

Clinicopathological Profile of Carcinoma Cervix and Their Impact on Survival of Patients

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Abstract

Introduction: Cervical carcinoma is one of the leading causes of death in female patients. In India, cervical cancer accounted for 9.4% of all cancers and 18.3% (123,907) of new cases in 2020. It still is among the most common cancers in India and a leading cause of cancer-related deaths in women in lower- and middle-income countries. FIGO stage, histological types, depth of stromal invasion, lymph vascular space invasion, and lymph nodes metastasis are aggressive characteristics of cervical cancer, which are regarded as significant factors for treatment, prognosis, and recurrence and have a great impact on survival.

Objectives: This study aimed to analyze the clinicopathological characteristics of women with cervical cancers in Kashmir and their impact on survival.

Materials and Methods: It was a retrospective study which was conducted in tertiary care hospital from year January 2017 to December 2021. A total of 31 patients histologically confirmed were taken for this study. The data were subdivided into two groups with histology adenocarcinoma and squamous cell carcinoma, respectively. Patients' characteristics were analyzed under the following parameters age, FIGO stage (I, II, III, and IV), grade (well-differentiated, moderately differentiated, poorly differentiated, tumor histology (squamous, and adenocarcinomas), nodal status (node-positive, node-negative), lymphovascular invasion, and correlated with and their impact on survival of patients.

Results: A total of 31 patients with cervical cancer were analyzed in the data. The majority of patients in the squamous cell carcinoma (group) were in the age group of 60 (35.29%) and 40–49 (35.29%) and while, in the adenocarcinoma group (Group B), the majority of patients were in the age group of 60 (35.71%), followed by 40–49 (28.57%). In Group A, majority of patients were having IIB stage 6 (35.29%) and in Group B, majority were having stage IIA 6 (42.85%). In Group A, 11 patients (64.70%) received concurrent chemoradiation and brachytherapy, while 3(17.64%) received adjuvant radiation and 3(17.64%) received chemotherapy. In Group B, two patients (14.28%) received adjuvant radiotherapy and 2 (14.28%) received chemotherapy and nine received concurrent chemoradiation followed by brachytherapy (64.28%), while 1(7.14%) received radiation followed by chemotherapy. At 1 year of follow-up 14 (82.35 %), patients were diseases free and 3(17.64%) had metastasis, 1 (5.88%) had died in Group A, while in Group B, two patients (14.28%) died, six patients (42.85%) were disease free, and one patient (7.14%) had local recurrence and five patient (35.17%) had metastasis. The disease-free survival was 33 months for Group A and 24 months for Group B. Overall survival percentage was more in Group A which is 59 months and 21 months for Group B.

Conclusion: Our results suggest that histology, lymphovascular invasion, parametrial involvement, and nodal involvement are independent predictors of shorter survival in patients with cervical adenocarcinoma. Adenocarcinoma was associated with a worse prognosis compared to squamous, particularly for patients who require post-operative treatment; such patients may benefit from individualized post-operative treatments that differ from those applied for squamous.

Key words: Carcinoma, Lymphovascular invasion, Survival

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INTRODUCTION

Cervical carcinoma is one of the leading causes of death in female patients. As per Globocan 2020, 604,100 new cases of cervical cancer were detected globally in 2020 and 341,831 deaths were attributed to this malignancy. In India, cervical cancer accounted for 9.4% of all cancers and

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18.3% (123,907) of new cases in 2020. It still is among the commoner cancers in India and a leading cause of cancer-related deaths in women in lower- and middle-income countries^[1] Although the age-standardized incidence rate of cervical cancer decreased substantially by 39.7% (95% UI 265–57.3) from 1990 to 2016, it is the second leading cause of cancer deaths for females in 12 Indian states.^[2] The peak age of incidence of cervical cancer is 55–59 years, and a considerable proportion of women report in the late stages of the disease.^[3] The situation is more alarming in the rural areas, where the majority of women are illiterate and ignorant about the hazards of cervical cancer as well as health-care resources are scarce as reported.^[4] The incidence of cervical carcinoma is low in Kashmir as per studies.^[5]

In addition to HPV infection, early coitus, number of pregnancies, genital hygiene, use of oral contraceptives, nutritional status, smoking, etc., are associated with the development of cervical cancer. Various methods of treatment are used for cervical carcinoma depending on the stage. The previous studies have revealed that age, FIGO stage, histologic types, depth of stromal invasion, lymph vascular space invasion, and lymph nodes metastasis are aggressive characteristics of cervical cancer, which are regarded as significant factors for treatment, prognosis, and recurrence.^[6,7] Consequently, this study aimed to analyze the clinical pathological characteristics of women with cervical cancers in Kashmir and their impact on survival.

PATIENTS AND METHODS

This study was performed in the Department of radiation oncology, Government medical college Srinagar, Kashmir India. It was a retrospective analysis of patients with cervical carcinoma. A total of 50 patients were registered at our hospital out of which 31 patients were taken for the study and the remaining patients were excluded due to a lack of follow-up. The study population included all the histopathologically confirmed 31 cases of cervical cancer between January 2017 and December 2021. The study group was divided into two groups; Group A included 17 patients with squamous cell carcinoma histology and Group B included 14 patients with adenocarcinoma histology. The sociodemographic, clinical, radiological, and histopathological findings were retrieved into a structured pro forma. The other details included the type of treatment provided and post-treatment assessment, patients, and characteristics were analyzed under the following parameters age, FIGO stages grade (well-differentiated, moderately differentiated, and poorly differentiated), tumor histology, nodal status, lymphovascular invasion, and survival. In addition, treatment modalities such as surgery, radiotherapy, and chemotherapy were also included in the study.

The follow-up was done at 3 monthly for 1 year and then 6 monthly for another 2 years and then annually, by interval history, gynecological examination, and by radiologically. Adjuvant radiotherapy or concurrent chemotherapy was given in patients with high post-operative risk factors.

Results: total of 31 patients with cervical cancer were analyzed in the data. Table 1 summarizes the demographic and clinicopathological characteristics of the study. The majority of patients in Group A were in the age group of 60 (35.29%) and 40–49 (35.29%), while, in Group B, majority of patients were also in the age group of 60 (35.71%) and 40–49 (28.57%), respectively.

The majority of patients in Group A were having stage IIB 6 (35.29%), while 3 (17.64%) were having stage IIA, 4 (23.52%) were having stage III, 2 (11.57%) were having Ib2, and one patient had stage IVA (5.88%) and 1 (5.88%) had IVB. However, in Group B, majority of patients 6 (42.85%) were having II A, followed by 4 patients (28.57%) who had stage II B and 1 patient had stage III (7.14%), and 1 had stage IVB (7.14%) and 2 (14.28%) had stage Ib2.

The majority of patients in Group A were having well-differentiated histology 7 (41.17%), while, in Group B, majority were moderately differentiated 8 (57.14.0%), as shown in Table 1.

Out of 17 patients in Group A, 11 patients (64.70%) received concurrent chemoradiation followed by brachytherapy,

Table 1: Demographic and clinicopathological characteristics

		Demographic profile			
Variables	Category	Histology			
		GROUP A (Squamous cell carcinoma)		GROUP B (Adenocarcinoma)	
		n (17)	%	n (14)	%
Age	<39	1	5.88	4	28.57
	40–49	6	35.29	4	28.57
	50–59	4	23.52	1	7.14
	60+	6	35.29	5	35.71
Mean±SD		53±11.85		47±12.80	
FIGO	1b2	2	11.57	2	14.28
	IIA	3	17.64	6	42.85
	IIB	6	35.29	4	28.57
	III	4	23.52	1	7.14
	IVA	1	5.88	0	0.00
	IVB	1	5.88	1	7.14
	Grade	Moderately differentiated.	6	35.29	8
	Poorly differentiated	4	23.52	2	14.28
	Well-differentiated	7	41.17	4	28.57
Total		17		14	

while three patients (17.64 %) received adjuvant radiation and three patients (17.64%) received chemotherapy, while as in Group B, two patients (14.28%) received adjuvant radiotherapy and two patients (14.28%) received chemotherapy, nine patients (64.28%) received concurrent chemoradiation and brachytherapy, and 1 (7.14%) received chemotherapy after radiation, as shown in Table 2.

In Group A, seven patients (41.17%) had undergone surgery, four patients (23.52%) out of seven had lymphovascular invasion, and four patients (23.52%), out of seven were lymph node-positive; however, in Group B, eight patients (57.14%) had undergone surgery, five patients (35.71%), out of eight had lymphovascular invasion and all 8 (57.14%) patients had lymph node-positive.

Follow-up at 3 months, 15 patients (88.23%) had no evidence of diseases and two patients (11.76%) had residual diseases in Group A, while, in Group B, nine patients (64.28%) had no residual diseases; however, five patients (35.71%) had residual diseases. After a follow-up at 6 months, 14 patients (82.35%) had no evidence of diseases and 3 (17.64%) were metastatic in Group A,

while, in Group B, 11 patients (78.57%) had no evidence of diseases, while three patients (21.42%) had metastasis.

At 1 year of follow-up, in Group A, 14 (82.35%) patients were diseases free and two patients (11.76%) had metastasis, and 1 (5.88%) had died, while, as in Group B, two patients (14.28%) died, six patients (42.85%) were disease free, and one patient (7.14%) had local recurrence; however, five patients (35.17%) had metastasis.

Statistic

Survival analysis was done using SPSS 26, overall survival Kaplan–Meyer survival analysis, log-rank (Mantel-Cox) test of equality for survival distribution was used to explore P value <0.05 , was considered statistically significant. Overall survival percentage was more in Group A which is 59 months and 21 months for Group B. Mean survival time was 29.3 months for Group A and 22.2 months for Group B and that was a significant difference between the survival of the two groups ($P = 0.018$). The disease-free survival was 33 months for Group A and 24 months for Group B. There was a statistically significant difference between the two histological types in terms of DFS ($P = 0.012$).

TABLE 2: TREATMENT, RISK FACTORS AND OVERALL SURVIVAL

	GROUP A (Squamous cell carcinoma. N=17)		GROUP B (Adenocarcinoma N=14)	
Surgery				
No	10	58.82%	6	42.85%
Yes	7	41.17%	8	57.14%
Lymph Node				
Yes	4	23.52%	8	57.14%
No	13	76.47%	6	38.46%
Lymphovascular Invasion				
Yes	4	23.52%	5	35.71%
No	13	76.47%	9	64.28%
Treatment				
Chemotherapy	3	17.64%	2	14.28%
Concurrent chemoradiation+Brachytherapy	11	64.70%	9	64.28%
Adjuvant Radiation+Brachytherapy	3	17.64%	2	14.28%
Radiation+Chemotherapy+Brachytherapy	0	0.00%	1	7.14%
Follow-up at 3months				
No evidence of residual disease	15	88.23%	9	64.28%
Residual disease	2	11.76%	5	35.71%
Follow-up at 6 month				
Metastatic	3	17.64%	3	21.42%
No evidence of disease	14	82.35%	11	78.57%
Follow-up at 12months				
Death	1	5.88%	2	14.28%
Disease free	14	82.35%	6	42.85%
Local recurrence	0	0.00%	1	7.14%
Metastasis	2	11.76%	5	35.17%
Survivalat2 years				
Alive	11	64.70%	7	50.00%
Died	4	23.52%	4	28.57%
Metastasis	1	5.88%	1	7.14%
Survival at 3 years				
Alive	10	58.82%	2	14.28%
Disease free	1	5.88%	3	21.42%
Died	1	5.88%	3	21.42%

In this study, we found that advanced clinical stage, vascular invasion, parametrial invasion, and lymph node metastasis were high-risk factors influencing the prognosis of cervical cancer. However, prognosis had no significant correlation with age and histological grade. Although treatment for adenocarcinoma and squamous carcinoma was the same, they seemed to respond differently to treatment, high nodal positivity and lymphovascular invasion seemed to affect survival more.

DISCUSSION

Cervical cancer is the most common malignancy in developing nations after breast cancer among malignant tumors in women. There are still unresolved controversies in domestic and foreign studies on the prognostic factors of cervical cancer, especially in terms of pathological factors which are consistent with findings by Lapresa *et al.*^[8] Therefore, exploring the prognostic factors of cervical cancer, improving early detection rate, and developing effective treatment measures to improve survival rate are of utmost importance.

In our study, 31 patients were taken in the final analysis, out of which 17 patients (54.83%) were having (Group A) squamous cell carcinoma histology and 14 patients (45.16%) were having (Group B) adenocarcinoma histology which is similar to the study conducted by Vinh-Hung *et al.*^[9] The mean age in squamous cell carcinoma group was 53 ± 11.85 belonging to the range of <39–60+ and the mean age in adenocarcinoma group was 47 ± 12.80 ranging from <39 to 60+ which is similar to study conducted by Sreedevi *et al.*^[3]

In our study, most of the patients in Group A had stage IIB 6 (35.29 %) and in Group B stage IIA (42.85%) at presentation, which is similar to a study conducted by Mohumud *et al.*^[10] that staging has a prognostic value. The proportion of patients in Group A who underwent surgery was 41.17% and post-operative lymphovascular invasion was found in 23.52% and node positivity was seen in 23.52%. However, in Group B, 57.14% of patients who underwent surgery, 35.71% patients had lymphovascular invasion and 57.14% patients had lymph node positivity which is similar to a study conducted by Wang *et al.*^[11]

At follow-up of 3 months in Group A, 88.23% were disease free and 11.76% were having residual disease, while in Group B, 64.28% were disease free and 35.71% were having a residual disease. Patients in both groups having residual were subjected to chemotherapy and again followed at 6 months, it was found that in Group A, 82.35% were disease free and 17.64% had developed metastasis,

while, in Group B, 78.57% were disease free and 21.42% had metastasis.

At follow of 1 year, 82.35% were disease free, 11.76% of patients had metastasis, and 5.88% of patients had died in Group A, while, in the adenocarcinoma group, 42.85% of patients were disease free, 14.28% of patients had died, 7.14% patients had local recurrence, and 35.17% had metastasis, which are similar to studies conducted by Hu *et al.*^[12]

Overall survival for Group A was 51%, while, in Group B, it was 21%. Disease-free survival for Group A was 33 months and 24 months for Group B, these findings are consistent with studies done by Yamauchi *et al.*^[13] who found that despite giving the same treatment adenocarcinoma tends to behave differently.

Investigations comparing the prognosis of cervical adenocarcinoma with squamous cell carcinoma came up with varying results, with certain studies reporting adenocarcinoma tends to have a poorer prognosis compared to squamous cell carcinoma as reported by Nakanishi *et al.*^[14-18] and while a study done by Park *et al.*^[14-18] reported no statistically significant differences between the two groups.

Lymph node metastasis is commonly more aggressive in adenocarcinoma compared to squamous cell carcinoma and some studies reported a higher incidence of lymph node metastasis and poorer prognosis in adenocarcinoma compared to squamous after controlling for stage and tumor size. Therefore, a shorter progression-free survival was found in patients with adenocarcinoma, especially those in the early FIGO stage. The study by Zheng *et al.*^[19] found that 91% of the literature considered lymph node metastasis as an independent risk factor for poor prognosis. In addition, we also demonstrated that positive post-operative pathological factors, such as lymphovascular invasion, lymph node metastases, and parametrial involvement, could worsen the prognosis of adenocarcinoma patients more as compared with squamous. A study conducted by Zheng *et al.*^[19] found that vascular invasion is also an important factor associated with prognosis, our study also reveals similar results.

Among patients who received postoperative irradiation alone, the adenocarcinoma Group B exhibited a significantly poorer prognosis compared to the squamous cell Group A; there was no significant difference between the two groups among patients who received postoperative chemotherapy or concurrent chemoradiation. Similarly, patients with adenocarcinoma experienced more local failure in our study. We found that patients with Group B were more

likely to have distant failure. Cervical adenocarcinoma is more radio resistant compared to squamous suggesting that post-operative irradiation alone does not improve overall survival in patients with cervical adenocarcinoma which is also similar to a study done by Margolis *et al.*^[19,20]

The limitations of this study are that it was a retrospective and single-center study and, therefore, had a lower level of evidence. In addition, the sample size was small.

CONCLUSION

Our results suggest that lymphovascular invasion, parametrial involvement, and nodal involvement as independent predictors of shorter survival in patients with cervical adenocarcinoma. Adenocarcinoma was associated with a worse prognosis compared to squamous, particularly for patients who require post-operative treatment; such patients may benefit from individualized postoperative treatments that differ from those applied for squamous.

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