Pattern of Recurrence in Locally Advanced Carcinoma Cervix Based on Platinum Sensitivity

Sarah Khan[1], Shazia Rafiq[2] and Muhammad Sami Ullah[3]

ABSTRACT

Objective: To validate the concept of platinum sensitivity in cervical cancer women and estimate its effect.

Study Design: Prospective study

Place and Duration of Study: This study was conducted at the Nishtar hospital Multan from May 2022 to April 2023.

Materials and Methods: A total of 60 patients diagnosed as IB2 and IVA proven histologically as squamous cell carcinoma or adenocarcinoma were enrolled. Platinum-based chemotherapy is a standard treatment for patients with advanced cervical cancer (ACC). Platinum drugs, such as cisplatin and carboplatin, are commonly used in combination with other chemotherapy agents to treat ACC.

Results: The mean age of the patients was 54.63±3.55 years. All the sixty patients were given chemotherapy with cisplatin-based regimens. Most of the patients 51.7% had <6 months of relapse, whereas, locoregional was the most common pattern of relapse, 73.3%. Most of the patients had loco-regional and <6 months of relapse time and 9 patients had distant relapse pattern and >18 months of relapse time, (p<0.001).

Conclusion: Platinum sensitivity concept can be applied to advanced cervical cancer patients, with evidence showing a significant role on survival of women after recurrence in women who were treated with platinum chemotherapy previously.

Key Words: Cervical cancer, Recurrence pattern, platinum sensitivity, Chemotherapy.

INTRODUCTION

Cervical cancer remains a significant public health issue worldwide. It is the fourth most common cancer globally, and in low- and middle-income countries (LMICs), it often ranks second after breast cancer in terms of prevalence[1]. In 2018, there were an estimated according to a report about 569,847 newly diagnosed women of cervical cancer in year of 2018 in the world. Additionally, cervical cancer caused approximately 311,365 deaths in the same year. These numbers highlight the substantial burden of this disease and its impact on affected individuals, families, and communities[2]. Among causes of cervical cancer human papillomavirus is leading cause with persistent infection.

[1.] Department of Clinical Oncology / Obstet & Gynae[2], Nishtar Hospital, Multan.

[3.] Department of Pathology, Nishtar Medical University, Multan.

Correspondence: Dr. Sarah Khan, Senior Registrar of Clinical Oncology, Nishtar Hospital, Multan
Contact No: 0321 6368774
Email: saarahk606@gmail.com

Several factors contribute to the higher incidence and mortality rates of cervical cancer in LMICs compared to high-income countries[3]. These factors include limited access to cervical cancer screening programs, lack of HPV vaccination programs, inadequate healthcare infrastructure, and limited resources for early detection, diagnosis, and treatment[4].

Advanced cervical cancer (ACC) is typically classified as stage IB3 to IV according to the FIGO (International Federation of Gynecology and Obstetrics) staging system, as updated in 2019[5]. It comprises both locally advanced cervical cancer (LACC) in stages IB3 to IVA and initially metastatic cervical cancer in stage IVB. ACC accounts for approximately 40% of all cervical cancer cases at the time of diagnosis[6].

Platinum sensitivity concept is indeed an important prognostic factor for ovarian cancer women. Platinum-based chemotherapy, such as carboplatin or cisplatin, is commonly used as a first-line treatment for ovarian cancer. The response to platinum-based chemotherapy can vary among patients, and the duration of response, or platinum sensitivity, has been recognized as a significant factor in predicting disease recurrence and overall survival[7].

In the context of ovarian cancer, platinum sensitivity is typically classified into three categories: sensitive, resistant, and refractory. Platinum-sensitive refers to patients who have a relapse more than six months after completing their initial platinum-based chemotherapy[8].

Platinum-resistant indicates a relapse within six months of completing chemotherapy, while platinum-refractory implies that the cancer did not respond to platinum-based chemotherapy[9].

MATERIALS AND METHODS

Study was conducted at Nishtar Hospital, Multan in 1 year period from May 2022 to April 2023. Study was approved by hospital committee of ethics. All participated patients were asked for written inclusion consent. Women with IB2 and IVA proven histologically as squamous cell carcinoma or adenocarcinoma, intact renal parameters, ECOG 0-1, age limit 20-60 years and received platinum based chemotherapy as neo adjuvant or with radiation were included in the study. Patients with ECOG above 1 and 4B stage were excluded from study. Pre-operative work up like history taking, physical examination, paravaginal examination, biopsy and magnetic resonance imaging were done for all patients. Initial demographic data along with clinical, pathological and surgical data was recorded.

Management plan was made by multidisciplinary team of hospital according to INCa (French National Institute of Cancer Guidelines. Recurrence was labeled on physical examination with CT or MRI involvement. Sensitivity was reported as Platinum Resistant (PR): This category includes patients whose cancer recurred less than 6 months after completing platinum-based chemotherapy. These patients have a poor response to platinum therapy and are considered resistant to further treatment with platinum-based drugs. Partially Sensitive (PPS): Patients falling into this category experienced cancer recurrence between 6 and 11 months after completing platinum-based chemotherapy. They have a modest response to platinum therapy, indicating partial sensitivity to these drugs. Sensitive (PS): Patients classified as sensitive had their cancer recur between 12 and 18 months after the completion of platinum-based chemotherapy. They demonstrate a good response to platinum therapy and are considered sensitive to further treatment with these drugs. Very Sensitive (PVS): This category includes patients whose cancer recurred more than 18 months after completing platinum-based chemotherapy. They have an excellent response to platinum therapy and are considered very sensitive to these drugs.

Data was recorded in SPSS version 23 and analyzed for mean (SD) and frequency (percentages) for numerical and categorical data respectively. Significant p value was below 0.05.

RESULTS

Sixty patients were included in this study. The mean age of the patients was 54.63±3.55 years. All the sixty patients were given chemotherapy with cisplatin-based regimens. Further, all the patients were given radiation.

Brachytherapy was given to 52(86.7%) patients. (Table.No. 1).

Most of the patients 31 (51.7%) had <6 months of relapse, whereas, locoregional was the most common pattern of relapse, 44 (73.3%). (Table.No. 2).

Most of the patients had locoregional and <6 months of relapse time and 9 patients had distant relapse pattern and >18 months of relapse time, (p<0.001). (Table No. 3).

Table No. 1: Demographic and previous treatment of the study patients

Variable	Frequency	%	Mean±S.D
Age (years)			54.63±3.55
Chemotherapy			
Yes	60	100.0	
No	0	0.0	
Radiation			
Yes	60	100.0	
No	0	0.0	
Brachytherapy			
Yes	52	86.7	
No	8	13.3	

Table No. 2: Relapse and its pattern of the study patients

Variable	Frequency	Percentage
Relapse		
<6 months	31	51.7
6-18 months	9	15.0
>18 months	20	33.3
Pattern of relapse		
Locoregional	44	73.3
Nodal	7	11.7
Distant	9	15.0

Table No.3: Association of pattern of relapse and relapse time

Relapse months	Patterns of relapse			Total	P-value
	Locoregional	Nodal	Distant		
<6	31	0	0	31	
6-18	2	7	0	9	<0.001
>18	11	0	9	20	
Total	44	7	9	60	

DISCUSSION

In this study recurrence was followed as per French National Institute of Cancer guidelines, similar approach was used by Takekumaet al[10] and classified patients into different categories based on the time interval between initial treatment and recurrence. These categories included patients with recurrence within 6 months, between 6 and 11 months, between 12 and 18 months, and beyond 18 months.

In this study most of the patients 51.7% had <6 months of relapse, whereas, locoregional was the most common pattern of relapse, 73.3%. Most of the patients had

locoregional and <6 months of relapse time and 9 patients had distant relapse pattern and >18 months of relapse time, (p<0.001). Study conducted by de Foucher T et al[11] found that the recurrence rates for a certain condition differed significantly based on the time frame after the initial occurrence. Specifically, the study found that 52% of cases recurred in less than 6 months, 21.6% recurred between 6 and 17 months, and 14.6% recurred after 18 months or more.

In cases of recurrent disease platinum sensitivity is an important prognostic factor that was reported in numerous previous reports. But platinum sensitivity in terms of pattern of recurrence, prognostic factor survival rate and practical implication is not well reported specialty in cervical cancer patients[12]. In case of advanced disease of cervix, chemotherapy based on platinum and taxane has been considered gold standard. Furthermore, acquired and primary platinum resistance has been associated with poor survival and low probability response[13].

Based on the research by Taniokaet al[14], it has been shown that the time to recurrence of 12 months is a significant independent predictive factor of tumour response. Additionally, a 6-month progression-free interval (PFI) has been identified as an independent prognostic factor for overall survival (OS) in patients with recurrent CC.

According to a study conducted by Matodaet al[15], a PFI of more than 24 months was the discriminating point between platinum-sensitive and platinum-resistant cervical cancer patients. This means that patients with a PFI of more than 24 months were considered platinum-sensitive, while those with a PFI of less than 24 months were considered platinum-resistant.

In this study locoregional recurrence was observed in 73.3% of patients, nodal recurrence was observed in 11.7% of patients and distant recurrence was seen in 15% women. Studies conducted by Quinn et al[16], Scatchard et al[17] and Kitagawa et al[18] reported locoregional recurrence 22%–55%, distant recurrence 22%–75% and 2%–50% combined recurrence.

A retrospective study by Foucher et al[11] conducted on women with advanced cervical cancer found that platinum sensitivity status was a strong predictor of overall survival (OS) after recurrence. The impact of prior platinum exposure on response rates in patients with advanced cervical cancer was also studied. The study found that the response rate of cisplatin based therapy was upto 8%after mono-therapy, cisplatin and topotecan combination shows 15% and paclitaxel shows 32%. The study by Tewari and Monk[19] reported 20% response rate with cisplatin mono-therapy, topotecan 39% and finally CT paclitaxel combination reported 37%.

CONCLUSION

Platinum sensitivity concept can be applied to women with ACC, with evidence showing a significant impact on patient survival after recurrence among those previously treated with platinum chemotherapy. This is particularly relevant as most recurrences are not treatable with curative intent. Therefore, a history of platinum exposure can be a major indicator for predicting the effectiveness of second-line systemic treatments.

Author's Contribution:
Concept & Design of Study:	Sarah Khan
Drafting:	Shazia Rafiq
Data Analysis:	Muhammad Sami Ullah
Revisiting Critically:	Sarah Khan,
Final Approval of version:	Sarah Khan

Conflict of Interest: The study has no conflict of interest to declare by any author.

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