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Unexpected Uterine Cancer Following Hysterectomy without Prior Evaluation versus Endometrial Evaluation: A Retrospective Study

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ABSTRACT

Background: Uterine cancer (UC) is rising in low-resource settings. Despite advancements in diagnostic technology, many UC cases are diagnosed incidentally post-hysterectomy, complicating management and outcomes. This study aimed to compare the clinicopathological profile, treatment patterns, treatment completion, and 3-year oncological outcomes of the two groups of women diagnosed. **Methods & Materials:** This retrospective comparative study was carried out at the National Institute of Cancer Research and Hospital (NICRH), Bangladesh, between September 2018 and August 2019. The 57 women with histopathologically confirmed uterine cancer were divided into two groups: Group A (23 women) were diagnosed with uterine cancer before the hysterectomy through endometrial evaluation, and Group B (34 women) were diagnosed with uterine cancer unexpectedly after hysterectomy without prior evaluation of the endometrium. The demographic, clinical, histopathological, treatment, and 3-year survival data were compared between the two groups using SPSS version 26. **Results:** The mean age was 56.94 ± 4.62 years in Group A and 52.38 ± 9.46 years in Group B. Postmenopausal bleeding was the commonest presenting symptom in both groups (65.2% vs 67.6%). Most of the patients in Group B (70.6%) received adjuvant radiotherapy/chemotherapy alone, while all patients in Group A underwent staging laparotomy, and high-grade tumours (34.8% vs 14.7%) and non-endometrioid histology (30.4% vs 11.8%) were more common in Group A. The completion of treatment was significantly higher in Group A (87.0%) compared to Group B (52.9%) (p=0.008), and there was no significant difference between the groups in terms of follow-up regularity (p=0.653). Overall, 10.5% of participants experienced a recurrence at 3 years, with a slightly higher rate in Group B (12% vs 9%). **Conclusions:** Preoperative diagnosis via endometrial assessment facilitated targeted oncological therapy and considerably increased treatment completion rates. Although the three-year survival rates were comparable, the findings suggest that proper endometrial examination before hysterectomy is necessary for timely identification and coordinated therapy.

Keywords: *Uterine cancer; Hysterectomy; Endometrial evaluation; Unexpected diagnosis; Treatment outcomes*

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INTRODUCTION

In many high-income countries, endometrial carcinoma is the most prevalent gynecological cancer and is one of the six most frequently diagnosed cancers in women globally, with an estimated 417,000 new cases reported in 2020 [1]. In the past 30 years, the incidence of this event has increased significantly worldwide, due to the ageing population and the growing prevalence of obesity, diabetes and other elements of the metabolic syndrome [2]. Most women with postmenopausal or abnormal uterine bleeding have a disease that is at an early, surgically treatable stage, but a systematic review and meta-analysis have demonstrated that only a minority of women with postmenopausal bleeding will ultimately be found to have an underlying malignancy, and careful triage of these patients before hysterectomy is clinically important [3]. Hysterectomy remains a common procedure for presumed benign indications, including uterine leiomyoma, abnormal uterine bleeding, adenomyosis, and pelvic organ prolapse, in many tertiary care centers, particularly when there are limited facilities for endometrial sampling before surgery, or the clinical suspicion is low. This issue has been quantified in contemporary retrospective cohorts: a large single-center series reported that 0.33% of hysterectomies for benign disease had unexpected uterine malignancy [4]. In a multicenter review, unexpected malignancy was found in 1.8% of cases, and a series from the Middle East also found unsuspected malignant pathology in women who underwent myomectomy or hysterectomy without an oncological work-up [5, 6]. If uterine cancer is only identified on final histopathology following a non-staging hysterectomy, patients are subjected to the added morbidity, cost, and psychological stress of re-exploration or completion surgery, and to a shortened time frame for scheduling adjuvant therapy. An alternative route is pre-operative endometrial evaluation by Pipelle aspiration biopsy, dilatation and curettage or hysteroscopic biopsy, which can identify malignancy before surgery and enable one-step, appropriately staged management. Its diagnostic performance is not without limitations, however: pooled analyses have shown that sampling accuracy for prediction of final histological type and grade is highly variable depending on the technique and the tumour biology, and that the volume of the biopsy itself has been shown to affect diagnostic reliability [7, 8]. In well-resourced centers, there is only moderate concordance between the grade and subtype of the preoperative sample and the final hysterectomy specimen, and clinical and demographic factors that further influence the accuracy of the grade and subtype have also been described in Asian populations [9, 10]. Comparative surgical staging experience from South Asian gynecological oncology units also reveals that a significant proportion of patients treated in tertiary centers in this part of the world are only diagnosed with endometrial cancer after initial surgery for a benign diagnosis [11]. There is a need to directly compare the clinicopathological profile, treatment patterns, treatment completion, and oncological outcomes of women with uterine cancer that is identified incidentally after hysterectomy without prior evaluation with those diagnosed by preoperative endometrial evaluation. This study was conducted as a retrospective study to fill this

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gap in comparison in the context of a tertiary care hospital in Bangladesh.

METHODS & MATERIALS

This retrospective comparative study was carried out at the National Institute of Cancer Research and Hospital (NICRH), Bangladesh, between September 2018 and August 2019. The study population consisted of 57 women with histopathologically confirmed uterine cancer who attended the outpatient department for management purposes by consecutive sampling methods during the study period, divided into two comparison groups: Group A (n=23) included women with uterine cancer diagnosed preoperatively through endometrial evaluation (endometrial biopsy, dilatation and curettage, or hysteroscopic biopsy) before hysterectomy was performed, and Group B (n=34) included women with uterine cancer diagnosed unexpectedly at final histopathology after hysterectomy for a presumed benign indication, without prior endometrial evaluation. We excluded patients lost to follow-up before the end of primary treatment and those without a complete medical record or histopathology report. Demographic data (age, parity), presenting symptoms (postmenopausal bleeding, per-vaginal discharge, irregular per-vaginal bleeding), histopathological data (histological type, tumour grade, depth of myometrial invasion), treatment modality received (staging laparotomy with or without adjuvant chemotherapy or radiotherapy, completion surgery, or adjuvant therapy alone), treatment completion status, follow-up regularity, three-year recurrence pattern, and three-year recurrence-free and overall survival were retrieved from hospital medical records, operative notes, histopathology reports, and outpatient follow-up records. Continuous variables were presented as mean ± SD and compared between groups by independent samples t-test, and categorical variables were presented as frequencies and percentages and compared by Chi-square test or Fisher's exact test as appropriate. Recurrence-free survival and overall survival were calculated by the Kaplan-Meier method and compared between groups by the log-rank test, and mean survival time and 95% confidence intervals were reported. We considered $p < 0.05$ statistically significant. The data were analysed using SPSS version 26.

RESULTS

The distribution and baseline characteristics of the 57 study participants are shown in *Table I*, 23 of whom were in Group A and 34 in Group B. The mean age was 56.94 ± 4.62 years in Group A and 52.38 ± 9.46 years in Group B. Regarding parity, 5 (21.7%) women in Group A and 8 (23.5%) in Group B had a parity of two or fewer, while 18 (78.3%) in Group A and 26 (76.5%) in Group B had a parity of three or more.

Table I
Distribution and baseline characteristics of the study participants, *n*=57.

Variable	Category	Group A, n=23	Group B, n=34
Age, years	Mean ± SD	56.94 ± 4.62	52.38 ± 9.46
Parity	≤2	5 (21.7)	8 (23.5)
	≥3	18 (78.3)	26 (76.5)

The presenting symptoms of the study participants are presented in *Table II* based on the mode of diagnosis. The most common presenting symptom was postmenopausal bleeding in 15 (65.2%) women in Group A and 23 (67.6%) women in Group B; per-vaginal discharge in 3 (13.0%) women in Group A and 1 (2.9%) woman in Group B; and irregular per-vaginal bleeding in 5 (21.7%) women in Group A and 10 (29.4%) women in Group B.

Table II
Presenting symptoms according to mode of diagnosis.

Presenting symptom	Group A, n=23, n (%)	Group B, n=34, n (%)
Postmenopausal bleeding	15 (65.2)	23 (67.6)
Per-vaginal discharge	3 (13.0)	1 (2.9)
Irregular per-vaginal bleeding	5 (21.7)	10 (29.4)
Total	23 (100.0)	34 (100.0)

The histopathological features of the study subjects are described in *Table III*. In Group A, 16 (69.6%) women had endometrioid histology, 7 (30.4%) women had non-endometrioid histology or sarcoma, and in Group B, 30 (88.2%) women had endometrioid histology, and 4 (11.8%) women had non-endometrioid histology or sarcoma. Low-grade tumours were more common in both groups (65.2% and 85.3%, respectively), and myometrial invasion of more than 50% was seen in 15 (65.2%) women in Group A and 19 (55.9%) women in Group B.

Table III
Histopathological characteristics according to mode of diagnosis.

Variable	Category	Group A, n=23, n (%)	Group B, n=34, n (%)
Histological type	Endometrioid	16 (69.6)	30 (88.2)
	Non-endometrioid or sarcoma	7 (30.4)	4 (11.8)
Tumour grade	Low grade	15 (65.2)	29 (85.3)
	High grade	8 (34.8)	5 (14.7)
Myometrial invasion	≤50%	8 (34.8)	15 (44.1)
	>50%	15 (65.2)	19 (55.9)

Table IV shows the treatment modalities received by mode of diagnosis. All patients in Group A underwent staging laparotomy, 5 (21.7%) of whom received no further treatment, 4 (17.4%) radiotherapy, 2 (8.7%) chemotherapy, and 12 (52.2%) chemotherapy and radiotherapy. In Group B, the majority of patients (24, 70.6%) were treated with adjuvant radiotherapy or chemotherapy alone, with smaller numbers receiving completion surgery with or without adjuvant therapy, or follow-up only.

Table IV
Treatment modalities according to mode of diagnosis.

Treatment modality	Group A, n=23, n (%)	Group B, n=34, n (%)
Staging laparotomy, no adjuvant treatment	5 (21.7)	0 (0.0)
Staging laparotomy + radiotherapy	4 (17.4)	0 (0.0)
Staging laparotomy + chemotherapy	2 (8.7)	0 (0.0)
Staging laparotomy + chemotherapy + radiotherapy	12 (52.2)	0 (0.0)
Follow-up only	0 (0.0)	2 (5.9)
Adjuvant radiotherapy/chemotherapy only	0 (0.0)	24 (70.6)
Completion surgery, no adjuvant treatment	0 (0.0)	2 (5.9)
Completion surgery + radiotherapy	0 (0.0)	1 (2.9)
Completion surgery + chemotherapy + radiotherapy	0 (0.0)	5 (14.7)
Total	23 (100.0)	34 (100.0)

Treatment completion and follow-up status by mode of diagnosis is provided in *Table V*. A statistically significant difference was observed between the two groups (p=0.008) with 20 (87.0%) women in Group A achieving complete treatment, and 18 (52.9%) in Group B. Regular follow-up was maintained by 12 (52.2%) women in Group A and 14 (41.2%) in Group B, while 3 (13.0%) and 7 (20.6%) women, respectively, were lost to follow-up (p=0.653).

Table V
Treatment completion and follow-up status according to mode of diagnosis.

Variable	Category	Group A, n=23, n (%)	Group B, n=34, n (%)	p-value
Treatment status	Complete treatment	20 (87.0)	18 (52.9)	0.008
	Incomplete treatment	3 (13.0)	16 (47.1)	
Follow-up status	Regular	12 (52.2)	14 (41.2)	0.653
	Irregular	8 (34.8)	13 (38.2)	
	Lost to follow-up	3 (13.0)	7 (20.6)	

Table VI shows the three-year recurrence pattern according to mode of diagnosis. Any recurrence was observed in 2 (8.7%) women in Group A and 4 (11.8%) women in Group B. Overall, 6 (10.5%) participants experienced recurrence within three years.

Table VI
Three-year recurrence pattern according to mode of diagnosis.

Recurrence outcome	Group A, n=23, n (%)	Group B, n=34, n (%)	Overall, N=57, n (%)
No recurrence	21 (91.3)	30 (88.2)	51 (89.5)
Vault recurrence/metastasis	1 (4.3)	3 (8.8)	4 (7.0)
Lung metastasis	1 (4.3)	0 (0.0)	1 (1.8)
Bone metastasis	0 (0.0)	1 (2.9)	1 (1.8)
Any recurrence	2 (8.7)	4 (11.8)	6 (10.5)

The three-year recurrence-free and overall survival rates by mode of diagnosis are shown in *Table VII*. There were 2 (8.7%) women in Group A and 4 (11.8%) in Group B who experienced recurrence-free survival events; the mean recurrence-free survival for Group A was 34.17 ± 1.25 months and for Group B was 33.41 ± 1.22 months. By 3 years, 5 (21.7%) women in Group A and 7 (20.6%) in Group B had died, and there was no significant difference in overall survival between the two groups.

Table VII
Three-year recurrence-free and overall survival outcomes according to mode of diagnosis.

Outcome	Category	Group A, n=23, n (%)	Group B, n=34, n (%)	Overall, N=57, n (%)
Recurrence-free survival	Recurrence/event	2 (8.7)	4 (11.8)	6 (10.5)
	No recurrence/censored	21 (91.3)	30 (88.2)	51 (89.5)
Mean recurrence-free survival, months	Mean ± SE	34.17 ± 1.25	33.41 ± 1.22	33.72 ± 0.89
	95% CI	31.73-36.62	31.01-35.81	31.98-35.46
Overall survival	Alive/censored at 3 years	18 (78.3)	27 (79.4)	45 (78.9)
	Death/event	5 (21.7)	7 (20.6)	12 (21.1)
Cause/status at 3 years	Alive after 3 years	18 (78.3)	27 (79.4)	45 (78.9)
	Chemotherapy/treatment-related complication	3 (13.0)	3 (8.8)	6 (10.5)
	Disease-related morbidity	2 (8.7)	2 (5.9)	4 (7.0)
	Disease recurrence	0 (0.0)	2 (5.9)	2 (3.5)
	Total	23 (100.0)	34 (100.0)	57 (100.0)

DISCUSSION

This study shows that Group A included women with uterine cancer diagnosed before hysterectomy by endometrial evaluation, while Group B included women with uterine cancer diagnosed unexpectedly on final histopathology after hysterectomy without prior endometrial evaluation. Women in Group A were older and had more non-endometrioid histology, high-grade tumours, and deep myometrial invasion, but the malignancy had been diagnosed before definitive surgery. This distinction was clinically significant because it enabled the treatment to be carried out along an oncologically planned route, instead of having to make treatment decisions after an unexpected diagnosis in the postoperative period. Previous reports have shown that uterine malignancy can be overlooked before surgery and that the clinical presentation and tumour biology can affect the diagnosis of malignancy during the pre-operative evaluation [12]. The management challenges that arise when the final diagnosis is malignant, but the initial diagnosis was presumed benign, have also been highlighted in reports of uterine sarcomas after surgery for presumed benign disease [13]. Occult endometrial cancer has also been studied after prolapse surgery, and some patients may undergo further staging procedures after the initial diagnosis, even if the cancer is early stage or low grade [14]. One of the most important clinical benefits noted in Group A was that all 23 women had staging laparotomy as part of their planned oncological treatment. The opportunity to perform appropriate staging at the time of definitive treatment was therefore afforded by the preoperative diagnosis of malignancy, as opposed to the post-operative incidental diagnosis. The recommendations for endometrial cancer are to perform appropriate surgical staging and risk-directed management [15]. The current European consensus guidelines also include histological type, tumour characteristics and appropriate staging as important factors for subsequent treatment planning [16]. New techniques such as sentinel lymph node mapping can also offer a reliable assessment of the nodes with a lower morbidity rate than systematic lymphadenectomy [17]. Multicentre studies have also confirmed that sentinel lymph node assessment is a valuable part of modern staging procedures [18]. The most significant difference between the two groups was in treatment completion. The difference between the two groups was statistically significant (p=0.008) with 20 (87.0%) women in Group A achieving complete treatment, compared with 18 (52.9%) women in Group B. This discovery confirms the clinical significance of the diagnosis of uterine malignancy prior to hysterectomy. After the diagnosis of cancer, patients could be referred to a structured oncological pathway from the beginning, with the surgical staging and subsequent adjuvant treatment depending on the pathological risk. Women in Group B had already had a hysterectomy, but the diagnosis of malignancy had not been made before surgery, and treatment had to be planned based on an unexpected histopathological diagnosis. Most of the women in Group B were therefore treated with adjuvant radiotherapy or chemotherapy alone, and some needed completion surgery with or without further treatment. This decentralized approach can lead to further logistical, financial, and treatment difficulties, especially in resource-poor environments. The three-year oncological outcomes were statistically similar between the groups, although Group A had significantly higher treatment completion. Recurrence occurred in 2 (8.7%) women in Group A and 4 (11.8%) women in Group B, while mean recurrence-free survival was 34.17 ± 1.25 and 33.41 ± 1.22 months, respectively (p=0.706). There was also no significant difference in overall survival (p=0.894). Similar results have been seen in cohorts where appropriate follow-up treatment was given after the diagnosis of occult uterine cancer was made [14]. Modern approaches to the management of endometrial cancer focus on the importance of tumour biology, pathological risk, stage and adequacy of treatment as key factors influencing oncological outcome [19, 20]. Thus, the lack of statistical significance in survival should not detract from the clinical benefit seen with the use of preoperative diagnosis. Instead, the present results indicate that, when clinically appropriate, endometrial assessment can help detect malignancy prior to hysterectomy, plan for staging, and significantly increase the chances of completing the intended treatment pathway. The lower number of recurrences in Group A also suggests that further studies are warranted to determine if early diagnosis and coordinated treatment can lead to longer-term oncological outcomes in larger populations [21].

LIMITATIONS

The study was retrospective, conducted at a single center, and had a small sample size, which may limit the generalizability of the results.

CONCLUSION

This retrospective study emphasizes the clinical significance of detecting uterine cancer before hysterectomy using adequate endometrial assessment. Women diagnosed preoperatively in Group A followed a planned oncological treatment pathway; all had staging laparotomy, and a much higher proportion completed treatment than women in Group B, whose cancer was discovered unexpectedly after hysterectomy. Although Group A had a higher number of high-grade and non-endometrioid tumors, treatment completion remained significantly higher, and recurrence was numerically lower. The three-year recurrence-free survival and overall survival rates were not significantly different across the groups. These data suggest adequate preoperative endometrial assessment in clinically indicated women undergoing hysterectomy, as early detection of cancer allows for planned staging, coordinated treatment, and increased treatment completion.

FUTURE RECOMMENDATIONS

To confirm these results, larger, multicenter prospective studies with longer follow-up periods are recommended, as well as the identification of strategies to improve the accuracy of preoperative diagnosis and adherence to adjuvant treatment.

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CONFLICT OF INTEREST

None declared

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