.32%	23.81%
	40-51 yrs	Count	37	23
		% within recurrence	31.62%	36.51%
	>51 yrs	Count	34	25
		% within recurrence	29.06%	39.68%

agnosis, while only 14.4% (n=26) do so after. The majority of patients' body mass indexes (BMI) ranged from 25 to 29.9 (26.1%, 47 patients) and 30 to 39.9 (35%, 63 patients). Furthermore, 45% (81 women) had histopathological abnormalities in their background endometrium, such as disordered proliferative endometrium and endometrial hyperplasia without atypia, whereas 55% (n=99) had normal background endometrium. Further details of the histological variants of the benign endometrial polyps in our series did not reveal significant correlation with the different clinical variables.

## Discussion

Endometrial polyps are a common gynecological condition in which the endometrium grows abnormally into the uterine cavity. Due to a lack of studies in our area, the current study focused on evaluating the various clinicopathological parameters of EP patients treated at a tertiary hospital.

This study shows that the polyps were presented more in the reproductive age groups, (group 30 to 40 years old and group 40 to 50 years old, respectively). This finding was supported by a study that found the majority of cases were between the ages of 40 and 49.<sup>[7]</sup> Other studies back up our findings, concluding that polyps were uncommon (0.9%) in young women, but prevalent (9.2%) in women over the age of 30.<sup>[8]</sup> These age groups are still reproductive, and they have high levels of estrogen and progesterone hormones, both of which contribute to polyp formation. Such findings might support the concept that EPs have high concentration of estrogen and progesterone receptors.<sup>[5]</sup> The overall prevalence of EP, in our study, tended to be toward the lower values of those that were previously reported in the literature.<sup>[1,2]</sup> Compared to what we have found (prevalence of 4.9%), a Danish study revealed the prevalence to be 7.8%, whereas another Turkish study demonstrated a prevalence of 9% in the geriatric population<sup>[8,9]</sup> Furthermore, it was reported that EPs can be found in 10% of females at autopsy.<sup>[1]</sup> Such variation could be attributed to sampling procedures and the fact that a large proportion of EP patients are asymptomatic.

The morphological features of EPs in our study were almost those of benign endometrial polyps, whereas only

one case was malignant. This was also observed in many previous studies where the benign cases were more prevalent than the malignant ones. A study conducted in Turkey shows that only 14.3% of the cases become hyperplastic and show malignant transformation compared with 85.7% that were benign endometrial polyps.<sup>[9]</sup> Moreover, a study from Denmark showed the presence of only one polyp with carcinoma and two with atypical hyperplasia.<sup>[8]</sup> Premenopausal women are less likely to have malignant endometrial polyps than postmenopausal women, and the risk of malignant transformation increases with age.<sup>[9]</sup> The reasons behind this could be due to the spontaneous regression mechanism that is characteristic of the cycling endometrium in women of reproductive age. Other factors that influence malignant transformation include obesity, hypertension, the size of the polyp, and the use of tamoxifen.<sup>[4]</sup>

In the current study, the majority of the cases had only a single polyp. This finding contrasts with another study that found patients with multiple polyps in more than half of the cases.<sup>[6]</sup> The reason behind this finding seems to be multifactorial, namely related to sampling. A previous study revealed that the group with multiple polyps (mean age 65.2 years) was older compared to the single polyp group (mean age 62.1 years).<sup>[10]</sup>

According to the symptoms reported by patients in our study, abnormal uterine bleeding was the most common, followed by infertility. These findings are consistent with those of a study conducted in Italy and Brazil, which found that 10%–40% of patients presented with abnormal bleeding and 15%–25% with infertility.<sup>[4]</sup> Abnormal bleeding in endometrial polyp patients could be due to stromal congestion within the polyp which leads to venous stasis and apical necrosis of the blood vessels. The link between endometrial polyps and infertility is unclear, but there are numerous hypotheses that explain it differently.<sup>[4,5]</sup> Recurrent implantation failure may also be the cause, as the polyp can cause mechanical obstruction, preventing sperm from reaching the oocyte for fertilization. Another reason could be an increase in the matrix metalloproteinase (MMPs) which leads to inhibition of the implantation.<sup>[5]</sup> Additionally, an increase in the levels of certain cytokines, such as interferon-gamma and glycodefin, can result in failure to fertilize.<sup>[5]</sup> Our study shows that 51.1% of cases give birth before being diagnosed with endometrial polyp, where-

as 14.4% give birth after the diagnosis of EP. This might support the concept that infertility is one of the major presentations of endometrial polyp. Another study found that 63.4% of patients became pregnant following hysteroscopic polypectomy, compared to 36.6% who did not become pregnant, indicating a strong causal effect of the polyp in the implantation process.<sup>[11]</sup>

Our study explored the relationship between age and the risk of recurrence of endometrial polyp. Increasing age increases the likelihood of recurrence, with the highest frequency recorded for those over the age of 50, though this was not statistically significant. Another study found that patients over the age of 35 have a recurrence rate of 72.45%, while those under the age of 35 have a rate of 27.55%.<sup>[12]</sup> A study conducted at the Department of Obstetrics and Gynecology in Taiwan found that the relationship between recurrent endometrial polyps after hysteroscopic polypectomy ranged between 2.5% and 43.6%, depending on factors such as follow-up duration.<sup>[13]</sup> Their findings show that a higher number of endometrial polyps and a longer follow-up period were associated with an increased postoperative recurrence potential of polyps, rather than the type of polyp or the patient's age.<sup>[13]</sup> Doobaly and colleagues, on the other hand, emphasized the importance of histological type in determining recurrence potential, which increased with polyps exhibiting endometrial hyperplasia characteristics.<sup>[14]</sup> We also propose that the presence of proliferative abnormalities of the associated background endometrium might play a role in this regard. About 45% of our cases showed abnormalities, such as disordered proliferative endometrium and non-atypical endometrial hyperplasia in adjacent background endometrium.<sup>[1]</sup> Therefore, different hormonal treatment options have been used as therapy for EPs and to prevent their recurrence, such as combined oral contraceptives (COCs).<sup>[14]</sup>

Our data showed that 76.1% of patients were diagnosed on a clinical basis and confirmed histopathologically. This could reflect the good practice of our gynecologists in considering the possibility of endometrial polyps as an etiology for many gynecological complaints. Only 12.8% of the cases without clinical impression of having a polyp were diagnosed by histopathological study. Such finding might be explained by suboptimal preoperative clinical and radiological workup. One of the used radiological tools is transvaginal ultrasound (TVUS) which allows visualization of the uterine cavity where endometrial polyp appears as a focal mass or thickening. However, this sign is considered non-specific and could be present in other abnormalities, such as leiomyomas. Combining TVUS with power Doppler increases the sensitivity for polyp detection to 91%–97%.<sup>[15]</sup> However, hysteroscopy and biopsy are considered the gold standard for diagnosing EP.<sup>[1,5]</sup> On the other hand, such suboptimal preoperative workup might also contribute to the possibility of recurrent polyps.<sup>[13,14]</sup>

The patients' BMIs ranged from 30 to 39.9, indicating obesity and, thus, a higher level of estrogen.<sup>[16]</sup> This highlights the role of obesity as a potential risk factor for develop-

ing endometrial polyps.<sup>[14,16]</sup> This is supported by a Turkish study showing that 52% of patients with a BMI of 30 or higher had a significantly higher number of endometrial polyps compared to 15% of patients with a BMI below 30.<sup>[16]</sup> In contrast, another study found a higher rate of endometrial polyps in people with a BMI between 25.0 and 29.9 (54% of cases), while only 10.4% had a BMI of 30 or higher.<sup>[17]</sup>

The current work has some limitations. First, because the data was gathered from medical records in the hospital information system, some information may be missing, such as follow-up results, Pap smear results, and radiological assessments. Additionally, the sample size was 180 patients, which is considered relatively small, and the data was collected for only five years. Since this study was conducted in one institution, the findings cannot be generalized to the entire community. Therefore, to avoid selection and recall biases, it is recommended to avoid overgeneralization of data and to exercise caution when claiming a cause-and-effect relationship in retrospective studies.<sup>[18]</sup>

## Conclusion

This study indicates that women over the age of 30 have a higher prevalence of endometrial polyps. Obesity could be one of the factors that contribute to the evolution of EP. Moreover, the results indicate that abnormal uterine bleeding and infertility are the most common clinical symptoms of EP. Healthcare providers should be aware of EP even if most of the cases are benign. The recurrence potential of EP depends on several factors such as patient's age and the number of the polyps. Finally, from a histopathological perspective, most endometrial polyps are benign. However, careful histopathological examination is highly recommended to exclude areas reminiscent of atypical endometrial hyperplasia, serous intraepithelial carcinoma or frankly invasive adenocarcinoma.<sup>[2,5,7,9]</sup>

## Competing interests

The authors have declared that no competing interests exist.

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