International Journal of Reproduction, Contraception, Obstetrics and Gynecology
*Dalal V et al. Int J Reprod Contracept Obstet Gynecol. 2024 Feb;13(2):247-251*
www.ijrcog.org
pISSN 2320-1770 | eISSN 2320-1789

DOI: https://dx.doi.org/10.18203/2320-1770.ijrcog20240117

**Original Research Article**

# Agreement level of preoperative histology with post-surgical histology in atypical hyperplasia and endometrial cancer patients

**Venus Dalal[1]*, Raghda Asal[2], Shipra Bharti[3], Vanitha Kumar[4], Varnit Toshyan[1]**

[1]Department of Obstetrics and Gynaecology, Royal Berkshire Hospital, Reading, UK
[2]Department of Obstetrics and Gynaecology, Leicester Royal Infirmary Hospital, Leicester, UK
[3]Department of Obstetrics and Gynaecology, Katihar Medical College, Bihar, India
[4]Department of Obstetrics and Gynaecology, North Hampshire and Basingstoke Hospital, Basingstoke, UK

**Received:** 11 December 2023
**Accepted:** 03 January 2024

***Correspondence:**
Dr. Venus Dalal,
E-mail: venusdalal@gmail.com



## ABSTRACT

**Background:** Endometrial cancer significantly contributes to gynecological cancers. The aim of the study was to assess the concordance between the preoperative endometrial biopsy and histology of hysterectomy specimens in patients surgically treated for endometrial hyperplasia and endometrial cancer. Concurrent malignancy was also assessed in cases of endometrial hyperplasia with atypia.
**Methods:** This study is a retrospective analysis of patients surgically treated for atypical hyperplasia (47 patients) and cancer (210 patients) at HHFT from January 2014 to March 2020. The preoperative histology was compared to the histological findings of hysterectomy. In cases of endometrial cancer, its histological type and grade were also assessed.
**Results:** In the endometrial cancer group, the majority were endometrioid adenocarcinoma (204 patients) and only 6 had a non-endometrioid type. In the endometrioid and non-endometrioid group, preoperative diagnosis was confirmed in 88.7% and 100% patients respectively in postoperative specimens. Tumor grade was reported in 193 patients. The present study shows the highest accuracy in grade 3 patients (88%) followed by grade 1 (82.8%) and grade 2 (62.5%). Out of these 47 patients who underwent surgical management for atypical hyperplasia, preoperative diagnosis was confirmed in 46.8% (22 patients). Importantly, concurrent endometrial cancer in hysterectomy specimens was found in 34% patients in atypical hyperplasia group.
**Conclusions:** High level of concordance was noticed in histology and grade in endometrial cancer patients. Only half of the patients in atypical hyperplasia group showed concordance as one-third of patients were found to have concurrent malignancy.

**Keywords:** Endometrial hyperplasia, Endometrial cancer, Histology, Grade, Hysterectomy

## INTRODUCTION

Endometrial cancer contributes to maximum number of gynaecological cancer cases in developed countries and is the second most common in developing countries.[1,2] The endometrial sampling is the best way to confirm the diagnosis. However, discrepancies between preoperative histology and post-hysterectomy histology is well-documented.[3-5] With a preoperative diagnosis of endometrial hyperplasia, the surgical procedure performed may be inadequate when endometrial carcinoma is diagnosed in postoperative specimen.[4,5] This shows that accuracy of preoperative histology is of utmost importance. When it comes to endometrial cancer, the hysterectomy specimens usually confirm the preoperative histology findings but inconsistencies are seen in histological type and grade of carcinoma.[6,7]

The surgical management of endometrial hyperplasia and cancer is guided by the preoperative histology from endometrial biopsy.[8] The prognosis of endometrial cancer

is affected by histological type and grade of cancer.[9] Outcome is mostly favourable in low grade endometrioid adenocarcinoma (grade 1 and 2) as compared to high grade endometrioid (grade 3) or non-endometrioid carcinoma.[8] The aim and objective of this study assess the concordance between the preoperative endometrial biopsy and histology of hysterectomy specimens in patients surgically treated for atypical hyperplasia and endometrial cancer. The second objective is to look for concurrent malignancy in patients undergoing hysterectomy for endometrial hyperplasia with atypia.

## METHODS

In this study, a retrospective analysis of medical records was carried out for patients surgically treated for endometrial hyperplasia and cancer at HHFT from January 2014 to March 2020. The patients' mean ages was 53.4±16 years and 59.2±16 years for endometrial hyperplasia and endometrial cancer group respectively. The histology results from endometrial sampling formed the basis for preoperative diagnosis, and it was compared to the histological findings from post-surgery specimen. Preoperative endometrial sampling was obtained by hysteroscopic guided endometrial curettage. In patients with a preoperative biopsy showing endometrial hyperplasia, total hysterectomy with or without bilateral salpingo-oophorectomy was performed. We have studied preoperative histology in these patients to see how accurate endometrial biopsy findings in hyperplasia cases are. In the subgroup with endometrial cancer, the surgery included total hysterectomy and bilateral salpingo-oophorectomy with or without pelvic and para-aortic lymphadenectomy.

In cases of endometrial cancer its histological type and grade was assessed. Grading was based on the criteria recommend by the WHO based on cytology and morphology. Three grades of tumour differentiation were: well-differentiated grade (G1), moderately differentiated (G2) and poorly differentiated grade (G3).

### *Statistical analysis*

Statistical package for the social sciences (SPSS) version 25 was used for statistical analysis. The percentage was used to measure the agreement between the preoperative and hysterectomy diagnosis, in hyperplasia and cancer group (with regard to the histology type and grade). Kappa statistics was used in endometrial cancer grade. The agreement strength was considered poor for weighted kappa values less than 0.2, fair for values of 0.21-0.40, moderate for value of 0.41-0.60, substantial for values of 0.61-0.80 and almost perfect for values of 0.81-1.00. Chi square test was used for comparing the misdiagnosis rate between each pair of groups (grade 1 versus grade 2, grade 2 versus grade 3 and grade 3 versus grade 1). The test for statistical significance was evaluated at 5% level of significance with a p value of $<0.05$ considered significant.

## RESULTS

### *Endometrial hyperplasia with atypia*

A comparison was made between preoperative and postoperative histology results. In the data collected, 176 patients were found to have endometrial hyperplasia from which 75 patients underwent surgical management for endometrial hyperplasia. Out of these 75 patients, endometrial hyperplasia with atypia contributed the most with 47 patients. Preoperative diagnosis was confirmed in 46.8% (22 patients) patients with atypical hyperplasia. Additionally, concurrent endometrial cancer in hysterectomy specimen was found in 34% patients (Table 1).

**Table 1: Comparison of initial histology with post-surgical histology in atypical hyperplasia and endometrial cancer patients.**

| Parameters | Post hysterectomy histology (%) | | | | | | |
|---|---|---|---|---|---|---|---|
| | Endometr-ioid carcinoma | Serous carcinoma | Clear cell carcinoma | Endometrial hyperplasia with atypia | Endometrial hyperplasia without atypia | Normal histology | Carcino sarcoma |
| **Atypical hyperplasia** | 16 (34) | 0 | 0 | 22 (46.8) | 4 (8.6) | 5 (10.6) | 0 |
| **Endometrioid (204)** | 181 (88.7) | 4 (1.9) | 2 (0.98) | 7 (3.4) | 7(3.4) | 2 (0.98) | 1 (0.49) |
| **Serous (3)** | 0 | 3 (100) | 0 | 0 | 0 | 0 | 0 |
| **Clear cell (3)** | 0 | 0 | 3 (100) | 0 | 0 | 0 | 0 |

### *Endometrial cancer*

Initial histology showing endometrial cancer was noted in 210 patients. A comparison was made between preoperative and postoperative histology results. Out of these 210 patients nearly half of them had laparoscopy (99 patients, 47.1%) and rest had laparotomy (111 patients 52.9%).

### *Tumor type*

There were 210 patients who had endometrial cancer on initial biopsy. Out of these, majority were endometroid

adenocarcinoma (204 patients) and only 6 had non-endometrioid type. Among these non-endometrioid type, 3 were serous carcinoma and 3 were clear cell carcinoma.

In endometrioid group, preoperative diagnosis was confirmed in 88.7% from postoperative specimen (Table 1). In those with different postoperative diagnosis, Histological type was reclassified as serous carcinoma and clear cell carcinoma and carcinosarcoma in 4 (1.9%), 2 (0.98%) and 1 (0.49%) patient respectively. Other results (16 patients) were endometrial hyperplasia with atypia (7 patients), endometrial hyperplasia without atypia (7 patients) and normal histology (2 patients). These 16 patients had confirmed preoperative histology finding of endometrioid cancer, we assumed that there was a small focus of endometrioid carcinoma in endometrium which was removed during preoperative endometrial curettage. Statistical analysis shows sensitivity and specificity of test as 100% and 46.15% respectively.

**Table 2: Concordance of initial grading with post-surgical grading in endometrial cancer patients.**

| Grade | Post hysterectomy histology (%) | | |
|---|---|---|---|
| | Grade 1 | Grade 2 | Grade 3 |
| **Grade 1 (128)** | 106 (82.8) | 17 (13.3) | 5 (3.9) |
| **Grade 2 (40)** | 10 (25) | 25 (62.5) | 5 (12.5) |
| **Grade 3 (25)** | 1 (4) | 2 (8) | 22 (88) |
| **Overall concordance** | 79.3 | | |

Observed agreement=0.83, expected agreement 0.53, Kappa value=0.64

***Tumor grade according to FIGO***

Tumor grade was available in the histology reports for comparison in 193 patients between preoperative and postoperative results. On initial endometrial biopsy, there were 128 patients with grade 1, 40 patients with grade 2 and 25 patients with grade 3. Tumor grades were then noted from the postoperative histology results. The weighted kappa value for agreement between preoperative and postoperative histopathological grade was 0.64, indicating that the rate of agreement was "substantial". Out of 128 patients classified as grade 1, 106 patients were confirmed to be grade 1 (82.8%), 17 (13.3%) were upgraded to grade 2 and 5 (3.9%) were upgraded to grade 3 (misdiagnosis rate-17.2%) (Table 2). Looking at data of patients with grade 2 on initial histology, 25 patients (62.5%) had similar tumor grade on final histology, 10 patients (25%) were downgraded to grade 1 and 5 patients (12.5%) were up graded to grade 3 (misdiagnosis rate-37.5%). Finally discussing the 25 patients with grade 3 on initial biopsy, 22 patients (88%) similar grading was confirmed but 3 patients were down staged to grade 1 (1 patient) and grade 2 (2 patients) (misdiagnosis rate-12%). Taken together, our results suggest that the level of differentiation as determined by histopathological analysis of preoperative biopsies may not always confirm the postoperative hysterectomy pathology, but concordance level is high specially in grade 3 and grade 1. The overall agreement rate was 79.3.0%. When we analyse on the basis of misdiagnosis rates in each grade, pairwise chisquare showed there was no significant difference between the rate of misdiagnosis of grade 1 compared to other two groups (Table 3). Similar was the case with grade 2 and grade 3 when compared with the grade 1/3 and grade 1/2 respectively.

**Table 3: Statistical analysis of misdiagnosis rate between each pair of groups (grade 1, grade 2, and grade 3).**

| Grade | Misdiagnosis rate | Chi square | P value |
|---|---|---|---|
| **Grade1/ grade 2** | 17.2/37.5 | 0.76 | 6.8 |
| **Grade 2/ grade 3** | 37.5/12 | 0.38 | 0.8 |
| **Grade3/ grade 1** | 12/17.2 | 3.3 | 0.19 |

## DISCUSSION

Abnormal uterine bleeding accounts for two-third of consultations in gynaecology in patients approaching menopause.[10] The main aim of investigating abnormal uterine bleeding is to exclude intrauterine pathology especially endometrial cancer.[11]

Histopathology is considered to be the most important method for preoperative evaluation of endometrial cancer, and its reliability in clinical practice has been recognized by experts for decades. In approximately 80% of patients, hormone dependent endometrial cancer is diagnosed preceded by atypical hyperplasia of the endometrium.[12-14] The treatment for endometrial cancer is mainly surgical and preoperative histological examination of endometrial samples is of key importance for deciding the extent of surgical management. However, the final surgical histology does not always confirm the preoperative diagnosis which may lead to either too extensive or too limited surgical treatment. If poorly differentiated endometrial cancers are diagnosed from the post-hysterectomy specimens, not conducting pelvic lymphadenectomy can adversely affect the treatment outcome even if invasion of the myometrium is superficial.[15]

When we discuss studies on comparison of histological type, a study by Kisielewski et al showed concordance level of 83.75%, 60% and 50% in patients with endometrioid, serous and clear cell carcinoma.[15] In another study by Garcia et al, the agreement rates were 93.2% and 68.9% for endometrioid and non-endometrioid tumors respectively but in present study agreement rates were 88.7% and 100% respectively.[16] In case of non-endometrioid endometrial cancer, there were only 6 cases in non-endometrioid group (3 serous carcinoma, 3 clear cell carcinoma) which shows that a different data may appear if a greater number of patients can be studied in this group. According to the literature, the agreement levels between the endometrial sampling diagnosis and the final

surgical pathology range from 30 to 60% in endometrial cancer cases.[4,7,17]

Histological grading helps in determining the scope of surgery specially planning for lymphadenectomy and adjuvant therapy later. The highest level of discrepancy is observed for histological grading.[4,17,18] In the present study overall concordance rate is 79.3% which is higher than recent study by Cokmez et al which shows concordance of 69.7%.[19] Looking at grade 1, grade 2 and grade 3 individually, grading was confirmed in 82.8%, 62.5% and 88% respectively showing highest agreement rate in grade 3. In study by Cokmez et al and Garcia et al agreement rate is 72.3%, 64.1%, 58.8% and 61.5%, 56%, 78.9% respectively for grade 1,2 and 3.[16,19] The concordance level increases with increasing aggressiveness according to study by Gracia et al. The present study also shows highest accuracy in grade 3 patients (88.5%) but followed by grade 1 which shows 82.5% accuracy followed by grade 3 (64.1%).

Discussing about patients with atypical hyperplasia, agreement rate in histology was 46.8%. One should keep in mind the small sample size while assessing these results. Here the main point of concern is concurrent malignancy. Concurrent endometrial cancer in hysterectomy specimen was found in 34% patients. In GOF study, endometrial cancer was found in 39.1% of patients getting surgically treated for atypical hyperplasia.[5] In these patients undertreatment of disease can be disadvantageous.

Every study has its own limitations. This study considers patients from single trust (2 centres) making the sample size small specially for non-endometrioid endometrial cancer and atypical hyperplasia. The other limitation is that it's a retrospective study.

The accuracy of histological finding in endometrial sampling is utmost important in deciding the extent of surgery and the counselling related to the follow up required. Differences in pre and post-operative findings can lead to under or overtreatment of the disease. Under-treatment increases the need of concurrent treatment and increases the chances of recurrence. On the other hand, overtreatment can pose increased risk of complications like lymphadenectomy increases chance of vessel injury. Both these possibilities are equally concerning. In case of endometrial hyperplasia patients undergoing surgical treatment, findings of concurrent cancer are more important than accuracy of histology.

## CONCLUSION

In endometrial cancer our findings from preoperative and postoperative biopsy demonstrate a reasonably high level of concordance between the histological type and grade. Similar results were not seen in the hyperplasia group, but we noticed the percentage of concurrent endometrial cancer was high in the atypical hyperplasia group.

*Funding: No funding sources*
*Conflict of interest: None declared*
*Ethical approval: The study was approved by the Institutional Ethics Committee*

## REFERENCES

1. Zhang Y, Zhao Y, Li Y. Comparison of Pre- and Postoperative Histopathology Results in Patients with Endometrial Carcinoma. Research Square. 2021 Available at: https://www.researchsquare.com/article/rs-166946/v1. Accessed on 09 September 2023.
2. Ferlay J, Colombet M, Soerjomataram I, Dyba T, Randi G, Bettio M, et al. Cancer incidence and mortality patterns in Europe: Estimates for 40 countries and 25 major cancers in 2018. Eur J Cancer Oxf Engl 1990. 2018;103:356-87.
3. Antonsen SL, Ulrich L, Høgdall C. Patients with atypical hyperplasia of the endometrium should be treated in oncological centers. Gynecol Oncol. 2012;125(1):124-8.
4. Wang X, Huang Z, Di W, Lin Q. Comparison of D&C and hysterectomy pathologic findings in endometrial cancer patients. Arch Gynecol Obstet. 2005;272(2):136-41.
5. Trimble CL, Kauderer J, Zaino R, Silverberg S, Lim PC, Burke JJ, et al. Concurrent endometrial carcinoma in women with a biopsy diagnosis of atypical endometrial hyperplasia: a Gynecologic Oncology Group study. Cancer. 2006;106(4):812-9.
6. Mitchard J, Hirschowitz L. Concordance of FIGO grade of endometrial adenocarcinomas in biopsy and hysterectomy specimens. Histopathology. 2003;42(4):372-8.
7. Petersen RW, Quinlivan JA, Casper GR, Nicklin JL. Endometrial adenocarcinoma--presenting pathology is a poor guide to surgical management. Aust N Z J Obstet Gynaecol. 2000;40(2):191-4.
8. Bogani G, Dowdy SC, Cliby WA, Ghezzi F, Rossetti D, Frigerio L, et al. Management of endometrial cancer: Issues and controversies. Eur J Gynaecol Oncol. 2016;37(1):6-12.
9. National Comprehensive Cancer Network. Guidelines With Evidence Blocks. Available at: https://www.nccn.org/guidelines/guidelines-with-evidence-blocks. Accessed on 09 September 2023.
10. Spencer CP, Whitehead MI. Endometrial assessment re-visited. Br J Obstet Gynaecol. 1999;106(7):623-32.
11. Mencaglia L. Hysteroscopy and adenocarcinoma. Obstet Gynecol Clin North Am. 1995;22(3):573-9.
12. Amant F, Moerman P, Neven P, Timmerman D, Van Limbergen E, Vergote I. Endometrial cancer. Lancet Lond Engl. 2005;366(9484):491-505.
13. Sherman ME. Theories of endometrial carcinogenesis: a multidisciplinary approach. Mod Pathol Off J U S Can Acad Pathol Inc. 2000;13(3):295-308.
14. Creasman WT, Odicino F, Maisonneuve P, Quinn MA, Beller U, Benedet JL, et al. Carcinoma of the

corpus uteri. FIGO 26th Annual Report on the Results of Treatment in Gynecological Cancer. Int J Gynaecol Obstet Off Organ Int Fed Gynaecol Obstet. 2006;95:S105-43.
15. Kisielewski F, Gajewska ME, Marczewska MJ, Panek G, Wielgoś M, Kamiński P. Comparison of endometrial biopsy and postoperative hysterectomy specimen findings in patients with atypical endometrial hyperplasia and endometrial cancer. Ginekol Pol. 2016;87(7):488-92.
16. Garcia TS, Appel M, Rivero R, Kliemann L, Wender MCO. Agreement Between Preoperative Endometrial Sampling and Surgical Specimen Findings in Endometrial Carcinoma. Int J Gynecol Cancer. 2017;27(3).
17. Vorgias G, Lekka J, Katsoulis M, Varhalama E, Kalinoglou N, Akrivos T. Diagnostic accuracy of prehysterectomy curettage in determining tumor type and grade in patients with endometrial cancer. MedGenMed Medscape Gen Med. 2003;5(4):7.
18. Soothill PW, Alcock CJ, MacKenzie IZ. Discrepancy between curettage and hysterectomy histology in patients with stage 1 uterine malignancy. Br J Obstet Gynaecol. 1989;96(4):478-81.
19. Cokmez H, Yilmaz A. Concordance of preoperative and postoperative histological grades in endometrioid type endometrial cancer. Eur J Gynaecol Oncol. 2020;41:208-13.

**Cite this article as:** Dalal V, Asal R, Bharti S, Kumar V, Toshyan V. Agreement level of preoperative histology with post-surgical histology in atypical hyperplasia and endometrial cancer patients. Int J Reprod Contracept Obstet Gynecol 2024;13:247-51.