



Retrospective analysis and treatment outcomes in patients of endometrial carcinoma: A single institutional study of Uttarakhand.

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ABSTRACT **Purpose:** The present study attempts to find out the factors that play a role in prognosis and survival of endometrial cancer amongst patients who have been treated at our institute.

Materials and methods: All patients of endometrial carcinoma who were registered in our centre from 2009 to 2015 were included in this analysis. The results were statistically analysed with SPSS latest version.

Results: Obesity was found in 22.36%, diabetes in 15.78% whereas hypertension was documented in 31.57% of patients. In histopathological analysis grade 1 endometrioid adenocarcinoma was found in 23.68%, grade 2 in 48.68%, and grade 3 in 18.42% of patients. The 1 year, 2 year and 5 year overall survival rate estimated by Kaplan Meir method for the cohort was 89%, 78% and 56% respectively.

Conclusion: We found that patients presenting at early stage and having low grade tumours do well than other patients.

KEYWORDS : FIGO stage, tumor grade, lymph-node involvement, recurrence, myometrial invasion

Introduction

Endometrial cancer is the sixth most common cancer in women worldwide, with 320,000 new cases diagnosed in 2012 [1]. The highest incidence of endometrial cancer was in Northern America and Europe; and the lowest incidence in Africa and Asia [1]. As per the age adjusted incidence rates Age Adjusted Rates (AARs per 1,00,000) Chennai (6.0), Delhi (5.5) and Thiruvananthapuram District (5.1) occupied the top three places among all the PBCR (Population based cancer registries) in India [2]. Compared to other genital malignancies endometrial cancer has got a relatively good prognosis because majority of the cases are diagnosed at an early stage [3]. Although stage of disease is the most significant prognostic variable, a number of factors such as increased age, higher tumor grade, aggressive histology have been shown to correlate with outcome within the same stage of disease. The state of Uttarakhand is poorly represented as far as cancer statistics is concerned and same holds true for cancer of endometrium. Cancer Research Institute (CRI), SRHU is a premier cancer centre for diagnosis and treatment of cancer in this region. It is situated in Dehradun and caters to majority of cancer patients in Garhwal region of the sub Himalayan belt. The present study attempts to find out the factors that play a role in prognosis and survival of endometrial cancer amongst patients who have been treated at our institute.

Material and Methods

This retrospective study was performed at the Cancer Research Institute, Swami Rama Himalayan University Dehradun. All patients with histopathological proven diagnosis of endometrial carcinoma who were registered in our centre from 2009 to 2015 were included in this analysis. Patients with uterine sarcoma and coexisting second malignancy were excluded from the analysis. Data analysis was also aided by Uttarakhand State council for Science and Technology (UCOST). Confidentiality of patients were taken care during the study and analysis of retrospective data was made by studying the patients files, electronic data and histopathology records available. The results were statistically analysed with SPSS latest version. Overall survival (OS) was calculated from date of first

diagnosis until death from any cause. The Kaplan-Meier test was used for calculating median survival time, and the differences between groups were evaluated by log-rank test. Statistical significance was defined as $P < 0.05$.

Results

A total of 76 patients of endometrial carcinoma were registered between 2009 to 2015 at our institute. Median age of the patients was 58 yrs (Range 28-82 yrs) [Table 1]. Majority of the patients were postmenopausal at the time of diagnosis (78.94%). Obesity was found in 17 patients (22.36%), diabetes in 12 (15.78%) whereas hypertension was documented in 24 patients (31.57%). Surgical staging was done in 36 (47.36%) patients at our institute whereas 31 (40.78%) patients were referred to our centre after incomplete surgical staging. Remaining 9 (11.84%) patients were advanced at the time of presentation and were taken up for palliative chemotherapy. In histopathological analysis 18 patients were grade 1 endometrioid adenocarcinoma (23.68%), 37 grade 2 endometrioid adenocarcinoma (48.68%), and 14 grade 3 (18.42%) endometrioid adenocarcinoma. In non endometrioid variety 2 patients were of clear cell (2.63%), 4 papillary serous (5.26%) and 1 patient was of squamous cell carcinoma (1.31%) [Refer to table 2]. Among the surgically staged patients 11 patients were in FIGO stage 1A (30.55%), 19 patients in stage 1B (52.77%), 2 patient in stage 2 (0.05%), 4 in stage 3 (0.02%). In patients who were referred after incomplete staging CECT scan abdomen and pelvis were done to assess for the stage prior to start of adjuvant treatment. All the slides and blocks were reviewed by pathologists at our hospital. On evaluation majority of patients were in stage 1B (17 patients/61.29%), 9 patients in Stage 1A (29.03%), 1 patient in stage 2 (0.03%) and 2 patient in stage 3 (0.03%). There were no mortality as a result of surgical staging, however one patient required colostomy due to rectal injury. Total 56 out of 66 patients (84.84%) received external beam radiotherapy on 6MV LINAC (median dose 50 Gy) followed by High dose rate (HDR) Ir¹⁹² brachytherapy (7 Gy/2 sessions). Of these 25 (44.64%) were surgically staged in our department whereas remaining were referred from

peripheral institutes(55.35%). Decision to start post operative adjuvant radiation was decided according to the HPE report and associated risk factors [11,12] . Survival analysis was done only in patients from study period 2009 to 2014 irrespective of initial stage in 46 patients. The Kaplan-Meier test was used for calculating median survival time, and the differences between groups were evaluated by log-rank test. Statistical significance was defined as $P < 0.05$. A total A total of 17 patients died(36%) during the follow up period.($p=0.001$) deaths have occurred during the study. The 1 year, 2 year and 5 year overall survival rate estimated by Kaplan Meir method for the cohort was 89%, 78.1% and 59.8% respectively. Whereas the 1 year, 2 year and 5 year progression free survival was 88.6%, 82.7% and 78.1%[figure 1 and 2].

There were 9 recurrences(19.56%) during the follow up period out of which 7 patients had disseminated abdominal disease, one patient had multiple pulmonary metastasis and 1 had local pelvic recurrence. One patient died due to intestinal obstruction post radiation therapy (5.88%). Remaining 7 patients had disseminated disease at the time of presentation(41.17%) and died as a result of advanced nature of disease.

Discussion

Endometrial carcinoma is the most common malignancy of the female genital tract in developed countries, and the 6th most common cancer in women after breast, lung, and colorectum [1]. The average age of patients with endometrioid cancer is approximately 63 years, and 70% or are confined to the corpus at the time of diagnosis. Their 5-year survival is approximately 83% [3]. In the study by Siegel RL et al the cumulative risk of endometrial cancer up to the age of 75 years has been estimated as 1.6% for high-income regions and 0.7% for low-income countries [4]. This difference was found to be associated with an epidemic of obesity and physical inactivity, two important risk factors, in high-income countries. In addition, endometrial cancer patients with obesity were also found to have a poorer outcome [4]. On the other hand, physical activity and long-term use of continuous combined estrogen–progestin therapy were associated with a reduced risk of endometrial cancer [5,6]. In our study we found that the median age of our patients was 58 yrs (Range 28-82 yrs) and majority of the patients were postmenopausal at the time of diagnosis (60 patients/78.94%). This is consistent with the known fact that advanced age is an important risk factor in endometrial cancer and also that it is a disease primarily of the postmenopausal women [3]. Obesity was found in 17 patients (22.36%), diabetes in 12(15.78%) whereas hypertension was documented in 24 patients(31.57%). However there was no correlation between these factors and the overall survival. Our findings suggest that even though obesity, hypertension and diabetes are documented in a significant number of patients they do not play any role in the prognosis of the patients as found in other studies[13]. However in the study by Siegel RL et al obesity was associated with poorer prognosis which differs with our finding[4]. In our study majority of patients were in stage 1(76.31%) which suggest that most patients presented early due to symptoms of abnormal uterine bleeding. Our finding is similar to other studies which have also shown that majority of endometrial cancer are at stage 1 at the time of diagnosis [3, 7]. Histopathologic diagnosis was available in all the patients and endometrioid adenocarcinoma constituted the majority whereas clear cell, papillary serous and squamous histopathology was identified only in 7 patients. Survival analysis was done only in patients from study period 2009 to 2014 in all the patients irrespective of the stage and histopathology, so that a minimum followup of 24 months could be obtained. The 1 year, 2 year and 5 year overall survival rate estimated by Kaplan Meir method for the cohort was 89%, 78.1% and 59.8% respectively. Whereas the 1 year, 2 year and 5 year progression free survival was 88.6%, 82.7% and 78.1%[figure 1 and 2]. Our results have shown that our 5 year overall and progression free survival are less as compared to other studies of Creasman et al[3] and Álvaro Tejerizo-García et al[14] . Our results reflect that inspite of having a overall survival of 89% at 1 year the 5 year survival dropped down to 59.8% which in turn reflects upon the poor followup due lack of connectivity in this region and thus presenting late with advanced disease after recurrence. However the numbers are very less as compared to other studies to make a definite conclusion. In univariate analysis we found that the survival rates for endometrial cancer varied widely by stage of the disease .Patients with stage 1 disease had an overall 1 year survival of 97.1% compared to 63.6% in advanced disease($P=0.0001$)[figure 3]. 70.1% of all patients with stage 1 were

still surviving at the end of the year study. Our findings are similar to study by Creasman W and Trimble EL which had also shown that early stage patients have better survival[3,7]. Our study has also shown that grade 1 and grade 2 endometrioid adenocarcinomas have better survival (5 year survival 66.5%) than grade 3 endometrioid and nonendometrioid histologies (28 months) [p value=0.005]. Clear cell carcinoma had the worst median survival of 8 months only[p value=0.005]. Our findings are similar to other studies which have also shown that patients low grade endometrioid carcinoma do better than high grade and non endometrioid histologies[8]. There were 9 recurrences during the follow up period out of which 7 patients had disseminated abdominal disease, one patient had multiple pulmonary metastasis and 1 had local pelvic recurrence. The results are similar to other studies which have shown that distant failures are more common than local recurrences in endometrial cancer[9,10]. To conclude in our institute endometrial cancer is the third common gynaecological cancer after cancer of cervix and ovary. Even though majority of the patients present in early stage of disease most patients are referred after simple hysterectomy as proper preoperative evaluation including endometrial biopsy was not done in majority of cases. In addition although our study is flawed by its retrospective design and small number it has given a fair insight into the nature of the disease. We found that patients presenting at early stage and having low grade tumours do well than other patients. We also found that a larger prospective study will be required to get a clear idea about the pattern and behavior of this cancer in this region.

TABLE 1: AGE

AGE	Number	Percentage
<40	1	0.01%
40-50 YEARS	8	10.5%
51-60 YEARS	37	48.68%
>60 YRS	30	39.47%
RANGE	(Range 28-82 yrs).	
MEDIAN	58YEARS	

Table 2: Clinicopathological factors:

FACTOR		NO	Percentage
AGE	PREMENOPAUSAL	16	16
	POSTMENOPAUSAL	60	78.94
WEIGHT	Body Mass Index>30kg/m ²	17	22.36
HYPERTENSION		24	31.57
DIABETES		12	15.78
FIGO STAGE	I	58	76.31
	II	3	3.94
	III	6	7.89
	IV	9	11.84
GRADE(ENDOMETRIOD)	1	18	26.68
	2	37	48.68
	3	14	18.42
HISTOPATHOLOGY	ENDOMETRIOD	69	90.78
	CLEAR CELL	2	2.63
	PAPILLARY SEROUS	4	5.26
	SQUAMOUS	1	1.31

FIGURE 1: OVERALL SURVIVAL IN MONTHS

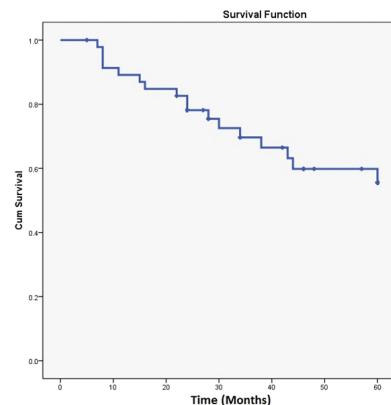
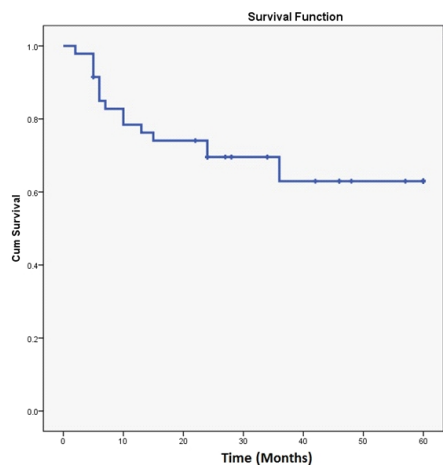


FIGURE2: PROGRESSION FREE SURVIVAL IN MONTHS



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