Experience with women having uterine cancer in Eastern India: a hospital based study

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ABSTRACT

Background: The changing lifestyle has led to a rise in obesity, diabetes and hypertension in India which the most important risk factors for developing uterine cancer. The treatment of uterine cancer is evolving and requires proper evaluation and often adjuvant treatment for better survival. The disease being associated with symptoms of abnormal uterine bleeding often ends up being inadequately managed by non-oncologists practicing in a generalist setting in India. The current study was aimed to audit and observe any difference in outcome of patients primarily treated in the oncology set-up of the Chittaranjan National Cancer Institute, which is a regional cancer center in India versus those receiving primary treatment in a non-oncological set-up.

Methods: Retrospective data was collected from hospital records after setting inclusion and exclusion criteria for the study.

Results: There is poor correlation between the endometrial biopsy and histopathology findings of patients operated in non-oncological setting as compared to that in the institute. The overall survival of patients operated in the institute was superior to those treated outside.

Conclusions: Patients having risk factors and symptoms akin to that of uterine carcinoma must be treated in an oncological set-up ideally.

Keywords: Endometrial carcinoma, Gynecologic oncology, Hysterectomy

INTRODUCTION

Endometrial cancer is a lifestyle related cancer with a higher incidence in the high-income countries as compared to India.¹,² It is among the ten leading cancer sites among seven out of twelve PBCRs in India.³ There has been a recent shift in the lifestyles of Indian urban population across the country leading to an increase in incidence of obesity and diabetes, which are both known risk factors for genesis of uterine cancer.⁴ Post-menopausal bleeding is the most common presentation of this malignancy.⁵ The present retrospective study describes the demographics, risk association, treatment and survival of patients presenting with uterine cancer at Chittaranjan National Cancer Institute, Kolkata between 2011 to 2018.

METHODS

An audit framework was designed to study the outcome in terms of survival of patients with uterine cancer presenting at the institute between years 2011 to 2018. Inclusion criteria was patients who had been histologically diagnosed as malignant and undergone complete treatment and follow-up at the institute, those who had registered but whose diagnosis could not be confirmed as malignant or had not undergone complete treatment and/or follow-up at the institute were excluded.
from the study. Therefore, the total number of participants eligible for the study was 60.

The patients’ records were searched for confirmation of diagnosis and staging, mode of primary and adjuvant treatment as per the patient’s stage and follow-up on a regular basis. The data of such patients was collected using Microsoft Excel datasheets and the analysis of data was done using IBM SPSS statistics version 20. The endpoint of the study was overall survival. The study group was analyzed by two major groups based on age ≤45 and >45 years and has undergone primary treatment in the institute or outside (non-oncological set-up).

**Statistical analysis**

Over-all survival was calculated using the Kaplan-Meier method where death was an event and those who could not be contacted were censored for the sake of the study. Agreement between preoperative endometrial biopsy and post-operative specimen histopathology was done using kappa statistics. All analysis was done using SPSS version 20.

**RESULTS**

Total number of patients registered with a diagnosis of uterine/endometrial cancer was one hundred and six, out of which thirty-six patients did not undergo any further assessment or treatment at the institute and ten patients had no follow-up at the institute. The remaining sixty patients were included in the study. The medical records of the patients included in the study were reviewed and data was collected under various heads.

Among the cases being studied majority were above 45 years of age with three patients having history of cancer of some site, in the family. Eighty percent of the patients were literate and around fifty-seven percent of the cases had a parity of more than one (Table 1). Around forty-seven percent patients had co-morbidities amongst which the commonest was diabetes mellitus, while fifteen percent patients had a combination of diabetes and hypertension (Table 2).

**Table 1: Patient characteristics with regard to age, literacy, parity, comorbidities and family history of cancer.**

| Characteristics                        | Number | %   |
|----------------------------------------|--------|-----|
| Total cases                            | 60     | 100.0% |
| Age years ≤45                          | 14     | 23.3% |
| >45                                    | 46     | 76.7% |
| Family history of cancer               |        |      |
| Nil                                    | 57     |      |
| Yes                                    | 3      |      |
| Literacy                               | 48     | 80.0% |
|                                         | 12     | 20.0% |
| Parity                                 |        |      |
| Parity less than/equal to 1            | 26     | 43.3% |
| Parity more than one                   | 34     | 56.7% |

**Table 2: Frequency of various co-morbidities among the patients.**

| Co-morbidities                        | Frequency | Percentage | Valid percentage | Cumulative percentage |
|---------------------------------------|-----------|------------|------------------|-----------------------|
| Diabetes mellitus                     | 10        | 16.7%      | 16.7%            | 16.7%                 |
| Hypertension                          | 6         | 10.0%      | 10.0%            | 26.7%                 |
| Hypothyroid                           | 1         | 1.7%       | 1.7              | 28.3%                 |
| Diabetes mellitus + hypertension      | 8         | 13.3%      | 13.3%            | 41.7%                 |
| Diabetes +hypertension+ischemic heart disease | 1     | 1.7%       | 1.7              | 43.3%                 |
| Diabetes+hypertension+COPD            | 1         | 1.7%       | 1.7              | 45.0%                 |
| CNS                                   | 1         | 1.7%       | 1.7              | 46.7%                 |
| No co-morbidity                       | 32        | 53.3%      | 53.3%            | 100.0%                |
| Total                                 | 60        | 100.0%     | 100.0%           |                       |

Figure 1: Distribution of symptoms among the patients.
The most common symptom of patients presenting to the hospital was post-menopausal bleeding (83.3%), followed by menorrhagia (10%) (Figure 1). Among the postmenopausal patients the most common histopathology was endometroid adenocarcinoma. Post-menopausal bleeding was also the commonest symptom for other histopathology types like, papillary serous adenocarcinoma and mixed mullerian tumour (Table 3).

Since the patients registered in the institute, some of them had already undergone primary treatment outside, the agreement between preoperative endometrial biopsy and
post-operative histopathology was seen using kappa statistics and it was found that there was poor agreement between the pre-operative and post-operative histopathology reports of those operated outside as compared to those operated in the institute (Table 4 and 5).

Table 6: Cross-tabulation showing age-wise distribution of patients in various stages.

| Staging | Total |
|---------|-------|
| Stage IA | Stage IB | Stage II | Stage IIIA | Stage IIIB | Stage IIIC1 | Stage IIIC2 |
| Age <=45 years | 6 | 5 | 2 | 0 | 1 | 0 | 0 | 14 |
| Age >45 years | 10 | 23 | 4 | 1 | 3 | 3 | 2 | 46 |
| Total | 16 | 28 | 6 | 1 | 4 | 3 | 2 | 60 |

Table 7: Mean survival in two groups compared in months.

| Hysterectomy at presentation | Mean* | Std. error | 95% confidence interval | Median | Std. error | 95% confidence interval |
|-----------------------------|-------|------------|-------------------------|--------|------------|-------------------------|
|                             | Estimate | Lower bound | Upper bound | Estimate | Lower bound | Upper bound |
| Yes                         | 75.597 | 64.098 | 87.095 | . | . | . |
| No                          | 105.917 | 91.784 | 120.050 | . | . | . |
| Overall                     | 98.410 | 84.973 | 111.847 | . | . | . |

a. Estimation is limited to the largest survival time if it is censored.

Table 8: Equality of survival distributions in the two survival curves with censoring.

| Overall comparisons | Chi-square | df | Sig. |
|---------------------|------------|----|------|
| Log rank (mantel-cox)| 2.786 | 1 | 0.095 |

Test of equality of survival distributions for the different levels of hysterectomy at presentation.

Table 9: Loss to follow-up.

| Sr. No. | Patient operated outside | Patient operated at Institute | Total lost to follow-up |
|---------|--------------------------|-------------------------------|-------------------------|
| Lost to follow-up | 4 | 2 | 6 |

The majority of patients presented in stage 1b followed by stage 1a, that is early stage cancer (Table 6). The survival of patients was analysed based on primary treatment (hysterectomy) done outside (non-oncology set-up) as compared to those treated at the institute. The survival was superior for those treated in the institute (Figure 2). The mean survival time was 105.92 months for those operated in the institute as compared to 75.6 months for those operated outside (Table 7). The equality of survival in the two populations (operated in the institute and outside) with censoring was compared using log rank test and the difference was 0.095 (Table 8).

**DISCUSSION**

Incidental diagnosis of endometrial cancer following hysterectomy poses a clinical dilemma to the gynecologic
The recommended management of women with postmenopausal bleeding is radiological assessment of the uterus and adnexa with measurement of endometrial thickness followed by endometrial aspiration or biopsy in case of thickened endometrium >4 mm. A diagnosed case of endometrial cancer should undergo complete surgical staging including assessment of the peritoneal cavity and retroperitoneal lymph node status. However, many such symptomatic postmenopausal women are inadequately investigated and then undergo inadequate surgery, following which they are referred to higher cancer centers for further management. As inferred from this study, such women have poorer survival (Figure 2).

With better oncological facilities, tissue specimens of endometrial cancer cases should be examined by oncopathologists as those not adept at diagnosing malignancy may be inaccurate at diagnosis, as what was observed in this study where correlation between pre-hysterectomy histopathology (outside the study institute) and post hysterectomy histopathology (at the study institute) was poor (Table 5 kappa 0.4).

Patients of all malignancies in general and those with endometrial cancer in particular require regular follow up to detect early recurrence or disease progression, if any. Authors observed from this study that patients who were operated at this study center have a tendency of continuing follow up better than those operated outside (Table 9).

Most of the patients find it difficult to reconcile to re-surgery as was observed in this study where none of the patients operated outside consented to undergoing surgical restaging. The survival of patients was not adversely affected by not undergoing surgical restaging. Most of the patients who required adjuvant therapy based on their radiological and histopathological findings had good survival. Subjecting patients to re-surgery just to adequately stage the disease, is an added risk to such patients who are suspected to have endometrial cancer, especially in a low-middle income country when the cost to treatment is increased as most of the treatment is borne by out of pocket expenditure.

It was finally observed that patients who were primarily operated in specialized gynecologic oncology setup had a superior survival as compared to patients in a non-oncology setup. Currently, there are no studies in the literature for endometrial cancer, however, a study by Engelen MJ et al, describes a superior survival in ovarian cancer patients treated primarily by a gynecological oncologist.

CONCLUSION

Patients with post-menopausal bleeding must always undergo an endometrial evaluation by biopsy before undergoing a hysterectomy, as the overall survival is better if women diagnosed as endometrial cancer are operated in an oncological set-up than in a general gynecological set-up.

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