
## College of health science

## School of medicine

## Department of Obstetrics and Gynecology

# Clinicopathologic characteristics, management outcome and its associated factors among patients managed with uterine cancer in Tikur Anbessa specialized Hospital: Addis Ababa Ethiopia: A Retrospective cohort study, 2024

Investigator: Dr. Esubalew Berihun (Obstetrics and Gynecology Year IV Resident)

A research thesis to be submitted to Addis Ababa University, school of medicine, department of obstetrics and gynecology in the Partial Fulfillment of the requirements for Specialty in Obstetrics and Gynecology

August, 2024

Addis Ababa

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**LETTER OF APPROVAL**

## Addis Ababa University,

## College of Health Sciences, Department of Obstetrics and Gynecology

## Research report attesting page

### Student declaration

I, Dr Esubalew Berihun hereby declare that this thesis entitled **"**Clinicopathologic characteristics, management outcome and its associated factors among patients managed with uterine cancer in Tikur Anbessa specialized Hospital: Addis Ababa Ethiopia**"** was fully undertaken by me under the guidance of my advisor and that I have, to the best of my knowledge and effort, I have cited all various sources of information used in this thesis, and I am also declaring that this thesis has not been submitted to any other institution for the award of any degree, certificate, masters or diploma.

Esubalew Berihun (MD) Signature _____ Date _____

**SUPERVISOR DECLARATION**

I hereby certify that I have read and evaluated this research thesis relating to **"**Clinicopathologic characteristics, management outcome and its associated factors among patients managed with uterine cancer in Tikur Anbessa specialized Hospital: Addis Ababa Ethiopia**"** under my guidance from its inception up to in its current format and that it can be submitted for final approval in partial fulfillment to the Degree of Specialty in Obstetrics and Gynecology. I also certify that the above declaration made by the investigator is correct to the best of my knowledge as an advisor.

## Advisors:

Dr Esayas Birhanu (MD, Gynecologic oncologist, Associate professor in gynecology and obstetrics, school of medicine, college of health science, Addis Ababa University)

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Dr Abera Bedada (MD, Assistant professor in gynecology and obstetrics)

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# Abbreviation

| | |
|---|---|
| CI | Confidence interval |
| EC | Endometrial cancer |
| EEC-A | Endometrial endometrioid carcinoma |
| FIGO | International Federation of Gynecology and Obstetrics |
| LVSI | Lymphovascular space invasion |
| OR | Odd Ratio |
| OS | Overall survival |
| TASH | Tikur Anbessa Specialized Hospital |

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## Abstract

**Background:** -: Most cases of endometrial cancer are found at early stage and have a good outcome overall. But about one-third of patients had a diagnosis of advanced disease. Patients who report with advanced stage or aggressive histologic subtypes have a higher rate of recurrence and, consequently, lower survival times, despite favorable outcomes in early-stage cancer. Over the last 20 years, the number of deaths from EC has climbed by more than 100%, with type II EC accounting for up to 40% of cases. The type of treatment was linked to a 36% lower chance of mortality or relapse. Since there is no studies that evaluate the treatment outcome of uterine cancer in our country this study was conducted.

**Objective:** -To assess Clinicopathologic characteristics, management outcome and its associated factors among patients with uterine cancer treated at Tikur Anbessa specialized Hospital: A five years retrospective cohort study, 2024.

**Method;** - Facility based retrospective cohort study design was conducted. Using a 2 months study period a five years data was recruited. 128 uterine cancer cases managed at TASH from Jan 1$^{st}$ 2015 to Dec 30$^{th}$ 2019 were involved. Data was gathered through the perusal of patient charts. Collected data was checked for completeness, consistency, clarity, and missed values and was entered into SPSS version 25 for data management and further statistical analysis. The clinicopathologic characteristic were described using symptoms, signs, and pathological findings related to a specific disease or condition. The management outcome was measured using logistic regression.. 95% confidence intervals were used to correlate the outcome variable with its independent variable. The threshold for statistical significance was established at p-value < 0.05 for all tests.

**Result:** - In this study 128 charts were reviewed and out of this 59(46.1%) of the study participants were in the age group 51-65 years with a mean and SD of 55.5±9.3 years respectively. 117(91.4%) of the participants were menopause and 64(50%) of the participants had presenting signs and symptoms of vaginal bleeding only and 37(28.9%) had vaginal bleeding and discharge. 53(41.4%) of the study participants had a symptom of 6-12 months duration and 19(14.8%) of the participants had ascites based on imaging. The study found that great majority (87.5%) of uterine cancer cases were endometrial cancer, and the rest is smooth muscle and mesenchymal cancer. The average age at diagnosis was 56 and 54 respectively. Metastasis

occurred in 20.3% of cases, predominantly in the peritoneum (19.2%). Recurrent metastases were observed in 33 patients, with 57.6% having both distant and local metastases. During the final follow up from 128 cancer cases 22% were were died. The determinant factor of patient death at last hospital follow up outcome were age of >60 years (AOR=1.3, 95%CI=1.11, 16.37), having metastasis (AOR=3.1, 95%CI=1.21, 7.69), tumor size of >2cm (AOR=1.4, 95%CI=1.18, 10.33) and provisional FIGO stage IV (AOR=16.3, 95%CI=1.23, 32.45).

**Conclusion and recommendation**- The study found that **great majority** (87.5%) of uterine cancer cases were endometrial cancer, and the average age at diagnosis was 56 and 54 respectively. Recurrent metastases were observed in 33 patients, with 57.6% having both distant and local metastases. During the final follow up from 128 cancer cases 22% were were died.Old age, metastasis, increasing tumor size and increasing the stage of disease are statistically significant factor for the death of the study participants. Further study is needed to address the final outcome of patients.

**Keyword**: - clinicopathologic, treatment outcome, uterine cancer, time of death

# 1. Introduction

## 1.2 Background

Endometrial cancer (EC) is the most common gynecologic malignancy in developed countries and the fourth most common cancer in women after breast, lung and colorectal cancers (1). EC most prevalent malignancy among women in developed countries is endometrial carcinoma. According to the latest data in 2018, there were 382,069 new cases and 89,929 deaths attributed to EC worldwide (2). The prognosis for patients with advanced endometrial cancer is quite bad, with metastasis being the main cause of death (3). Globally, uterine cancer ranks second among gynecologic cancers when nations with abundant and restricted resources are taken into account. Over 90% of uterine cancers are endometrial, originating in the epithelium; most of the remainder are mesenchymal and less commonly the endometrial stroma (2)

Over the previous 20 years, there has been a more than 100% increase in the death rates from EC, with type II EC accounting for up to 40% of cases. (4). Endometrial carcinoma is divided into two different subtypes. Type 1 endometrial carcinomas are low-grade, diploid, and have either well-differentiated or moderately-differentiated hormone receptors (hormone-receptor positive). Type 2 endometrial cancer is high-grade and histologically non-endometrioid (5).

Endometrioid adenocarcinomas, commonly referred to as type I tumors, are typically low-grade cancers that are associated with unopposed estrogen stimulation. They have a good prognosis and a low risk of metastasis or recurrence (6). On the other hand, type II tumors are less prevalent yet still cause most EC-related deaths. Type II cancers are not estrogen dependent and develop independently of the endometrial hyperplasia pathway (7). These have a worse prognosis and are more likely to be high grade, papillary serous or clear cell histologic types, with an increased chance of metastasis or recurrence (6).

Endometrioid carcinoma is the most prevalent subtype of endometrial cancer. Unrestricted estrogen exposure, obesity, nulliparity, and tamoxifen use are risk factors for endometrial cancer (8.).

Most cases with EC have an early diagnosis and a favorable outcome overall. But about one-third of patients receive a diagnosis of advanced disease (9). Patients who enter with an advanced stage or with aggressive histologic subtypes have a higher likelihood of recurrence and, consequently, a shorter survival time, even when early-stage cancer results are excellent. For stage IV illness, the reported 5-year overall survival (OS) is a pitiful 0–18% (10-11).

The majority of endometrial malignancies in their early stages can be cured with surgical excision alone, and success is guaranteed. However, when clinical or pathological unfavorable variables are present, disease recurrence may occur and have an impact on patient outcomes. Tumor stage, growing patient age, tumor size, high-risk histological type, grade 3 adenocarcinoma, myometrial invasion, and lymphovascular space invasion (LVSI) are the traditional risk factors for recurrence in early-stage endometrial cancer (12-14).

Furthermore, because it is uncommon, there are no evidence-based treatment plans. Nonetheless, long-term survival was achieved in certain advanced stage cases that underwent multimodal treatment (surgery, chemotherapy, and radiation therapy)(15-16).

Endometrial cancer (EC) is often treated with a hysterectomy and bilateral salpingo-oophorectomy, followed in certain cases by lymph node dissection. The decision regarding adjuvant treatment (observation versus radiation and/or chemotherapy) is made based on post-operative risk classification. The disease stage, tumor histo-type and differentiation grade, depth of myometrial invasion, LVSI, and patient age are the factors that determine the current treatment regimens (17).

Moreover, a study on 521 individuals with stage I endometrioid endometrial cancer found that, in patients with stage IB, histologic grade was the sole risk factor linked to tumor recurrence. In this patient group, the 5-year recurrence-free survival rates were 94% for grade 1, 79% for grade 2, and 74% for grade 3 (18).

Three to seven percent of uterine cancers are uterine sarcomas, which are uncommon mesodermal tumors (33). These are a diverse set of tumors, and each lesion has a limited amount

of personal experience. Historically, endometrial stromal sarcomas (10–15%), carcinosarcomas (40%), leiomyosarcomas (40%), and undifferentiated sarcomas (5–10%) have been the four main categories for uterine sarcomas. The majority of Subgroups exhibit aggressive behavior and have unfavorable prognoses, with high rates of distant metastases and local recurrence ( 35).

Ten patients (0.7%) out of 1,432 who had hysterectomy for suspected fibroids at the University of Southern California had leiomyosarcoma in the hysterectomy material, according to the review (36). A more recent analysis of 10,119 hysterectomies for benign causes carried out at one Dallas-area facility between 2000 and 2014 revealed that only nine patients (0.089%) had uterine sarcomas, five of which were leiomyosarcomas (37). From 1988 to 2005, information on 819 patients with 2009 FIGO stage I leiomyosarcoma was taken from the SEER database. For patients with stage IA disease, the 5-year overall survival rate was 76.6%, whereas for those with stage IB disease, it was 48.4% ($p < 0.001$)(38)

## 1.2 Statement of the problem

In high- and intermediate-income nations, endometrial cancer, also known as corpus uteri cancer, is the most frequent gynecological malignancy. 2020 saw the registration of 417,367 new instances of endometrial cancer, or 2.2% of all newly diagnosed cancer cases globally. Asia was the location of over 40% of these new cases, with China accounting for about half (81 964) of the cases. In China, endometrial cancer is the third most frequent malignancy among women. In turn, endometrial cancer was accountable for 97,370 cancer-related deaths, or 1% of all cancer-related deaths globally (39).

In the United Kingdom, endometrial cancer has become more common in recent years, accounting for about 9400 diagnoses and 2400 deaths per year. When compared to patients with advanced (Stage III or IV) disease, the majority of patients with endometrial cancer are discovered at an earlier stage (Stage I or II) and have a better prognosis (five-year survival rates of >74% vs ≤15%, respectively). Patients with distant recurrent disease have a dismal prognosis as well (median survival of less than a year) (40)

Patients who enter with an advanced stage or with aggressive histologic subtypes have a higher risk of recurrence and, consequently, a shorter survival time, even with an excellent prognosis in early-stage cancer. Since lymphatic or direct extensions are the most prevalent ways that EC spreads, most recurrences of the condition occur locally in the pelvis and abdomen (21).

Currently, surgery is the main treatment for EC, with adjuvant radiation therapy and chemotherapy coming next (22). These treatments haven't, however, successfully lowered the chance of EC death. Recurrence rates for EC range from 60% to 80%, and they typically happen two to three years following surgery (23).The type of treatment was linked to a 36% lower chance of mortality or relapse. A significant difference was observed in cancer specific survival, with adjuvant chemotherapy being preferred over radiation therapy (24). The features, course of treatment, and prognosis of uterine cancer patients in Ethiopia have not received adequate

research attention. As a result, little is known about the management and clinical features of uterine cancer patients, their prognosis, and the factors that influence mortality in this nation. Thus, the clinicopathologic and management outcome of patients treated for uterine cancer were evaluated in this study.

## 1.3 Significance of the study

Studying the characteristics, management outcomes, and associated factors among patients with uterine cancer important for analyzing the characteristics (age, stage at diagnosis, histopathological types) helps in understanding the population most affected by uterine cancer and identifying high-risk groups By studying the outcomes of different management strategies (surgery, chemotherapy, radiotherapy and combination), healthcare providers can identify the most effective and safest interventions.

Understanding which treatment works best for specific subgroups of patients (e.g., based on tumor type, patient age, or comorbidities) helps in tailoring treatment plans for better outcomes. By studying factors associated with better or worse outcomes (e.g., stage of cancer, tumor grade, and patient comorbidities), researchers can help clinicians predict patient survival rates and guide discussions on prognosis.

Studies of uterine cancer characteristics can lead to more effective public health campaigns, early identification of symptoms, and better awareness of risk factors. It can also lead to better guidelines for monitoring patients during and after treatment, reducing recurrence rates or managing complications more effectively. These findings would help other researchers to use as baseline data to conduct further research

# 2. Literature review

## 2.1 The clinicopathologic characteristics

An investigation was conducted on the clinicopathologic features and survival rates of endometrial cancer in conjunction with endometrial endometrioid carcinoma (EEC) that develops in adenomyosis (EEC-A or EEC-AIA). In this study, endometrial cancer without adenomyosis was compared with EEC-A and EEC-AIA. Three groups of endometrioid subtypes were compared in terms of epidemiological features, clinicopathological traits, and survival outcomes: group A consisted of patients with stage IA endometrial carcinoma who did not have coexisting adenomyosis; group B included patients with EEC-A; and group C included patients with EEC-AIA. The results showed that the groups representing endometrial endometrioid carcinoma (EEC-A) and EEC-AIA included 230 (11.06%) and 28 (1.35%) cases, respectively, and 1043 cases (50.14%) were confirmed to have stage IA ECC without adenomyosis (AM). 199 (86.5%), 19 (8.3%), 2 (0.9%), 2 (0.9%), 1 (0.4%), 6 (2.6%), and 1 (0.4%) cases of stage IA, IB, II, IIIA, IIIB, IIIC, and IVB occurred among the 230 patients in group B. There were 24 (85.7%), 1 (3.6%), 2 (7.1%), and 1 (3.6%) cases of stage IA, IB, IIIA, and IIIC among the 28 patients in group C. The stage distributions of groups B and C were similar (p=0.267), particularly the ratios of stages IA and IB (p=0.364) (25)

According to clinicopathological features and potential risk factors, the most common location of the EC in endometrial cancer was discovered in peritoneal metastasis (91.3%), with ovaries (82.9%), lymph nodes (78.9%), lungs (76.9%), and liver (50%). Poorly-differentiated tumors (G3) in lymph node metastasis had the highest risk of extra uterine metastasis (68.4%), followed by the peritoneum (56.5%), ovaries (53.7%), and liver (50%). Of the patients with pulmonary metastases, 8 individuals (41%), with moderately differentiated tumors (G2) had the highest rate of extra uterine metastasis. Nearly all patients (94.7%) had more than half of the lymph nodes

metastasized from the myometrium, followed by the ovaries (92.7%), lungs (84.6%), and liver (50%). Conversely, in almost all cases of peritoneal metastasis (95.7%), the depth of myometrial invasion was less than half. The incidence of extra uterine metastasis increased significantly ($p<0.001$) as the degree of tumor differentiation worsened, with the G2 group exhibiting the highest proportion (23.8%) and the G1 group displaying the lowest percentage (4%) (26).

A retrospective observational study on clinicopathological characteristics and risk factors showed that 32 (8.3) patients had serous and clear cell tumor (type II) and 343 (91.7) patients had endometrioid adenocarcinoma (Type I). Patients with type II EC presented with a mean age of 64.97 (SD±6.59), whereas patients with type I EC had a mean age of 57.56 (SD±10.42). Among patients with EC, hypertension and diabetes were the most prevalent comorbidities (27).

Following primary staging surgery, clinicopathologic features and treatment outcomes in patients with stage I, high-risk histology, or high-grade endometrial cancer revealed that, out of 267 patients, 175 were at stage IA and 92 were at stage IB. Furthermore, 37 patients had papillary serous carcinoma, 27 patients had clear cell carcinoma, and 203 patients had grade 3 endometrioid cancer. 57 years old was the median age at diagnosis (range: 31–83 years old).A follow-up time of 67.9 months was the median (range: 4–201 months). Thirteen percent of the 37 individuals experienced recurrence (28).

## 2.2 Risk factors of endometrial cancer

Risk factors for endometrial cancer in patients with endometrial hyperplasia revealed that there were no significant differences between the EC and no EC groups in terms of hyperlipidemia, preoperative CA125, number of deliveries, menopause, or endometrial thickness (all $P>0.05$). However, there were significant differences in terms of age, BMI, diabetes, hypertension, and pathology of EH. The risk factors of EC in patients with EH (all $P<0.05$) that were found through logistic regression analyses were age >50 years (OR 3.064, 95% CI 1.945–5.931), BMI ≥25 kg/m2 (OR 2.705, 95% CI 1.121–3.889), diabetes (OR 3.049, 95% CI 1.781–5.114), hypertension (OR 2.725, 95% CI 1.108–3.431), and severe hyperplasia (OR 3.181, 95% CI 1.496–4.228).

In Sri Lanka, a cross-sectional study on the risk factors for endometrial carcinoma in postmenopausal women found that having a first-degree relative with a family history of cancer

(AOR = 12.6; 95% CI:5.14–30.9), generalized obesity (BMI ≥25 kg/m2) (AOR = 11.85; 95% CI:5.12–27.4), never having children (AOR = 3.84; 95% CI:1.37–10.7), age at menarche of ≤11 years (AOR = 4.07; 95% CI:1.16–14.2), age > 55 years (AOR = 4.69; 95% CI:2.16-20.25), suboptimal consumption of deep-fried food (AOR = 0.17; 95% CI:0.06–0.46), and low level household activities (AOR = 2.82; 95% CI:1.34–5.92) (30)

In a hospital-based study assessing risk factors for endometrial cancer, it was found that the following factors were associated with an increased risk: nulliparity (OR 6.23, 95% CI 2.86-13.59), null gravidity (OR 5.94, 95% CI 2.51-14.06), a positive family history of reproductive cancer (OR 4.97, 95% CI 2.33-10.59), a history of infertility (OR 2.38, 95% CI 1.32-4.31), obesity (BMI ≥25) (OR 1.71, 95% CI 1.16-2.52), early menarche age (<12 years) (OR 2.10, 95% CI 1.17-3.75), and the use of hormonal contraception (OR 1.69, 95% CI 1.15-2.49). (31).

## 2.3 Treatment outcome of endometrial cancer

A study on the clinicopathological features and survival rates of endometrial cancer found that, during a median follow-up period of 57.0 months (range 3.8–105.4 months), 1297 patients (99.69%) had definitive survival results. There were 35 (3.36%), 14 (6.17%), and 0 (0%) occurrences of recurrence and 11 (1.05%), 6 (2.64%), and 0 (0%) cases of cancer-related death in Groups A, B, and C, respectively. For groups A, B, and C, the corresponding median disease-free survival (DFS) intervals were 57.70 (range 3.8 to 105.4), 50.30 (3.8 to 93.8), and 39.40 (24.1 to 93.2) months. For groups A, B, and C, the corresponding median OS intervals were 58.40 (range 9.4 to 105.4), 50.90 (3.8 to 93.8), and 39.40 (24.1 to 93.2) months, respectively(25)..

Nine (24.3%) of the 37 patients who experienced disease recurrence had a local recurrence, 24 (64.9%) had a distant recurrence, and four (10.8%) had both a local and a distant recurrence. These findings are reported in the Clinicopathologic Features and Treatment Outcomes in Patients with Stage I, High-Risk Histology or High-Grade Endometrial Cancer after Primary Staging Surgery. In comparison to both local recurrence ($p < 0.001$) and local plus distant recurrence (Z-test, $p < 0.001$), the probability of distant recurrence was substantially higher. Following the initial staging procedure, 102 patients (38.2%) underwent observation without receiving any additional adjuvant treatment, 114 patients (42.7%) underwent radiation, and 28

patients (10.5%) underwent chemotherapy. In 23 patients (8.6%), chemotherapy and radiation were administered together. The recurrence site ($p = 0.390$) and recurrence rate ($p = 0.440$) did not differ. Additionally, there was no difference in the four patient groups' overall survival ($p = 0.621$). Nine (24.3%), 24 (64.9%), and four (10.8%) of the 37 individuals who experienced a recurrence of the disease were local recurrences, while the remaining 24 patients had distant recurrences. In comparison to both local recurrence ($p < 0.001$) and local plus distant recurrence (Z-test, $p < 0.001$), the probability of distant recurrence was substantially higher. In univariate and multivariate analyses, patients with stage IB disease were linked to a worse overall survival (149.7 months vs. 201.8 months, $p < 0.001$) as well as a higher recurrence rate (22.8% vs. 9.1%, $p = 0.003$). Patients who were over 60 years of age experienced a greater rate of recurrence (21.7% vs. 9.7%, $p = 0.008$ in univariate analysis and $p = 0.022$ in multivariate analysis) compared to those who were under 60. They also fared worse overall than the younger patients, with 102.0 months compared to 196.8 months ($p = 0.001$). Tumor recurrence and overall survival were not significantly correlated with tumor size (<2 cm vs. ≥2 cm) or the status of LVSI (positive vs. negative). (28).

Individuals with advanced stages of endometrial cancer may experience metastases outside of their uterus. The most frequent locations for endometrial carcinoma metastatic sites are retroperitoneal and pelvic lymph nodes; distant metastases, such as those to the brain, liver, and lung, are less common. Remote tumor metastasis primarily arises via hematogenous, lymphatic, and transcoelomic pathways. Moreover, localized tumor spread inside the gynecologic tract is also possible. In this investigation, the multivariate analysis revealed that tumor differentiation grading (OR 3.69, 95% CI 2.10-6.50) and myometrial invasion (OR 2.84, 95% CI 1.12-7.25) were independent risk factors for extrauterine metastases in endometrial cancer patients..(26)

## 2.4 Associated factors for clinicopathologic characterstics

In stage IA patients, comparisons between groups A and B and A and C had statistical power ($1-\beta$) of 0.8249 and 1.000 for 5-year DFS and OS, respectively, and had statistic power of 0.8698 and 1.000 for 5-year OS, according to a study on the clinicopathological features and survival outcomes of endometrial carcinoma. In the Cox regression mode, we added variables such as age, co-existing endometriosis, surgical routes, differentiation, FIGO stages, maximum tumor

diameter, LVSI status, and postoperative adjuvant therapy. The deep invasive endometriosis protein is not included in the model because it was not tested in all of the patients. In this model, all patients showed equal DFS and OS when compared to group A patients (reference); in contrast, EEC-A patients showed similar DFS but were linked to inferior OS (HR 5.033, 95% CI 1.803–14.048, p=0.002). In contrast to group A patients, EEC-AIA and EEC-A both exhibited comparable DFS and OS in this manner for stage IA patients. In the Cox model, EEC-AIA patients had similar DFS and OS in patients of all stages (both HRs were 0.000, 95% CI 0.000-not available, p=0.971 and 0.985, respectively) and in patients in stage IA (both HRs were 0.000, 95% CI 0.000-not available, p=0.989 and 0.987, respectively) when compared with EEC-A patients (reference) (25). Clinicopathological features and potential risk factors for extrauterine metastases in endometrial carcinoma revealed that tumor differentiation grading (OR: 3.69; 95% CI: 2.103–6.504) and myometrial invasion (OR: 2.84; 95% CI: 1.127-7.205) had the strongest correlations, ranging from the strongest to the weakest. There was a 20.4% chance of extrauterine metastases. In a comparison analysis, the presence of lymph node metastasis was a significant indicator for ovarian metastatic prediction. The rate of ovarian metastasis in the context of lymph node metastasis was 26.5% ($p<0.001$) (26). The question of whether the patient was taking hormone replacement therapy (HRT) at the time of the endometrial cancer diagnosis was found to have a chi square test correlation with the frequency of endometrial cancer, according to a retrospective observational study on clinicopathological characteristics and risk factors. Patients who were not taking hormone replacement therapy (HRT) prior to being diagnosed with EC had an 80% lower risk of getting endometrial cancer (CI: 0.056-0.114, p=0.016) than those who were (27)

# 3.Objective

## 3.1 General objective

To assess the Clinicopathologic characteristics, management outcome and associated factors of uterine cancer among women who were managed in Tikur Anbessa specialized Hospital; Addis Ababa Ethiopia; 2024

## 3.2 Specific objective

- To assess the clinicopathologic characteristics of uterine cancer among women managed at TASH in the last five years
- To assess the management outcome of uterine cancer among patient managed at TASH in the last five years
- To identify associated factors for treatment outcome of uterine cancer among women managed at TASH in the last five years

# 4. Methods

## 4.1 Study Area and Period

The study was done in TASH which is the teaching hospital of Addis Ababa University and the study was conducted retrospectively for five years (from Jan 1, 2015 up to Dec 30, 2019). TASH, school of medicine, college of health science, Addis Ababa University is the main referral hospital in Ethiopia which is found in Addis Ababa city. Since its founding in 1964, it has served as the primary teaching facility for the majority of specialties' preclinical and clinical training.

## 4.2 Study Design

Facility based retrospective cohort study was conducted

## 4.3 Source Population

All uterine cancer patients who were managed in TASH

## 4.4 Study Population

All patients diagnosed to have uterine cancer managed at TASH

## 4.5 Inclusion and Exclusion Criteria

### 4.5.1 Inclusion criteria

All TASH patients managed with uterine cancer within the specified time frame (2015–2019) were included.

### 4.5.2 Exclusion criteria

Patients' charts that were missed during data collection and those without a histopathology result

## 4.6 Sample Size Determination

In this study, sample size will be determined by using the single population proportion formula taking 91.7% patients had endometrioid adenocarcinoma (27), with 5% marginal error, 95% CI.

Therefore $n = \frac{Z(_{1/2})^2 P(1-P)}{d^2}$

Sample size = $(1.96)^2*0.917(1-0.917)/0.05)^2=116$

Then after adding 10% none response rate the final sample size will be 128.

## 4.8 Study Variables

### 4.8.1 Dependent Variable

- Treatment outcome of uterine cancer at last follow up

### 4.8.2 Independent Variables

- Clinicopathologic characteristics (Clinical presentation, Stage of disease ,Type of histology, Imaging finding
- Socio-demographic characteristics
  - ✓ Age, educational level, marital status
- Reproductive characteristics
  - ✓ Gravidity, parity, presence of abortion
- Age of menarche
- Health related characteristics
  - ✓ HTN, DM ,BMI, family History, Smoking

## 4.9 Operational definitions

- ***Uterine cancer***- includes endometrium, smooth muscles and mesenchymal tumor of the uterus that confirmed by histopathology and secondary tumors or both uterine and cervical but not include cervical cancer only
- **Stage at diagnosis**- stage that was documented on the chart by most senior physician
- **Treatment outcome-** The treatment/ mangment outcome of the patient were assessed until the status of the patient at last visit.
- **Status of outcome at last hospital visit :** this outcome was alive or dead
- **Survival-** calculated from confirmed diagnosis to status of outcome at last hospital visit

## 4.10 Data Collection methods

The standard questionnaires were adapted from the literature by the author. The principal investigator trained the data collector for 1 day about the questionnaires to collect the data from the chart. The patient card numbers were obtained from the regular gynecologic OPD HMIS register and oncology department HMIS register. All patient cards were collected from the card office.

## 4.11 Data Quality Control Measures

By creating a suitable data extraction tool, data quality was ensured. Expert researchers assessed the modified data extraction tool. Patients enrolling in 2015 and 2019 had a pretest on 5% of their medical records reviewed based on a confirmed diagnosis two weeks before the time when the data is actually collected. The recorded variables were checked using that action. Consequently, the data extraction technique reduced the number of unrecorded variables. Every day the filled questionnaires were checked before a chart returned to the chart office. The principal investigators controlled the data collection procedure and data collectors and a close supervision, honest communication and on spot decision in the data collection phase was implemented. Double data entry using epi data 4.2 was carried out to assure the quality.

## 4.12 Data Processing and Analysis

Collected data was checked for completeness, consistency, clarity, and missed values and was entered into SPSS version 25 for data management and further statistical analysis. The collected data analyzed for mortality, overall survival and recurrence rate in relation to option of management and associated factors. Frequency counts were performed to assess completeness of all variables. 95% confidence intervals were used to correlate the outcome variable with its independent variable. All tests were two sided and statistical significance were set at p-value < 0.05.

## 4.13 Ethical Considerations

The proposal was presented to my advisors for feedback and approval before conducting the study, then ethical approval was sought from obstetrics and gynecology research and ethical review committee and formal letter of permission was obtained from the department of obstetrics and gynecology. Permission was obtained to the outpatient department to get the patient's chart.

All information collected from the charts was used solely for the purpose of this study. No identifier such as name or mobile numbers or house number are collected other than address as AA or outside AA.

## 4.14 Dissemination plan and use of findings

The result of the study was presented to TASH, department of obstetrics and gynecology. The final report was submitted to the department of obstetrics and gynecology. Moreover, efforts

may be done to publish the findings of the study and disseminate through different journals and scientific publications.

# 5. Result

## 5.1 Socio-demographic characteristics of the study participants

In this study 128 charts were reviewed and out of this 59(46.1%) of the study participants were in the age group 51-65 years with a mean and SD of 55.5±9.3 years respectively. The majority

of them 75(58.6%) were from Addis Ababa and 93(72.7%) of them were married and 37(28.9%) of them were unable to read and write.

Table 1.Socio-demographic characteristics of the study participants among patients managed with uterine cancer in TASH; Addis Ababa, Ethiopia.

| **Variable** | Frequency | **Percent** |
|---|---|---|
| **Age in years** | | |
| 35-50 | 53 | 41.4 |
| 51-65 | 59 | 46.1 |
| >65 | 16 | 12.5 |
| **Addresses** | | |
| AA | 75 | 58.6 |
| Amhara | 7 | 5.5 |
| Harari | 4 | 3.1 |
| Oromia | 38 | 29.7 |
| SNNPR | 4 | 3.1 |
| **Residence** | | |
| AA | 75 | 58.6 |
| Out of AA | 53 | 41.4 |
| **Marital status** | | |
| Married | 93 | 72.7 |
| divorced | 13 | 10.2 |
| widowed | 22 | 17.2 |
| **Educational level** | | |
| unknown | 8 | 6.3 |
| Unable to read and write | 37 | 28.9 |
| primary | 31 | 24.2 |
| secondary | 25 | 19.5 |
| collage and above | 27 | 21.1 |

## 5.2 Endometrial cancer risk related characteristics of the study participants

Forty participants (1.7%) percent of the study participants had normal body mass index of and thirty-seven participants (28.9%) of the participants were the age of menarche at the age of 14 and 55(43%) of the participants were grand multiparous. Almost 51(39.8%) of the study participants had a history of contraceptive use for at least one year and 24(18.8%) the participants had a history of infertility. 48(37.5%) of the participants had a history of comorbid disease as shown in the table below.

Table 2.Endometrial cancer risk related characteristics of the study participants among patients managed with uterine cancer in TASH; Addis Ababa, Ethiopia.

| Variable | Frequency | Percent |
|---|---|---|
| BMI in kg/m2(n=96) | | |
| 18.5-24.9 | 40 | 41.7 |
| 25-29.9 | 35 | 36.5 |
| ≥30 | 21 | 21.9 |
| Age of menarche( n=128) | | |
| 13 | 20 | 15.6 |
| 14 | 37 | 28.9 |
| 15 | 19 | 14.8 |
| 16 | 16 | 111.7 |
| 17 | 1 | 0.8 |
| UK | 36 | 28.1 |
| Parity ( n=128) | | |
| nulliparous | 18 | 14.1 |
| primiparous | 14 | 10.9 |
| multiparous | 41 | 32.0 |
| grand multiparous | 55 | 43.0 |
| Exposure to active or passive smoking( n=128) | | |
| No | 128 | 1100 |
| Hormonal Contraception use at least for 1year ( n=128) | | |
| Yes | 51 | 39.8 |
| No | 77 | 60.2 |
| History of Reproductive Cancers ( n=128) | | |
| Yes | 2 | 1.6 |
| No | 126 | 98.4 |
| History of HRT or tamoxifen use ( n=128) | | |
| Yes | 3 | 2.3 |
| No | 125 | 97.7 |
| Family History of endometrial or other cancer ( n=128) | | |
| No | 128 | 100 |
| History of Infertility ( n=128) | | |
| Yes | 24 | 18.8 |
| No | 104 | 81.3 |
| Any comorbid disease ( n=128) | | |
| Yes | 48 | 37.5 |
| No | 80 | 62.5) |
| The list of comorbid disease (n=48) | | |
| Hypertension | 20 | 41.7 |
| DM | 16 | 33.3 |
| RVI | 10 | 20.8 |
| Asthma | 7 | 14.6 |
| DVT | 3 | 6.3) |
| Epilepsy | 3 | 6.3 |
| Stroke | 1 | 2.1 |

| | | |
|---|---|---|
| CKD | 1 | 2.1 |

## 5.3 Clinicopathologic characteristics of the uterine cancer

117(91.4%) of the participants were menopause and 64(50%) of the participants had presenting signs and symptoms of vaginal bleeding only and 37(28.9%) had vaginal bleeding and discharge. 53(41.4%) of the study participants had a symptom of 6-12 months duration and 19(14.8%) of the participants had ascites based on imaging.26(20.3%) of the participants had metastasis of disease on imaging and 5(19.2%) were metastasis to the peritoneum and 64(50%) of the participants had Grade III cancer.

Table 3.Clinicopathologic characteristics of the uterine cancer patients managed in TASH; Addis Ababa, Ethiopia

| **variable** | Frequency | Percent |
|---|---|---|
| **Menopause** | | |
| Yes | 117 | 91.4 |
| no | 11 | 8.6 |
| **Presenting sign and symptom** | | |
| Abdominal pain and swelling | 3 | 2.4 |
| Abdominal swelling | 1 | 0.8 |
| Vaginal bleeding | 64 | 50 |
| Vaginal bleeding and discharge | 37 | 28.9 |
| Vaginal bleeding and lower abdominal pain | 9 | 7.0 |
| Vaginal bleeding, discharge and lower abdominal pain | 12 | 9.4 |
| Vaginal discharge | 2 | 1.6 |
| **Duration of symptom** | | |
| <6 month | 52 | 40.6 |
| 6month-1years | 53 | 41.4 |
| ≥1 years | 23 | 18.0 |
| **Imaging modalities for diagnosis** | | |
| US | 13 | 10.2 |
| CT | 2 | 1.6 |
| MRI | 1 | 0.8 |
| US, CT, MRI | 2 | 1.6 |
| US &CT | 94 | 73.4 |
| US & MRI | 16 | 112.5 |
| **Ascites on imaging** | | |
| Yes | 19 | 14.8 |
| No | 109 | 85.2 |

| | | |
|---|---|---|
| **Metastasis based on imaging** | | |
| Yes | 26 | 20.3 |
| no | 102 | 79.7 |
| **Area of metastasis based on imaging (n=26)** | | |
| Abdominal wall and momentum | 1 | 3.8) |
| Adnexa | 3 | 11.5 |
| Bladder wall | 3 | 11.5 |
| Bladder wall, Inguinal LAP | 1 | 3.8 |
| Cervix | 3 | 11.5 |
| Cul-de-sac, peritoneum | 1 | 3.8 |
| Liver | 3 | 11.5 |
| Lung | 1 | 3.8 |
| Lymph node | 1 | 3.8 |
| Peritoneum | 5 | 19.2 |
| Rectum and pelvic lymph node | 1 | 3.8 |
| Vaginal wall | 3 | 11.5 |
| **FIGO grade based on endometrial biopsy (n=118)** | | |
| I | 35 | 29.7 |
| II | 24 | 20.3 |
| III | 59 | 50 |

## 5.4 The relationship between type of uterine cancer and area metastasis among patients managed in TASH

| Types uterine cancer Vs area of metastasis | | | |
|---|---|---|---|
| Types uterine cancer and histologic type of uterine cancer diagnosis | Area of metastasis | | Total |
| | Local | distal | |
| Endometroid adenocarcinoma | 12 | 5 | 17 |
| Clear cell carcinoma | 1 | 0 | 1 |
| Carcinosarcoma | 1 | 0 | 1 |
| Clear cell adenocarcinoma | 0 | 1 | 1 |
| Leiomyosarcoma | 1 | 2 | 3 |
| Serous adenocarcinoma | 0 | 2 | 2 |
| Aden squamous carcinoma | 0 | 1 | 1 |
| Total | 15 | 11 | 26 |

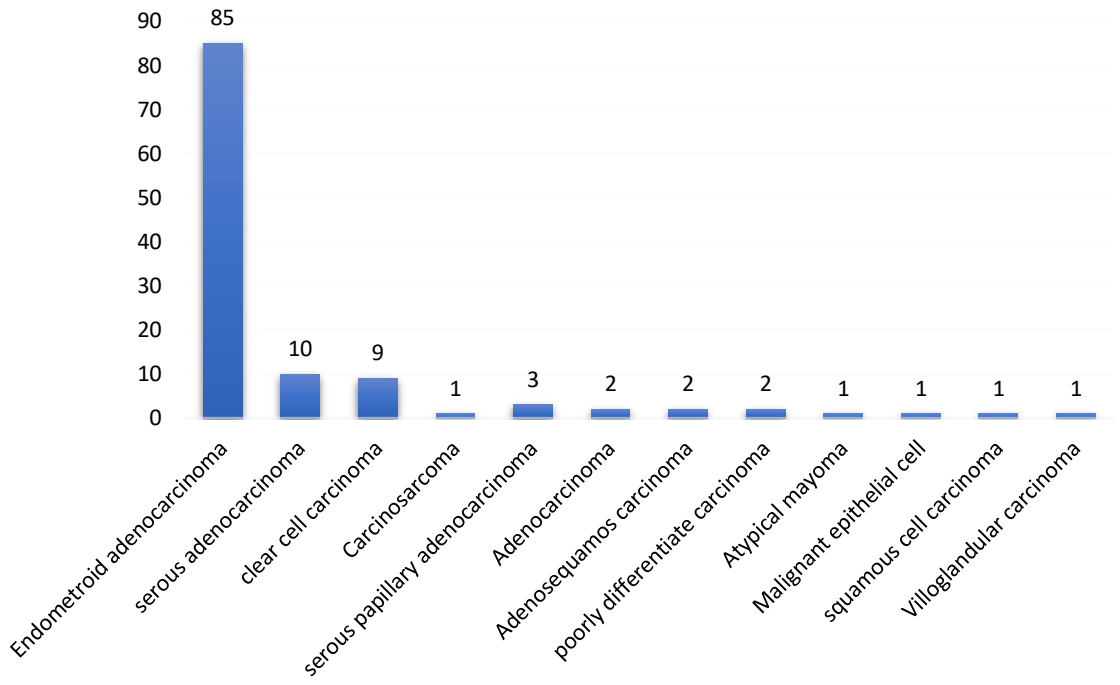



Figure 1.Types of tumors based on endometrial biopsy among patients managed with uterine cancer in TASH; Addis Ababa, Ethiopia

## 5.5 Histopathology results related characteristics of the study participants

Fifty-two participants (69.3%) of the participants had >2cm of tumor size. 69(65.1%) participants had myometrium involvement and 67(52.3%) of the Participants were FIGO stage I. 19(14.8%) of the participants had lympho-vascular invasion and 13(7.8%) had cervical stromal involvement. 4(3.5%) of the study participants had peritoneal involvement and 10 (7.8%) the cancer had distant metastasis.

Table 4. Histopathology results related characteristics of the study participants among patients managed with uterine cancer

| Variable | category | frequancy | percent |
|---|---|---|---|
| Tumor size(n=75) | ≤2cm | 23 | 30.7 |
| | >2cm | 52 | 69.3 |
| Macroscopic involvement (n=114) | Myometrium | 86 | 75.4 |
| | cervix | 7 | 6.1 |
| | parametrium | 2 | 1.8 |
| | serosa | 19 | 16.7 |
| FIGO grade (n=122) | 1 | 33 | 29.5 |
| | 2 | 33 | 20.5 |
| | 3 | 56 | 50 |
| Myometrial | <50% | 37 | 34.9 |

| | | | |
|---|---|---|---|
| invasion (n=106) | >50% | 69 | 65.1 |
| Lympho-vascular invasion | Not assessed | 59 | 46.1 |
| | Not involved | 50 | 39.1 |
| | involved | 19 | 14.8 |
| Cervical stroma | not assessed | 34 | 26.6 |
| | not involved | 81 | 63.3 |
| | involved | 13 | 10.1 |
| Vagina | Not assessed | 42 | 32.8 |
| | Not involved | 86 | 67.2 |
| Adnexa | not assessed | 38 | 29.7 |
| | not involved | 86 | 67.2 |
| | involved | 4 | 3.1 |
| Uterine serosa | not assessed | 33 | 25.8 |
| | not involved | 75 | 58.6 |
| | involved | 20 | 15.6 |
| Parametrium (n=30) | not assessed | 7 | 23.3 |
| | not involved | 17 | 56.7 |
| | involved | 6 | 20 |
| Lymph node(n=103) | sampled | 86 | 76.9 |
| | not sampled | 23 | 23.1 |
| Pelvic lymph node | negative | 67 | 78.8 |
| | positive | 17 | 21.3 |
| Peritoneal involvement (n=113) | not assessed | 15 | 13.3 |
| | not involved | 94 | 83.2 |
| | involved | 4 | 3.5 |
| Distant metastasis | yes | 10 | 7.8 |
| | no | 118 | 92.2 |
| Provisional FIGO stage | I | 67 | 52.3 |
| | II | 13 | 10.2 |
| | III | 34 | 26.6 |
| | IV | 14 | 14(10.9 |

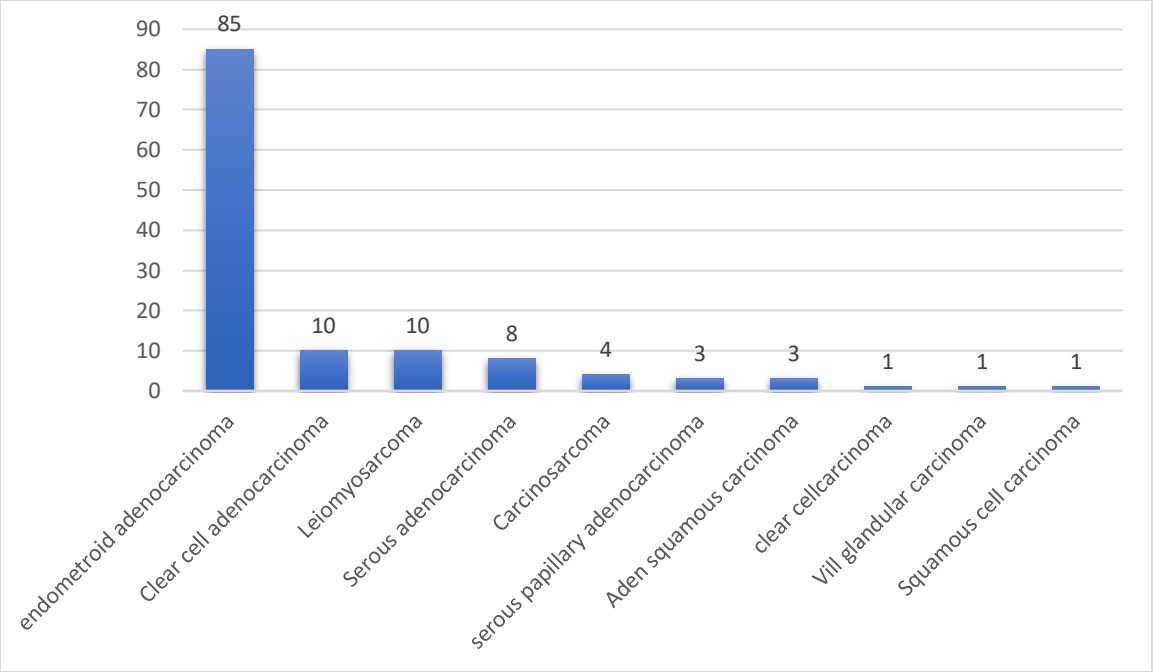



Figure 2.Types of uterine cancer based on histopathology among patients managed with uterine cancer in TASH.

## 5.6 The uterine cancer biopsy grade comparison between endometrial biopsy and final histopathology

The finding of the study showed that 103 participants had a biopsy grade in both endometrial biopsy and final histopathology. From those 98(95.1%) of the participants had similar biopsy grade results while the remaining five had different pathologic results as shown in the table below.

Table 5.The uterine cancer biopsy grade result comparison between endometrial biopsy and final histopathology among patients managed with uterine cancer

| **Tumor grade by endometrial biopsy* Tumor grade by final histopathology** | | | | | |
|---|---|---|---|---|---|
| | | Final histopathology | | | Total |
| | | I | II | III | |
| endometrial biopsy | | 0 | 0 | 9 | 9 |
| | I | 32 | 0 | 0 | 32 |
| | II | 0 | 21 | 2 | 23 |
| | III | 1 | 2 | 45 | 48 |
| Total | | 33 | 23 | 56 | 112 |

## 5.7 The relation between surgical histopathology and endometrial biopsy result

In this study 103(87.3%) of participants had similar endometrial biopsy and final histopathology result. 85(66.4%) of participants were diagnosed with endometrioid adenocarcinoma by final histopathology results. From those 92.9% (n=79) similar result with endometrial biopsy, form the remaining 6 cases, 4 of them hadn't endometrial biopsy and 2 of them had different endometrial diagnosis (1 adenocarcinoma and malignant epithelial cell) from final histopathology as shown the table below

Table 6.The relation between surgical histopathology and endometrial biopsy result among patients managed with uterine cancer in TASH

| | | Endometroid adenocarcinoma | Clear cell carcinoma | Vill glandular carcinoma | Carcinosarcoma | Clear cell adenocarcinoma | Leiomyosarcoma | Serous adenocarcinoma | Carcinosarcoma | Serous papillary adenocarcinoma | Aden squamous carcinoma | Squamous cell carcinoma | Total |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Endometrial biopsy | | 4 | 1 | 0 | 0 | 0 | 5 | 0 | 0 | 0 | 0 | 0 | 10 |
| | Adenocarcinoma | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 2 |
| | Adenosequamose carcinoma | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 2 |
| | Atypical myoma | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 1 |
| | Carcinosarcoma | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 |
| | Clear cell carcinoma | 0 | 0 | 0 | 0 | 8 | 0 | 0 | 1 | 0 | 0 | 0 | 9 |
| | Endometroid Adenocarcinoma | 79 | 0 | 0 | 1 | 0 | 3 | 0 | 2 | 0 | 0 | 0 | 85 |
| | Malignant epithelial cells | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| | Poorly differentiated carcinoma | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 2 |
| | Serous adenocarcinoma | 0 | 0 | 0 | 1 | 2 | 1 | 6 | 0 | 0 | 0 | 0 | 10 |
| | Serous papillary adenocarcinoma | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 3 | 0 | 0 | 3 |
| | Squamous cell carcinoma | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 |
| | Vill glandular carcinoma | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| Total | | 85 | 1 | 1 | 2 | 10 | 10 | 8 | 4 | 3 | 3 | 1 | 128 |

## 5.8 Treatment related characteristics of uterine cancer

All (n=128) of the participants received treatment and from those 51(39.1%) of the participants were managed with surgery and chemotherapy. Surgery was done for 111(86.7%) and all the procedures were laparotomy. 64(57.7%) of the surgical patients received postoperative therapy and from those 60(93.7%) were received chemotherapy. 77(60.2%) percent of the study participants received chemotherapy and from those 62(80.5%) of them received adjuvant therapy and 70(90.9%) of them received a regimen of Paclitaxel and carboplatin. 53(68.8%) of the participants received cycle 6 chemotherapy and 48(62.3% had improvement after treatment.

Table 7.Treatment related characteristics of the study participants among patients managed with uterine cancer in TASH; Addis Ababa, Ethiopia

| variable | category | Frequency | *percent* |
|---|---|---|---|
| Treatment given | Yes | 128 | 100 |
| Types of treatment (n=128) | Surgery | 47 | 36.7 |
| | Chemotherapy | 15 | 11.7 |
| | Surgery and chemotherapy | 51 | 39.8 |
| | Surgery, chemotherapy, radiotherapy | 9 | 7.0 |
| | Surgery and radiotherapy | 4 | 3.2 |
| | Chemotherapy and radiotherapy | 2 | 2(1.6 |
| Hormonal therapy (n=125) | Yes | | |
| | no | 125 | 100 |
| Surgery done | Yes | 111 | 86.7 |
| | no | 17 | 13.3 |
| Route of surgery | laparotomy | 111 | 100 |
| Types of surgery (n=111) | Staging | 78 | 70.3 |
| | TAH+BSO | 14 | 12.6 |
| | Unknown (surgery done other facility) | 19 | 17.1 |
| Post-operative therapy given (n=111) | Yes | 64 | 57.7 |
| | no | 47 | 42.3 |
| Types of post-operative therapy (n=64) | Chemotherapy | 52 | 81.3 |
| | chemo and radiotherapy | 8 | 12.5 |
| | Radiotherapy | 4 | 6.3 |
| Chemotherapy given | Yes | 77 | 60.2 |
| | no | 51 | 39.8 |
| Types of chemotherapy | Adjuvant | 62 | 80. |

| | | | |
|---|---|---|---|
| | Neoadjuvant | 7 | 10.4 |
| | Palliative | 8 | 9.5 |
| chemotherapy regimen (n=77 | Doxorubicin and Adriamycin | 1 | 1.3 |
| | Doxorubicin | 3 | 3.9 |
| | Doxorubicin and Ifosfamoid | 3 | 3.9 |
| | Paclitaxel and carboplatin | 70 | 90.9 |
| Number of cycles | 1 | 4 | 5.2 |
| | 2 | 1 | 1.3 |
| | 3 | 9 | 11.7 |
| | 4 | 9 | 11. |
| | 5 | 1 | 1.3 |
| | 6 | 53 | 68.8 |
| Chemotherapy discontinued | Yes | 24 | 31.2 |
| | no | 53 | 68.8 |
| Reason for discontinuation | Death | 15 | 62.5 |
| | Unknown | 9 | 37.5 |
| Radiotherapy given | Yes | 15 | 11.7 |
| | no | 113 | 88.3 |
| Time from diagnosis of uterine cancer to initiation of treatment in month | <=3 month | 59 | 47.2 |
| | >3 month | 66 | 52.8 |

### 5.9 Site and treatment modality of reccurent uterine cancer patient at last visit

In this study 33(25.8%) of the study participants had recurrence after treatment and from those having recurrence 24(72.7%) recurrent into the vaginal cuff. From those having recurrence, 32(96.9%) received treatment and 22(68.8%) received chemotherapy.

*Table 8. Site and treatment modality of reccurent uterine cancer patient who were managed in TASH*

| Variable | Category | frequancy | Percent |
|---|---|---|---|
| Recurrence after treatment | Yes | 33 | 25.8 |
| | no | 95 | 74.2 |
| Recurrence sites (n=33) | Abdominal wall | 2 | 6.1 |
| | Abdominal wall, peritoneum, vaginal cuff | 2 | 6.1 |
| | Para aortic LN, Peritoneum | 2 | 6.1 |
| | Pelvis | 2 | 6.1 |
| | Peritoneum liver, kidney | 1 | 1(3 |
| | Rectum, bladder, vulva | 2 | 6.1 |
| | Vaginal cuff | 7 | 21.2 |

| | | | |
|---|---|---|---|
| | Vaginal cuff, peritoneum | 2 | 6.1 |
| | Vaginal cuff and lung | 4 | 12. |
| | Vaginal cuff, liver | 2 | 6.1 |
| | Vaginal cuff, pancreas, lung, Rt iliac LN | 1 | 3 |
| | Vaginal cuff, pelvis, lung | 4 | 12.1 |
| | Vaginal vault | 2 | 6.1 |
| Recurrence treatment | Yes | 32 | 96.9 |
| | no | 1 | 0.1 |
| Treatment recurrent disease (n=32) | Chemotherapy | 22 | 68.8 |
| | Chemotherapy and radiotherapy | 2 | 6.3 |
| | Radiotherapy | 4 | 12.4 |
| | surgery | 3 | 9.4 |
| | surgery and chemotherapy | 1 | 3.1 |
| Post treatment Surveillance for the first 2 years(n=128) | no surveillance | 35 | 27.3 |
| | Surveillance | 90 | 72. |

## 5.10Treatment outcome of uterine cancer patients at last hospital follow up

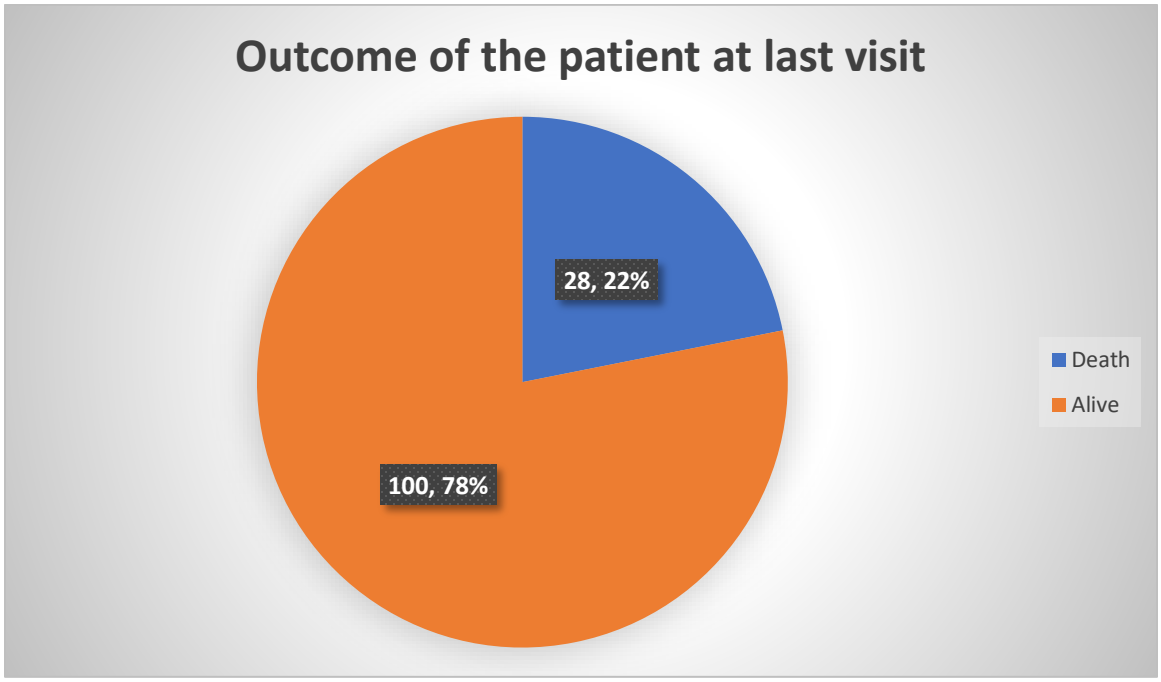


Figure 3.The status of the patients at last hospital follow up who were managed with uterine cancer in TASH; Addis Ababa, Ethiopia.

## 5.9 The relation between surveillance with recurrence

In this study 35 cases had no surveillance, from those 9-case had recurrence and 26 case had non-recurrence. On the other hand, 93 cases had surveillance, from those having surveillance, 27 cases had recurrence and 66 cases had non-recurrence.

Table 9.The relation between surveillance with recurrence and mortality among patients managed with uterine cancer in TASH

| **Recurrence * Post treatment Surveillance for the first 2 years** | | | |
|---|---|---|---|
| Post treatment Surveillance for the first 2 years | | | Total |
| no surveillance | Recurrence | yes | 9 |
| | | no | 26 |
| | Total | | 35 |
| surveillance | Recurrence | yes | 27 |
| | | no | 66 |
| | Total | | 93 |
| Total | Recurrence | yes | 33 |
| | | no | 92 |
| | Total | | 125 |

## 5.10 The determinant factor of patient status at last follow up

Body mass index, ascities, metastasis and provisional FIGO were an association with death of the patient at last visit by bivariate logistic regression. The multivariate logistic regression revealed that study participant whose age of >60 years had 1.3 times incease its death compared to those of age 35-50 years (AOR=1.3, 95%CI=1.11, 16.37) and study participant having metastasis were 3.1 times increase its death compared to its counterpart (AOR=3.1, 95%CI=1.21, 7.69). Study participants whose tumor size of >2cm were 1.4times increase its death compared to tumore size of <2cm (AOR=1.4, 95%CI=1.18, 10.33). Study participant whose provisional FIGO stage IV were 16.3times increase its death compared to provisional FIGO stage I (AOR=16.3, 95%CI=1.23, 32.45).

Table 10.The bivariable and multivariable logistic regression analysis association between independte and dependet variable of uterine cancer patients managed with uterine cancer in TASH; Addis Ababa, Ethiopia.

| Variable | Status of the patient at last hospital follow up | | p-value | CORwith 95%CI | p-value | AOR with 95%CI |
|---|---|---|---|---|---|---|
| | died | alive | | | | |
| Age in years | | | | | | |
| 35-50 | 3 | 25 | 1 | | 1 | |
| 51-65 | 17 | 46 | 0.095 | 3.1(0.82, 11.53) | 0.403 | 2.5(0.29, 22.13) |
| >60 | 8 | 29 | 0.254 | 2.3(0.55, 9.61) | 0.033 | **1.3(1.11, 16.37)** |
| BMI | | | | | | |
| 18-5-24.9 | 5 | 35 | 1 | | 1 | |
| 25-29.9 | 10 | 25 | 0.040 | **2.8(1.85, 9.20)** | 0.116 | 16.6(1.67, 64.79) |
| ≥30 | 5 | 16 | 0.264 | 2.2(0.55, 8.64) | 0.832 | 1.5(0.04, 54.72) |
| Ascities | | | | | | |
| Yes | 7 | 12 | 0.044 | **2.4(1.86, 6.96)** | 0.603 | 3.1(0.04, 21.27) |
| No | 21 | 88 | 1 | | 1 | |
| Metastasis | | | | | | |
| Yes | 9 | 17 | 0.043 | **2.3(1.89, 5.98)** | 0.010 | **3.1(1.21, 7.69)** |
| no | 19 | 83 | 1 | | 1 | |
| Tumor size | | | | | | |
| ≤2cm | 4 | 19 | 1 | | 1 | |
| >2cm | 15 | 37 | 0.118 | 1.9(0.56, 6.61) | 0.045 | **1.4(1.18, 10.33)** |
| Provisional FIGO | | | | | | |
| I | 10 | 57 | 1 | | 1 | |
| II | 4 | 10 | 0.228 | 2.3(0.59, 8.71) | 0.264 | 6.3(0.25, 57.69) |
| III | 4 | 29 | 0.704 | 0.79(0.23, 2.72) | 0.127 | 0.05(0.01, 2.37) |
| IV | 10 | 4 | 0.000 | **14.3(3.73, 54.43)** | 0.000 | **16.3(1.23, 32.45)** |

## 5.12 Survival analysis

### 5.12.1 Survival analysis by Life time table

Finding of the study showed that the median survival time of survival were 40.97 month. The life time tables were arranged by the interval of 6 months. The table showed that 5% (n=6) of the participants died in the first six months. From 128 participants and 121 were censored. During the first 6 months of assessment from 128 participants 14 patients were withdrawn, 28(22%) participants died and 100 (78%) participants were censored/ alive in the last clinical follow up as shown in the table below.

*Table 11.The life time table of the study participants among patients managed with uterine cancer in TASH*

| Interval Start Time | Number Entering Interval | Number Withdrawing during Interval | Number Exposed to Risk | Number of Terminal Events | Proportion Terminating | Proportion Surviving |
|---|---|---|---|---|---|---|
| 0 | 128 | 3 | 126.5 | 4 | .03 | .97 |
| 6 | 121 | 11 | 115.5 | 6 | .05 | .95 |
| 12 | 104 | 15 | 96.5 | 5 | .05 | .95 |
| 18 | 84 | 15 | 76.5 | 0 | .00 | 1.00 |
| 24 | 69 | 23 | 57.5 | 5 | .09 | .91 |
| 30 | 41 | 22 | 30 | 3 | .10 | .90 |
| 36 | 16 | 10 | 11 | 4 | .36 | .64 |
| 42 | 2 | 1 | 1.5 | 1 | .67 | .33 |
| a. The median survival time is 40.97 | | | | | | |

### 5.12.2 Survival analysis by Kaplan Meir curve

The K-C showed that as the date of diagnosis increases its survival decreases. during the month 40 the survival rate was around 45%.

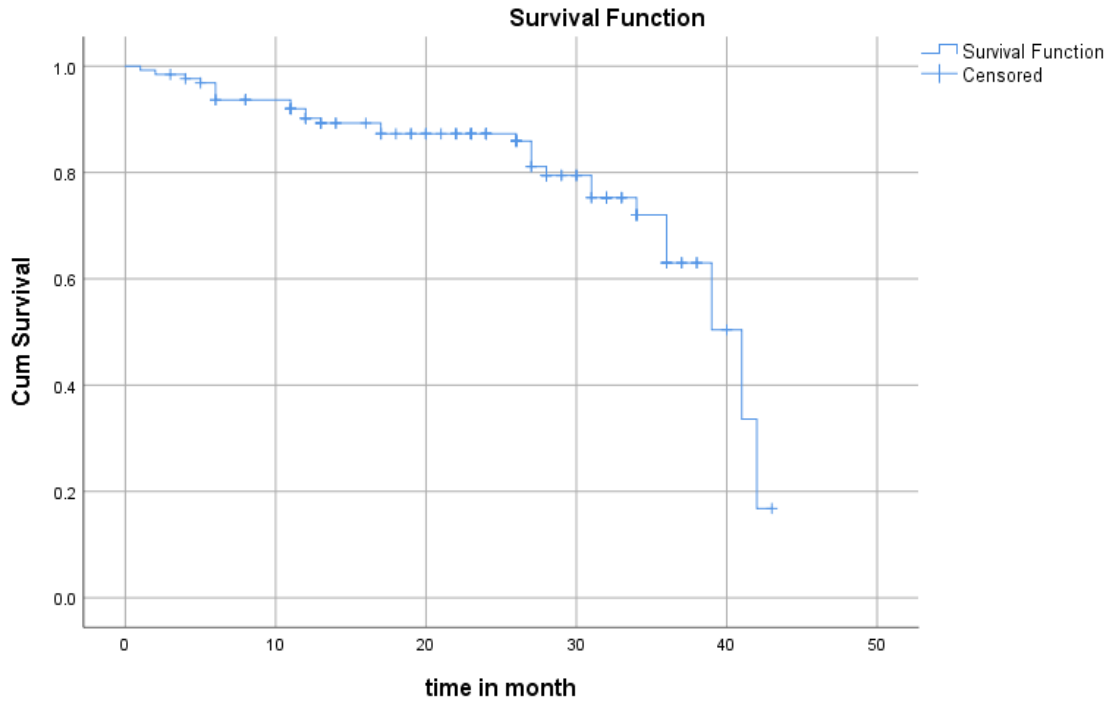
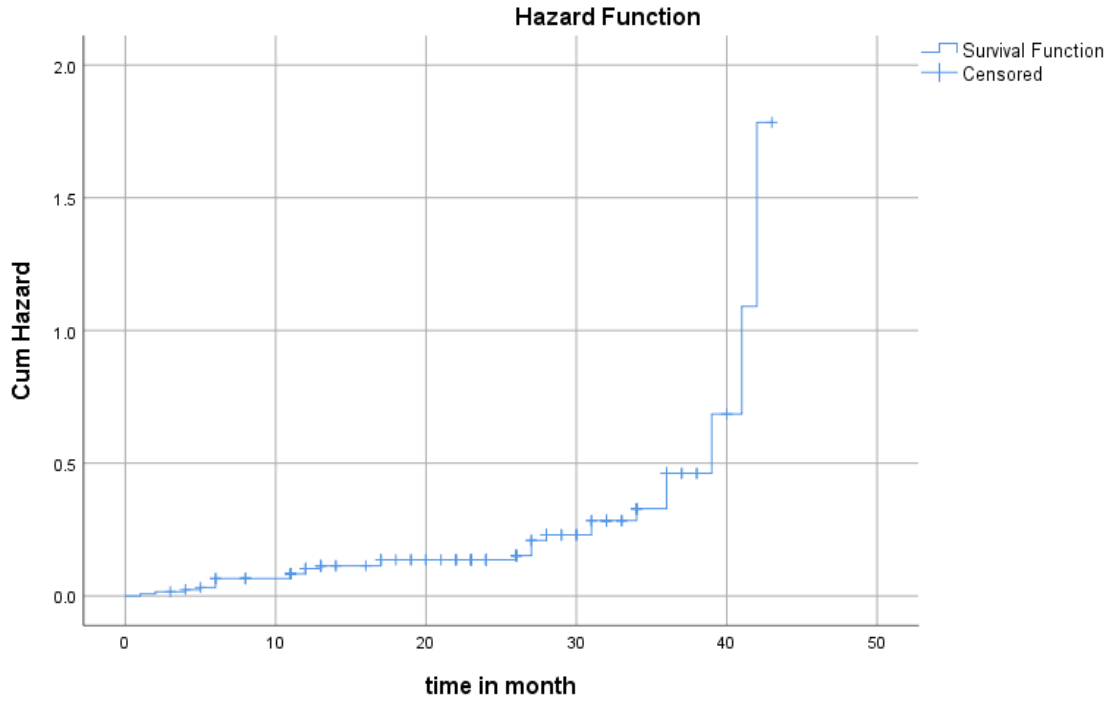
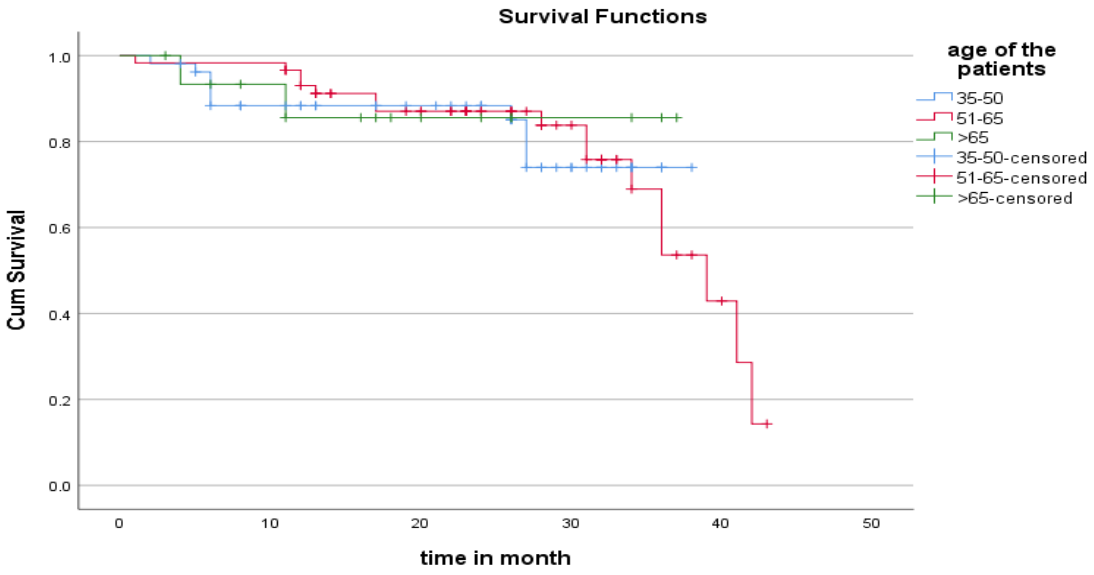


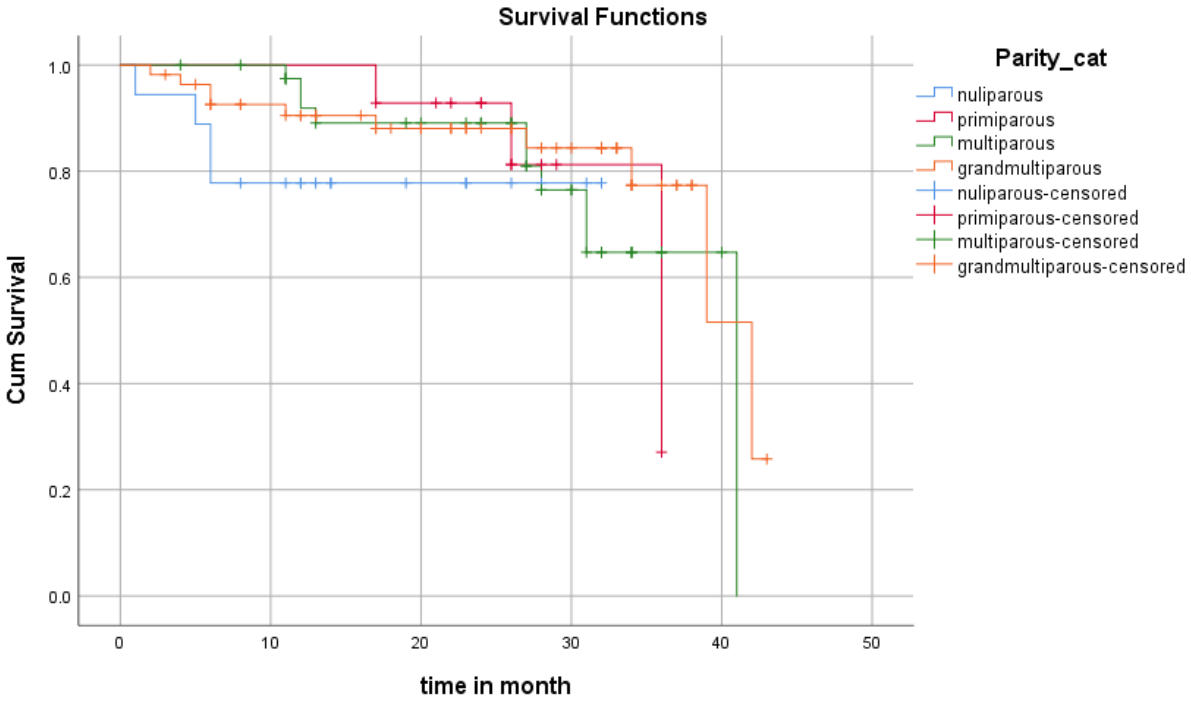

*Figure 3.The Kaplan-Meier survival curves compare survival time of uterine cancer patients with date of diagnosis in TASH , Addis Ababa ,Ethiopia*



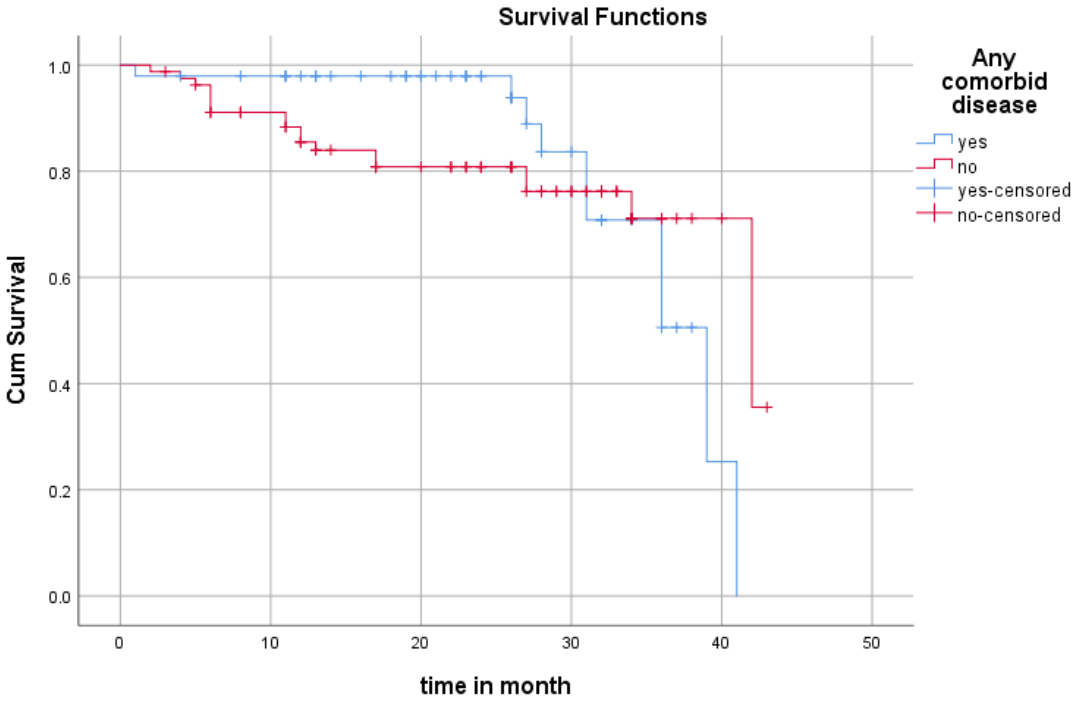
Kaplan Meir curve regarding to age of the study participants



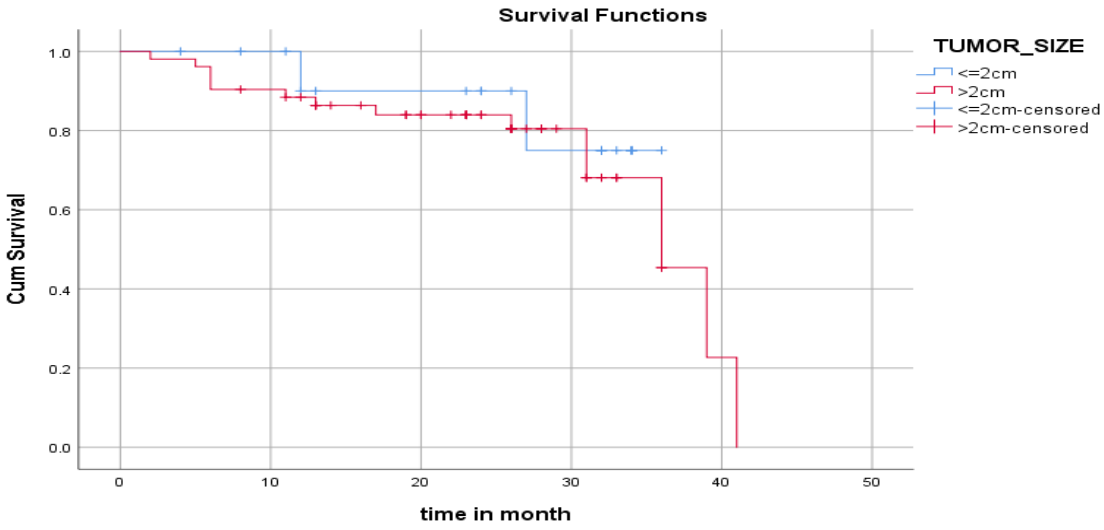

Kaplan Meir curve regarding to parity of the study participants



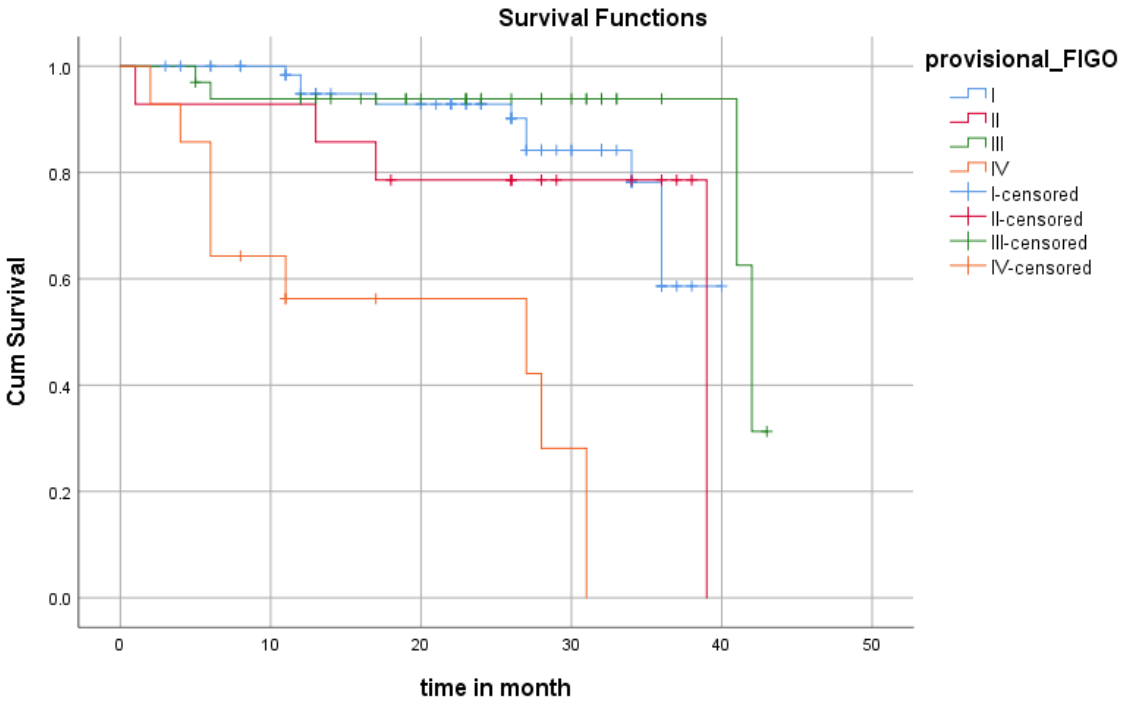

The Kaplan-Meier survival curves compare survival time of uterine cancer patients with comorbid disease in TASH



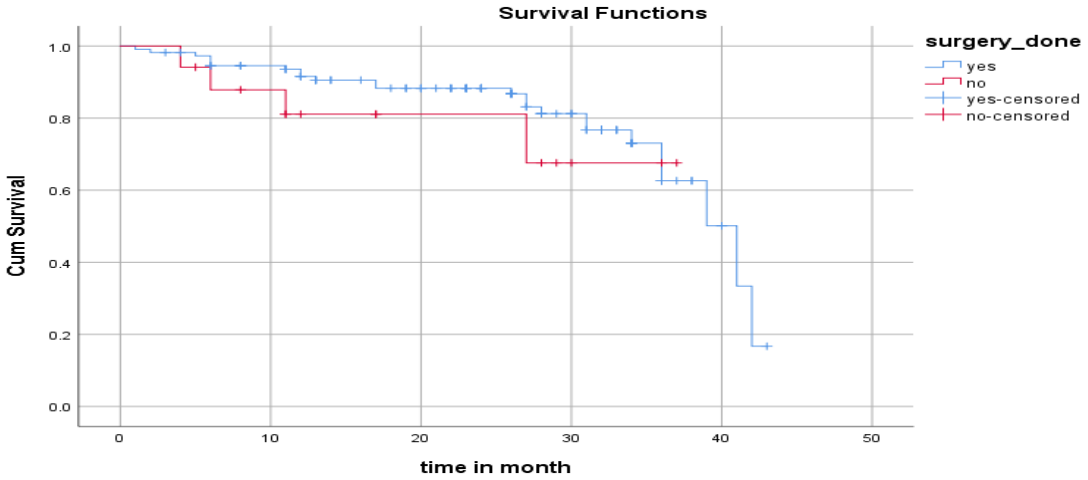

Kaplan Meir curve regarding to tumor size



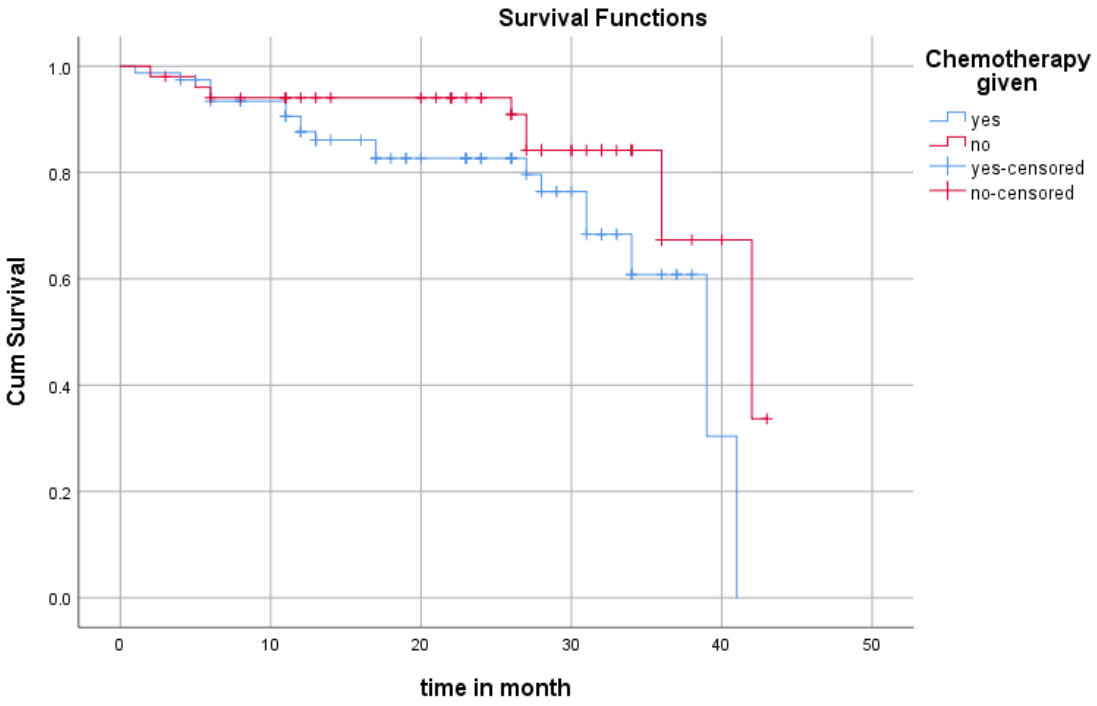

The Kaplan-Meier survival curves compare survival time of uterine cancer patients with stage of the disease in TASH



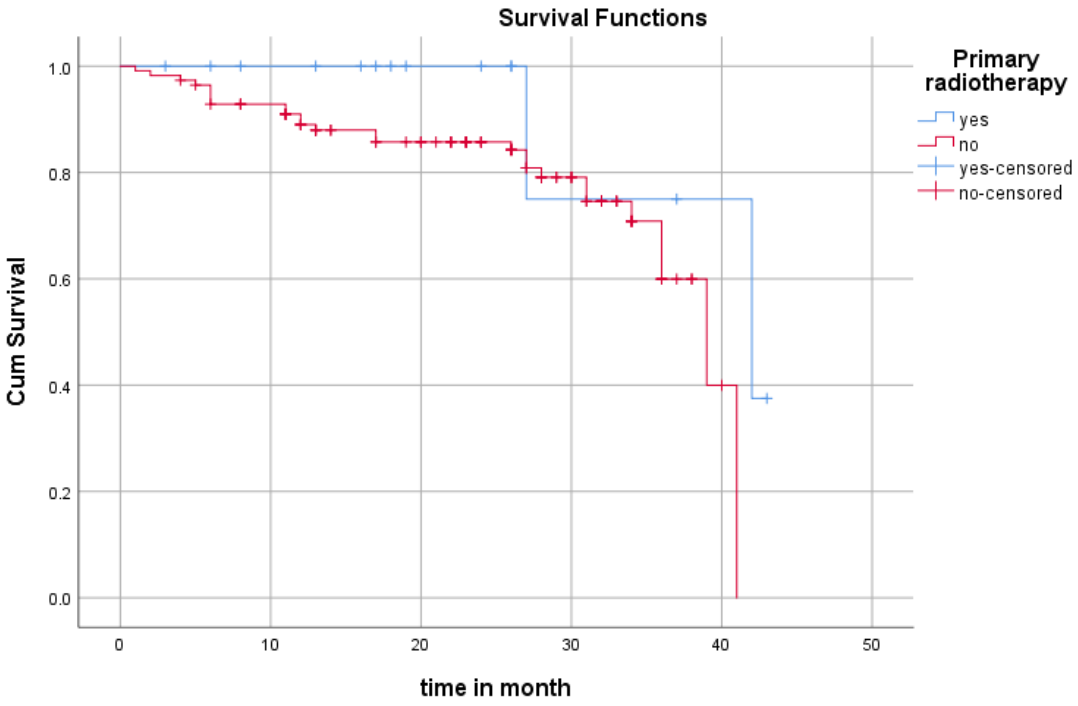

The Kaplan-Meier survival curves compare survival time of uterine cancer patients with surgery in TASH



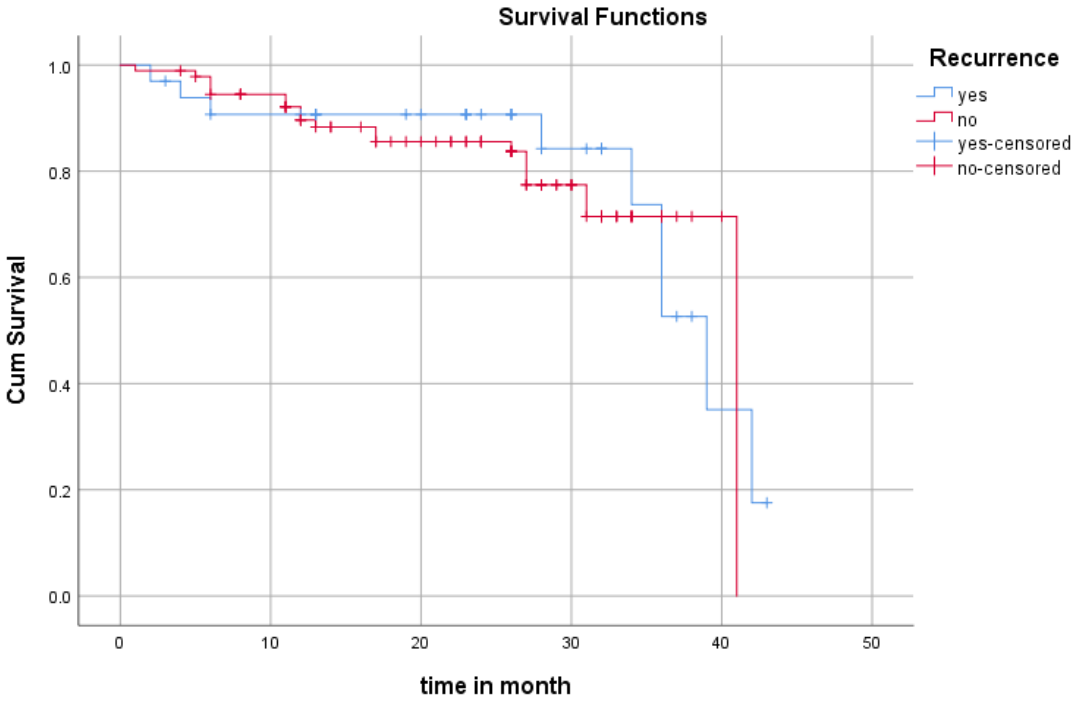

Kaplan Meir curve with regarding to chemotherapy management




The Kaplan-Meier survival curves compare survival time of uterine cancer patients managed with primary radiotherapy




K-M-C compare survival time of uterine cancer patients recurrency after treatment


Survival Functions
Recurrence
yes
no
yes-censored
no-censored
Cum Survival
1.0
0.8
0.6
0.4
0.2
0.0
0
10
20
30
40
50
time in month

## 6. Discussion

The aim of this retrospective follow-up study was to evaluate clinicopathologic characterstics and management outcome of patients at last follow up with proven uterine cancer treated at TASH.

The finding of the study revealed that 87.5 % of the uterine cancers were endometrial cancer and 12.5% of the cancer was smooth muscle and mesenchymal cancer. This finding was different from the study done in Pakistan in terms of proportional occurrence (27). This may be due to difference in genetic, age and lifestyle of the participants, difference in risk factor and clinical Presentation and Symptom.

Among 128 cancer cases 20.3% were metastasized from those endometroid adenocarcinoma accounts 17(65.3%) followed by leiomyosarcoma 3(11.5%). From the metastasized area peritoneum accounts 19.2% followed by bladder wall (11.5%), cervix (11.5%) and liver (11.5%). This finding was different with the study done by Iskandar, T.M et al by areas of metastasis and the most common site was ovary (26). This may be due to advanced-stage at diagnosis and high-grade endometrial cancers types

The finding also showed that, from 33 of having reccurence , 57.6% (n=19) were reccurence to distant and local areas, 33.3% (n=11) had local reccurence and 10.1(n=3) had distant reccurence. This finding was different from the study in China in which the majority of their findings was distant reccurence (28). This difference may be due to differences in patient age, genetic background, and overall health can status. Different populations might have different genetic susceptibilities or lifestyle factors influencing cancer recurrence. The histological subtype, grade, and molecular profile of the tumor can influence cancer recurrence. The initial stage of cancer at diagnosis plays a critical role in recurrence. Differences in treatment protocols, including the type and extent of surgery, chemotherapy, radiation therapy, and hormone therapy, can impact where and how cancer recurs. Other possible explanation for this difference may be due to study period and detection capability.

Study participant whose age of >60 years had 1.3 times incease its death compared to those of age 35-50 years (AOR=1.3, 95%CI=1.11, 16.37). This finding was supported by the study done in China (28).This may be due to older women being more likely to be diagnosed at a later stage of the disease. This can be due to a variety of factors, including delayed presentation of

symptoms, less frequent use of gynecological services, and potentially less diagnostic follow-up in older populations. On the other hand, older patients are more likely to have multiple comorbid conditions such as hypertension, diabetes, cardiovascular disease, and obesity. The immune system weakens with age, reducing the body's ability to fight cancer cells effectively.

Study participant study participant having metastasis were 3.1 times increase its death compared to its counterpart (AOR=3.1, 95%CI=1.21, 7.69)and Study participant whose provisional FIGO stage IV were 16.3times increase its death compared to provisional FIGO stage I (AOR=16.3, 95%CI=1.23, 32.45). This finding was in line with the study done malasia,Iskendar(26). This was may be due to asctes may show extrauterine metastasis and higher stage of tumor. In addition acites may related to aggressive histologic types that have poorer outcome

On therhand, Study participants whose tumor size of >2cm were 1.4times increase its death compared to tumore size of <2cm (AOR=1.4, 95%CI=1.18, 10.33). This finding was in line with the study done in USA(36). This may be due to larger tumors often indicating more advanced disease, which may have spread beyond the uterus to other parts of the body. This can complicate treatment and reduce survival rates. On the other hand, it may be due to larger tumors that can be more difficult to remove surgically and may require more extensive surgical procedures. This can increase the risk of complications and may not completely eliminate the cancer, leading to recurrence. How ever, this finding was different from study done in China(28). This may be due to small sample size, different methodologies and different patient characterstics

The finding of the study also revealed that the 44month clinical follow up survival of endometrial cancer was 40.78%. And that survival related to its stage grading were 79%, 40%, 39% and 30% on stage I, II, III, and IV respectively. This finding was lower in five-year survival rate compared to the study done in China (25). This difference may be due to variations in the characteristics of patient populations, including age, race, comorbidities, and genetic factors, which can influence survival rates. Some populations may have higher or lower incidences of aggressive cancer subtypes, which can impact outcomes. Different studies may use varying criteria or staging systems to classify endometrial cancer stages. Difference in treatment approaches; including the types of surgery, use of radiation therapy, chemotherapy regimens, and hormonal treatments. Difference in the quality of follow-up can influence reported survival

rates. Differences in study design, sample size, statistical methods, and adjustment for confounding factors can result in varying survival rates.

## 7. Limitation of the study

Selection bias may have been introduced during the secondary data collection process since patients with incomplete records were not included, potentially leading to an under- or overestimation of the rate of death.

Due to the study doesnot include on the last outcome of the patient the finding may not indicate the final outcome of the patient

Several major indicators, including biological biomarkers, treatment adherence, physical exercise, and multidisciplinary care, were overlooked in the secondary source data collection process, despite their potential to significantly predict the death of uterine cancer

## 7. Conclusion

The study found that great majority (87.5%) of uterine cancer cases were endometrial cancer, and the rest is smooth muscle and mesenchymal cancer. The average age at diagnosis was 56 and 54 respectively. Metastasis occurred in 20.3% of cases, predominantly in the peritoneum (19.2%). Recurrent metastases were observed in 33 patients, with 57.6% having both distant and local metastases. During the final follow up from 128 cancer cases 22% were were died. The determinant factor of patient death at last hospital follow up outcome were age of >60 years (AOR=1.3, 95%CI=1.11, 16.37), having metastasis (AOR=3.1, 95%CI=1.21, 7.69), tumor size of >2cm (AOR=1.4, 95%CI=1.18, 10.33) and provisional FIGO stage IV (AOR=16.3, 95%CI=1.23, 32.45).

## 8. Recommendations

According to the study finding, the following recommendations could be forwarded to:

- Better if FMOH work with public media to raise awareness about the importance of early identification and treatment for uterine cancer
- The pathology department should report the biopsy finding of all specimen components
- Additional prospective follow-up research could be carried out by incorporating significant mortality predictors such as financial difficulties, laboratory results, and factors connected to society and the healthcare system.
- Further investigation is needed by interested researchers to address the final outcome of patients

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## Annexes

**Questionnaire**

**Part I. Socio-demographic characteristics**

1. Age the study participants during diagnosis in years_____
2. Address_____
3. Marital status: Single……..Married……..Divorced …….Widowed……...
4. Educational level_____

**Part II**: **Characteristics of Endometrial cancer risk factor**

5. BMI(kg/m2)_____Menarche Age(years)_____Parity_____Age at menopause_____
6. Generalized Obesity: Obese…….. Non-obese……..
7. Central Obesity: Centrally obese…… Normal…….
8. Exposure to active or passive smoking : Yes…… No……..
9. Hormonal Contraception use at least for 1 year: Yes…….. No……..
10. History of Reproductive Cancers: Yes…… No……..
11. History of HRT or tamoxifen use: Yes…… No…….. If yes specify _____
12. Family History of endometrial or other cancer: Yes…… No……..
13. History of Infertility: Yes…… No……..
14. Any comorbid disease: Yes…… No…….. If yes specify_____

**Part III. Clinicopathology characteristics of the uterine cancer**

15. Menopause : Yes… No.
16. Presenting sign and symptom: ……
17. Endometrial thickness (mm) : TVU……..TAU_____
18. Diagnostic modalities used and (finding):
    I. Ultrasound (finding, diagnosis, stage)……..

II. CT(finding, diagnosis, stage )……..

III. MRI(finding, diagnosis, stage)……..

19. Ascites: Yes clinical……..… imaging…….. No…….

20. Is there metastasis: Yes…….No…….. If yes where_____

21. Endometrial biopsy result if done……..not done……..

I: Typeofsample: Pipelle……. Currettings ……Other specify……..

II: Tumour type:……..

III: FIGO grade:……

## II: Final histopathology result

22. Specimencomponents

I:Adnexa

II:Vaginalcuff

III:Parametrium

IV:Omentum

V:Lymphnodes:pelvic

VI:Lymphnodes:para-aortic

VII: Other specify…….

23. Maximum diameter of the tumor size (mm)_____

24. Macroscopicinvolvement

I.Myometrium

II.Cervix

III.Serosa

IV.Parametrium

25. FIGO grade ……..

26. Myometrial Invasion

I. <50%

II. >50%

27. Lymphovascular invasion: present……..Not identified……

28. Microscopic involvement

I: Cervical stroma: Involved…… Not involved…… Not assessed…….

II: Vagina: Involved…… Not involved…… Not assessed…….

III: Adnexa: Involved…… Not involved…… Not assessed…….

IV: Uterine serosa : Involved…… Not involved…… Not assessed…….

V: Parametrium : Involved…… Not involved…… Not assessed…….

29. If adnexa is involved, is this considered to beaseparate primaryneoplasm: Yes….No...Uncertain……..

30. Lymph node : Sampled……..Not sampled…….If sampled

I: Right pelvic lymph node: Total number……..Positive LN number……

II: Left pelvic lymph node: Total number……..Positive LN number……

III: Para-aortic lymph node: Total number……..Positive LN number……

31. Peritoneal involvement: Involved……Not involved…… Not assessed…….

32. Distant metastasis: Yes……..No……If yes specify……..

33. Provisional FIGO Stages ……

34. Types uterine cancer and histologic type of uterine cancer diagnosed…….

35. Date of provisional histological diagnosis……

**Part III. Management of uterine cancer**

36. Is treatment given: Yes…… No…….If yes specify……

37. Date of treatment started……

38. Hormonal therapy: yes……..No……..If yes specify_____

39. Date of surgery…….

40. Surgical routes: Laparoscopy …… Laparotomy ……Vaginal……..

41. Surgical procedures

I: Hysterectomy (Total, subtotal, radical)…….

II: Additional surgery ( uni/bilateral SO, salpingectomy, omentectomy)……

III: Staging surgeries : sampling, cytology……..

IV: Pelvic Lymphadenectomy/sampling……..

V: Paraaortic lymphadenectomy /sampling…….

42. Post operative therapy given: yes……No…….If yes specify……...

43. Chemotherapy given: yes……..No……..If yes

I: chemotherapy started date…….

II: Type of chemotherapy……

III: chemotherapy regimen……..

IV: Number of cycles…….

V: Chemotherapy stop date…….

44. Clinical response after chemotherapy……..

45. Chemotherapy Discontinued? Yes……. No…….. If yes, specify reason…….

46. Tumor diameter after chemotherapy: Increased……Decreased……..The same……

47. Primary radiotherapy: Yes……No……..If yes specify_____

48. Date of diagnosis of uterine cancer……..

49.Time from diagnosis of uterine cancer and initiation of treatment----------

50. if treatment is not initiated immediately ;specify the reason……

**Part IV. Characteristics of treatment outcome**

51.Recurrence: Yes……No……..

52.Recurrent sites……

53.Mortality: Yes……No……

54.Mortality due to cancer :Yes……..No…….

55.If cancer related death, death time after initiation of treatment_____

56.Treatment of recurrent disease

I. surgery

II. Chemotherapy

III.Radiotherapy

IV.Combination

57. . Post treatment Surveillance for the first 2 years

I. No surveillance
II. Every 3 month
III. Every 6 month
IV. Every year

58. Date of last follow up……..

59. Status at last follow up…….