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ORIGINAL ARTICLE

Recurrence Patterns and Predictive Factors in Early-Stage Endometrial Carcinoma: Insights from a Pakistani Cohort Study

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ABSTRACT

Background: Endometrial carcinoma incidence has surged in the Western world over the last two decades and is now increasing in the Eastern regions. Despite diverse treatment approaches, recurrence remains a significant concern, prompting the need to identify prognostic factors to target interventions and improve overall survival rates, thereby alleviating disease burden.

Objectives: To identify the frequency of recurrence in its earlier stages and factors influencing it specifically in our part of the world (Pakistan).

Methods: A cohort of 250 women who were diagnosed with endometrial carcinoma during 2018 and 2020 underwent treatment (hysterectomy) was studied for up to three years ending till 1 January, 2023following the treatment to identify the rates of recurrence and any predictive factors affecting the illness. The information utilized in this research was acquired from a database of all the patients who visited the Gynae Oncology unit, Lady Willingdon Hospital (King Edward Medical University) Lahore during these years.

Results: Out of 250 patients, 13 had a recurrence (5.2%), the various predictive factors identified were FIGO stage 1B (OR 1.89), a score of 3 or more for Charlson comorbidity index (OR 1.88), a histology which is not endometroid and the site of recurrence of the disease.

Conclusion: Early-stage endometrial cancer has a low risk of recurrence within 3 years following the initial treatment.

Keywords: Endometrial cancer; diagnosis; prognosis; treatment

INTRODUCTION

Endometrial carcinoma is one of the most common malignancies encountered in the field of gynaecology, it is in fact the commonest malignancy related to gynaecology in the developed world. However, in the past few decades, the incidence is rapidly rising in the developing countries as well[1]. Talking about uterine cancers in general, they are most commonly seen in the regions of North America and Northern European countries, their incidence is intermediate in Southern parts of Europe and South American temperate regions, and is lowest in South Asia, East Asia and in most of the African region. This likely reflects prevalence differences in risk factors, including obesity and reproductive patterns[5]. It is predicted that in the upcoming decades, the developing and poor nations are also going to get hit hard by the increased incidence of this disease[4].

Endometrial carcinomas broad classes or divisions, which are type 1 and type 2. Type 1 account for majority of the cancers and have a good prognosis and low recurrence rate and are mainly endometroid adenocarcinomas. Type 2 carcinomas are aggressive, clear or serous cell type and have a higher recurrence rate (about 50%), with 5-year survival rate around 55%[2]. The most common histologic type is endometroid, which has excellent survival (97.5%). The non-endometroid type, however has a poorer prognosis and is more frequently associated with recurrences[6].

The FIGO staging and the cancer histology largely determine the survival outcome of the disease. There are four stages of endometrial cancer according to international Federation of Gynaecology and Obstetrics (FIGO) which determine the mode of treatment depending on the size and severity. Stage I is confined to the uterus; it is further divided into stage IA (no or less than 50% myometrial invasion) and IB (equal to or more than 50% myometrial invasion). Stage II tumours extend to cervical stroma but do not go beyond uterus. Stage III tumours are those which extend beyond uterus but do not involve pelvic wall. Stage IV tumours involve bladder or bowel or cause distant metastasis[7].

Hysterectomy along with bilateral salpingo-oopherectomy is the procedure of choice when it comes to management. Pelvic and para-aortic lymph node removal may provide better outcomes in intermediate to high-risk disease (stage II and higher) but has no role in low-risk tumours. In case of cervical involvement, radical hysterectomy is carried out. For advanced and recurrent disease, cytoreduction is carried out (if fulfil the criteria). Adjuvant options include radiotherapy (for stage II or higher), can be given locally (brachytherapy), externally or in combination with chemotherapy. Chemotherapy alone can be used but evidence regarding its efficacy is still lacking. Additionally, hormonal therapy and immunotherapy are also being used[8].

Despite all the treatment modalities, recurrences do occur, for type I (20%) and type II (50%) and median survival rarely exceeding 12 months. Once the initial treatment fails and disease recurs, palliation is usually the only remaining option.

The median time for recurrence is 1 year and most (78% of the recurrences) take place within 2 years of the initial disease. The various sites of recurrences are pelvic (34.3%), extra-pelvic including, peritoneum, lymph nodes, bones, brain, lung, liver and bowel (43.3%) and 22.4% occur at multiple sites[9]. Factors which involve recurrence are old age, menopausal state, elevated BMI, lympho-vascular invasion, myometrial invasion, lower uterine segment involvement, tumour size>20mm and use of adjuvant therapy[10].

The purpose of conducting this study is to evaluate the incidence of recurrence of endometrial carcinoma, the factors affecting it, the commonest sites of relapse and the efficacy of re-treatment of the recurrent disease in our part of the world.

METHODOLOGY

In a retrospective study conducted at Gynaecological oncology Unit, Lady Willingdon Hospital Unit 2 Lahore, data from 250 women diagnosed with endometrial carcinoma between 2018 and 2020 were analysed. These patients underwent hysterectomy as part of their treatment regimen. The study tracked the recurrence rates and investigated potential predictive factors, including clinicopathologic and socio-demographic variables, over a three-year period post-treatment. Utilizing information sourced from the hospital's comprehensive database of patient visits during the specified timeframe, researchers aimed to identify patterns and associations that could inform future interventions and improve outcomes for individuals battling endometrial carcinoma. This research holds promise for enhancing our understanding of the

disease's progression and aiding in the development of targeted strategies to mitigate recurrence risks and optimize patient care.

RESULTS

A total of 250 women were included in the study, out of them 13 acquired a recurrence (5.2%) within 3 years of starting primary treatment. International Federation of Gynaecology (FIGO) stage 1B (OR 1.89), a score of 3 or more for Charlson comorbidity index (OR 1.88), a histology which is not endometroid (OR 1.77) were among the predictive factors for recurrence.

Table 1: Sub Site Distribution

Site	No.	%
Vaginal	4	80
Extra-vaginal	9	17

Site of recurrence also influenced the overall survival. For vaginal recurrence, the 5-year survival was 75% and for women with distant metastasis, it was only 15%.

Table 3: Predictive Multivariate Logistic Regression Model for Disease Recurrence

Potential co-variates	Recurrence vs non-recurrence	
	OR	95%CI
Charlson comorbidity score		
0	1.00	--
1	0.76	--
2	0.85	--
3	1.86	1.18-2.19
FIGO stage		
1A	1	--
1B	1.9	1.32-2.7
Histology		
Endometrioid	1	--
Non-endometrioid	1.8	1.8-2.6

FIGO staging was the only predictive factor involved in vaginal recurrence (OR: IB 1.66) whereas for extra-vaginal disease, FIGO staging (OR: IB 1.88), Charlson comorbidity index of 3 (OR 1.77) and non-endometrioid histology (OR 2.31) were the predictive factors.

Table 2: Disease Recurrence and Associated Factors

Variables	No	%
Age at diagnosis		
<66	9	43
>66	4	
BMI		
<25	3	24
25-30	6	
>30	4	
FIGO staging		
1A	5	14
1B	8	
Histology		
Endometrioid	3	8
Non-endometrioid	10	

DISCUSSION

Our study found out the recurrence rate of early-stage endometrial carcinoma to be 5.2% and the various predictive factors affecting the recurrence were FIGO stage of the disease, Charlson comorbidity index and site of recurrence. The 5-year survival rate following recurrence is highly dependent on the site of recurrence and is 75% for vaginal and 15% for extra-vaginal recurrences.

Comparing this with other studies, a study conducted by Sasada S et al[11] showed the recurrence rate for stage I endometrial carcinoma to be 4.1% which is quite close to our research. This research also indicated a higher 5-year survival rate (>90%) for stage 1 and also mentioned higher rates in ages >60%. This research also showed that the rate of recurrence was higher in stage IB as compared to stage IA and survival was better with recurrences in stage IA.

Another research conducted by Samual R. Francis et al[12] showed the recurrence rate of early-stage endometrial carcinoma to be 7.2% which is once again quite close to our results. The recurrence was mostly extra-vaginal (4.2% as compared to 1.7% vaginal recurrence), and patients with non- endometroid histology had a poorer prognosis. This research also showed that the 5-year survival for vaginal recurrence to be higher (61.2%) as compared to extra-vaginal (38.8%) which agrees with our results.

A study conducted by E. Vizza et al[13] showed that the recurrence rates for low grade (stage IA and IB with low grade histology) was 9.6%, which is again closer to our findings and the risk increased with increasing severity of the disease. It also agrees with the fact that patients with non-endometroid histology and had a poorer prognosis and increased recurrence rates. This study showed that for low-risk endometrial carcinoma, there are no differences between local and distant recurrences. This study showed 5-year survival for low-risk disease to be quite higher (99%)

Tanja Ignatov et al[14] conducted a study and showed the recurrence rates in low-risk disease to be 6%. It showed the 10-year survival rate to be highest (83%) in low-risk group. According to this study, most common site of recurrence was local (at the vaginal vault)

Study by Ming-Shyen Yen [15] et al found FIGO staging and age to be the most important prognostic factors for tumour recurrence. The recurrence rates were higher in their case (22.8% for stage IB and 9.1% for stage IA). Stage IB had a higher recurrence rate as well as a poorer 5-year survival rate between the two stages. They also state that patients with age> 60 years had an increased rate of recurrence than younger patients. The recurrence was more common at distant sites than at the local site. Their study did not find any corelation between the use of adjuvant treatment and the rate of recurrence. According to their results, endometroid histology poses a greater risk when it comes to recurrence, which contradicts with our results.

So far, there is not much work available on this topic in our part of the world. By comparing the results of our study with rest of the world, we can see that the trends are almost similar, we have similar rates of recurrence for early-stage endometrial carcinoma with some common predictive factors such as age, site of recurrence etc.

Limitations of this study: the size of our cohort was relatively small. Only those patients were included which had undergone total hysterectomy alone without any adjuvant treatment so we could not find out about the impact adjuvant radio or chemotherapy could have on our population. Despite these limitations, this study is the first of its kind conducted in Pakistan and will prove to be a key which unlocks further progress in research on this topic.

CONCLUSION

Endometrial carcinoma when diagnosed and treated in its earlier stages (FIGO stages 1A and 1B), has a low risk of recurrence in the next 3 years following initial treatment (hysterectomy). The site of recurrence has an important role in determining the survival, vaginal recurrence has a better prognosis than extra-vaginal recurrence. Even though this research helped to identify some prognostic factors, more research is required to establish a relationship or to understand the underlying mechanisms behind these findings. Conducting such studies will help to reduce the morbidity and mortality associated with the condition.

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