

## Uterine Cancer Treatment: Experience in Two Centers in Nepal

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### ABSTRACT

#### Background:



Information and studies regarding uterine cancer are limited in Nepal. The aim of this study is to assess the clinical characteristic features and treatment outcomes of uterine cancer managed in two hospitals of Nepal.

**Methods:** A retrospective descriptive study was conducted of all uterine cancer cases managed in gynecology department of Civil Service Hospital and National Cancer Hospital from August 2014-January 2016. The case record of all women diagnosed to have uterine cancer were retrieved and demographic characteristics, clinical presentations, histological type, treatment modalities and outcome were obtained and analyzed. Patients were followed up to five years and information regarding recurrence and mortality were obtained.

**Results:** There were 30 uterine cancers cases during study period with age ranging from 33-72 years (mean 53.3years). One case was unmarried while rest 29 (96%) were married, with parity ranging from 0-11. Abnormal uterine and postmenopausal bleeding were the commonest presentations. Histopathologically, endometrial adenocarcinoma accounted for 25 cases (83%), uterine sarcoma four cases (13%) and malignant mixed mullerian tumour one case (4%). All the endometrial cancers were preoperatively diagnosed by endometrial biopsy whereas all cases of uterine sarcomas were reported as leiomyoma radiologically, had benign findings in endometrial biopsy and were only diagnosed post-operatively by histopathology. All cases were treated primarily with surgery. Twenty four patients (80%) received adjuvant therapy according to stage and grade of the disease. Clinical follow-up showed 18 (62%) cases were disease free; 11 (36.67%) developed recurrence, mortality occurred in 9 (31%), two are living with disease and one case is lost to follow up.

**Conclusions:** Endometrial cancer can be usually diagnosed pre-operatively by endometrial biopsy, however, uterine sarcoma is often missed. Surgery is the main treatment modality of uterine cancers.

**Keywords:** Endometrial cancer, Sarcoma, Uterine cancer.

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## INTRODUCTION

Uterine cancer is the second common malignancy of the female genital tract in the world and according to the GLOBOCAN cancer statistics, there are an estimated 417,367 new cases and 97,370 deaths attributed to endometrial cancer worldwide in 2020.<sup>1</sup> In Nepal it is the 3rd most common gynecologic malignancy after cervical and ovarian cancer with 180 new cases and 93 deaths in the year 2020.<sup>1</sup> The incidence rates are found to be generally higher in developed countries compared to developing countries.<sup>2</sup> However, the mortality due to endometrial cancer has been found to be the highest among women of low socioeconomic status.<sup>3</sup> Significant increase of endometrial cancer has been seen in Asian countries like Japan, Korea and others which has been a matter of concern.<sup>4,5</sup>

The mean age at diagnosis of uterine cancer is 61 years although 5–30% of cases appear in women younger than fifty.<sup>6</sup> Abnormal uterine bleeding has been proven to be the most significant symptom of all types of uterine cancer. However, its specificity is low with a large number of benign pathologies also presenting with similar symptoms.<sup>7</sup> Postmenopausal women with high risk factors such as older age and obesity appear more likely to develop uterine cancer.<sup>8</sup>

Surgery is the mainstay of treatment for uterine cancer<sup>9</sup> and the International Federation of Gynecology and Obstetrics (FIGO) staging procedure includes: total hysterectomy, bilateral salpingo-oophorectomy with/without pelvic and para-aortic lymphadenectomy.<sup>10</sup> Adjuvant treatment in the form of radiation therapy and chemotherapy are required when there are unfavorable clinicopathological prognostic factors such as old age, non-endometrioid histology, high grade tumor, deep myometrial invasion, cervical

involvement, extrauterine extension including pelvic and para-aortic lymph nodes metastasis. The most common form of adjuvant therapy is pelvic radiation which gives good control of loco-regional but not distant or systemic disease<sup>11</sup> so chemotherapy may have a role in advanced disease or in early-stage disease with high risk of distant recurrence.<sup>12</sup>

Generally, prognosis of women with endometrial cancer is good, with a high overall survival rate; the 5-year survival rate was reported to be 81.2%.<sup>13</sup>

This study was undertaken to address the limited study and information available in our country regarding uterine cancer. The main aim of the study is to assess the clinical characteristic features and treatment outcomes of uterine cancer managed in two hospitals of Nepal.

## MATERIALS AND METHODS

A retrospective descriptive study was conducted of all uterine cancer cases managed in gynecology department of Civil Service Hospital and National Cancer Hospital from August 2014 to January 2016. Case record of all women with uterine cancer were retrieved from the hospital cancer database at the end of January 2016 and demographic characteristics, clinical presentations, histological type, treatment modalities and outcome were obtained and analyzed. Patients were followed up three monthly for the first two years then six monthly thereafter for five years. Patients who missed their follow up schedule were contacted over phone to inquire about their health and asked to follow up. Any mortality were recorded. Patients who could not be contacted at the end of five years were noted as lost to follow up. The last patient to complete her five year follow up was on January 2021. At follow up, history, clinical examination,

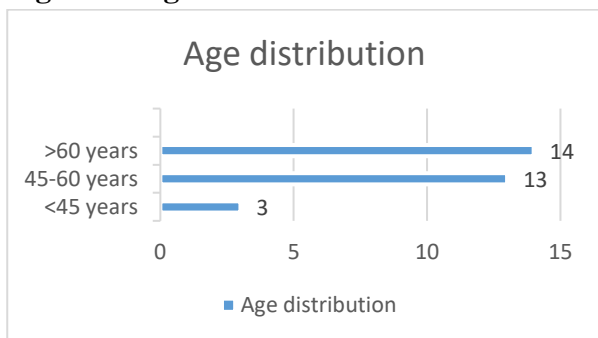
vault smear cytology, ultrasound abdomen and pelvis and CA 125 (in cases where it was raised preoperatively) were done. Those patients with suspicious clinical, biochemical, cytological or radiological findings were subjected to CT scan abdomen and pelvis. Those patients with recurrence were referred to clinical oncologist and further treatment were decided after multidisciplinary team discussion.

Data were entered in the Microsoft Excel and exported to SPSS 16 and descriptive analytical tools such as frequency percentage, mean and range were used for analysis. Approval for the study was taken from the administration and the Ethical Review Committee of the respective hospitals.

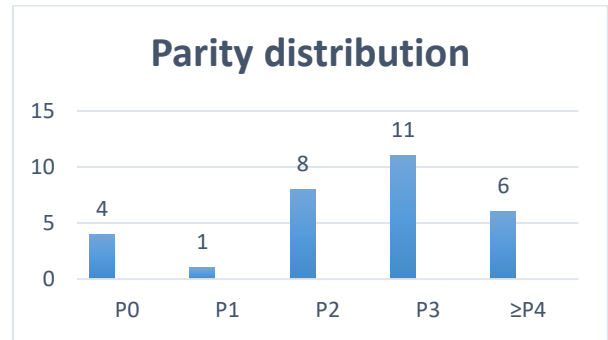
**RESULTS**

Thirty cases of uterine cancer were managed during the study period in the two hospitals of Nepal. Among them 22 cases were from Civil Service Hospital and eight cases were from National Cancer Hospital. The age ranged from 33-72 years with the mean age being 53.3 years (Figure 1). One case was unmarried and all other 29 (96%) were married. Their parity ranged from 0-11 with majority being para 3 (Figure 2). Majority of the cases 20 (66.67%) were postmenopausal and 10 (33.33%) were premenopausal. Abnormal uterine and postmenopausal bleeding per vaginum were the commonest presentations (Table 1).

**Figure 1: Age distribution**



**Figure 2: Parity distribution**



**Table 1: Clinical presentation and associated comorbid conditions**

Presentation and comorbid conditions	Number (n=30)	Percentage
Abnormal uterine bleeding	23	76.67
Postmenopausal bleeding	16	53.33
Pain lower abdomen	11	36.67
Hypertension	5	16.67
Diabetes	5	16.67

All the endometrial cancers were preoperatively diagnosed by endometrial biopsy whereas all cases of uterine sarcomas were misdiagnosed pre-operatively as myoma radiologically, had unremarkable endometrial report and were only diagnosed by post-operative histopathology. Majority of the cases (80%) were diagnosed at stage I (Table 2).

**Table 2: Stage at presentation**

FIGO Stage	Number (n=30)	Percentage
Stage IA	6	20
Stage IB	18	60
Stage II	2	6.67
Stage III	3	10
Stage IV	1	3.33

Histopathologically, endometrial adenocarcinoma accounted for 25 cases (83.33%), uterine sarcoma four cases (13.33%) and malignant mixed mullerian tumour one case (3.33%) (Table 3).

Clinical follow-up was done three monthly for the first two years then six monthly thereafter for five years where one patient of endometrial cancer was lost to follow up after one year when recurrence was diagnosed and her status at end of the study could not be known. There was mortality in nine (31%) patients: seven endometrial cancer among which six cases due to recurrence and one case due to severe post-radiation enteritis and sarcoma (N=2) both due to recurrence (Table 4). The overall survival at

five years was 68.9% (20/29) and disease-free survival was 62% (18/29).

All cases were treated primarily with surgery: total abdominal hysterectomy with bilateral salpingo-oophorectomy with or without pelvic, para-aortic lymph node dissection and some even omentectomy according to the histopathology; 24 (80%) of cases required adjuvant therapy in the form of radiation therapy and chemotherapy which were given according to stage, grade and risk factors of the disease (Table 5 and 6).

**Table 2: Histopathological Patterns**

Histopathology	Number (n=30)	Percentage
<b>1. Adenocarcinoma (n=25) 83.33%</b>		
1.1 No residual tumour	1	3.33
1.2 Endometrioid adenocarcinoma (G I: 6, G II: 6 and G III: 5)	17	56.67
1.3 Mucinous carcinoma (G I)	1	3.33
1.4 Clear cell carcinoma (G III)	1	3.33
1.5 Uterine serous papillary carcinoma	5	16.67
<b>2 Uterine sarcoma(n=4) 13.33%</b>		
2.1 Endometrial stromal sarcoma	1	3.33
2.2 Leiomyosarcoma	3	10
<b>3 Malignant mixed mullerian tumour (n=1) 3.33%</b>	1	3.33

**Table 4: Mortality review**

Case	Histology and Stage	Treatment	Remarks
1	Endometrioid Adenocarcinoma, Grade 2, Stage IB	TAH+BSO+B/L pelvic, para-aortic LND + Adjuvant External Beam RT + Intracavitary Radiotherapy (EBRT+ICR)	Recurrence after 2 years: metastasis in liver and upper abdomen. Died in about 3 years
2	Uterine serous papillary cancer, Stage IIIC	Neoadjuvant Chemotherapy, TAH+BSO+Omentectomy, Adjuvant Chemotherapy	Died in about 2.5 years due to recurrence.
3	Endometrioid Adenocarcinoma, Grade 2, Stage IA	TAH+BSO+B/L pelvic, para-aortic LND + Adjuvant EBRT+ICR	Died due to severe RT complications (Subacute intestinal obstruction, malabsorption due to severe Radiation Enteritis)
4	Endometrioid Adenocarcinoma, Grade 3, Stage IB	TAH+BSO+B/L pelvic, para-aortic LND. Defaulted Adjuvant RT	Recurrence after 1 year: metastasis in liver and upper abdomen. Died in about 3 years.
5	Uterine serous papillary cancer, Grade 3, Stage IB	TAH+BSO+Omentectomy. Adjuvant Chemotherapy	Recurrence after 3yrs: abdomen. Died in about 4 years.

6	Endometrioid Adenocarcinoma, Grade 2, Stage IB	TAH+BSO+B/L pelvic, para-aortic LND. Defaulted Adjuvant RT (EBRT+ICR)	Recurrence after 1.5 years in para-aortic, mediastinal nodes, liver and lungs. Died in about 2.4 years.
7	Endometrioid Adenocarcinoma, Stage IV	Neoadjuvant Chemotherapy, TAH+BSO, Adjuvant Chemotherapy	Recurrence after 1 year and died within 2 years despite treatment
8	Uterine sarcoma IB	TAH+BSO. Defaulted adjuvant treatment	Recurrence after 1 year and died despite treatment with chemotherapy
9	Uterine sarcoma IB	TAH+BSO. Defaulted adjuvant treatment	Recurrence after 1 year and died despite treatment

**Table 5: Primary treatment modality of uterine cancer**

Surgical types	Number (n=30)	Percentage
Total Abdominal Hysterectomy with Bilateral Salpingo-Oophorectomy (TAH BSO)	4	13.33
TAH BSO with omentectomy	2	6.67
TAH BSO with Bilateral Pelvic Lymph Node Dissection (B/L PLND) +/- Para-aortic LND	19	63.33
TAH BSO with B/L PLND+ Para-aortic LND with omentectomy	3	10.0
Radical Hysterectomy with B/L PLND	2	6.67

**Table 6: Adjuvant Treatment of uterine cancer**

Adjuvant treatment	Number (n=24)	Percentage
Radiation Therapy	16	66.67
Radiation Therapy and chemotherapy	6	25
Chemotherapy	2	8.33

## DISCUSSION

Uterine cancer is known to be a disease of elderly, studies showing the mean age at diagnosis to be 61 years and only 5–30% of cases in women younger than fifty.<sup>6</sup> But in the present study, significant number of cases 16 (53.3%) were young aged  $\leq 60$  years with the mean age of 53.3 years.

Several observational studies have shown an association between parity and endometrial cancer as parity is shown to modulate risk of endometrial cancer through affecting estrogen and progesterone levels.<sup>14</sup> In comparison to

nulliparous women, parous women was associated with decreased risk of developing endometrial cancer in several studies<sup>15-17</sup> and pooled analysis.<sup>18</sup> However, such an inverse association was not detected in several other studies.<sup>19,20</sup> In the present study only 13.33% were nulliparous and thus did not show the inverse association.

Abnormal uterine bleeding including pre and post-menopausal bleeding was one of the commonest presenting features which is similar to other studies. Tangjitgamol S, et al<sup>9</sup> has also noted abnormal uterine bleeding as the

most common presenting symptom in 87.3% of cases. Several other studies have shown that postmenopausal bleeding is the presenting symptom in more than 90% of confirmed endometrial cancer cases<sup>21,22</sup>. However not all cases of abnormal uterine bleeding have endometrial cancer and only 5-10% of patients presenting with postmenopausal bleeding will be actually diagnosed with endometrial cancer.<sup>23,24</sup>

The primary treatment of endometrial cancer is surgery and all the patients in our study underwent surgery with TAH BSO with B/L Pelvic LND+/- Para-aortic LND (63.33%) in majority of cases which is similar to 79.3% in other study by Therasakvichya S et al.<sup>25</sup>

Early stages of endometrial cancer are often curable with surgery whereas stage IV endometrial cancer has a five-year survival of approximately only 22%.<sup>7</sup> The overall survival was seen to be good in stage II and Stage IA in our study group but this may be due to small

study population of only 30 cases. Therefore, early detection remains the most important factor to increase the overall survival so we should initiate investigations to diagnose endometrial cancer in all cases presenting with postmenopausal bleeding.

## CONCLUSION

Abnormal uterine bleeding among perimenopausal or postmenopausal women is the main presenting symptom of uterine cancer; thus, endometrial biopsy should be performed for prompt and pre-operative diagnosis. However, pre-operative diagnosis of uterine sarcoma could be difficult even with endometrial biopsy. Surgery is the main treatment modality of uterine cancers. Adjuvant radiation therapy and chemotherapy based on stage and pathological risk factors contributes to better disease control and survival.

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