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Research Article

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Survival and prognostic factors for cervical cancer: a hospital based study in Mysuru, India

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ABSTRACT

Background: Cervical cancer is an important cause of morbidity and mortality among women and India has the largest burden of cervical cancer patients in the world. Survival studies measure the overall performance of patients after diagnosis or treatment. Knowledge of survival is essential to design strategies for prolonging the life of cervical cancer patients. The objectives of the study were to determine the survival rate and prognostic factors for cervical cancer.

Methods: This combined prospective and retrospective study was conducted during January 2012 to December 2012 among all the newly diagnosed cervical cancer patients from January 2006 to December 2007 at a tertiary care cancer hospital. Baseline data was collected by reviewing the medical records and cases were followed up for the next five years from the date of diagnosis to assess their survival status. Data was entered in Microsoft Excel and analyzed using SPSS 18. Survival analysis was done using the Kaplan Meier method. The Cox proportional hazards regression model was used to find the prognostic factors associated with cervical cancer.

Results: Among the 380 cervical cancer patients, overall survival rate was found to be 48.1%, 38.7% were dead and 13.2% lost to follow up. Age at diagnosis, performance status at presentation, staging and treatment duration were the prognostic factors for cervical cancer.

Conclusions: Five year survival rate for cervical cancer was found to be 48.1%. The prognostic factors of cervical cancer were potentially modifiable.

Keywords: Cervical cancer, Survival, Prognostic factors, Survival analysis

INTRODUCTION

Cervical cancer continues to have a major impact on women worldwide, particularly women in developing countries. Cervical cancer has been the most important cancer among women in India, over the past two decades. One in every five women in the world suffering from cervical cancer belongs to India which has the largest burden of cervical cancer patients in the world. It is predicted that if conditions remain the same

in India, by 2020, the number of women newly diagnosed with cervical cancer will be 1,82,027 and over a lakh (1,01,362) will succumb to the disease each year.³

Along with Human Papilloma Virus (HPV), there are various risk factors associated with cervical cancer such as early age at marriage, early age at first sexual intercourse, number of sexual partners, high parity, smoking, use of oral contraceptives, immunosuppressed states such as HIV infection.

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Survival refers to the life of a person after diagnosis of the disease. Survival studies measure the overall performance of a group of patients in terms of quality and quantity of life after diagnosis or treatment. It gives an overview of differences among populations pertaining to age, ethnicity, socio economic status, stage of diagnosis, treatment etc. Besides incidence and clinical stage at presentation, knowledge of survival is essential to monitor and evaluate cancer control programme. The lower survival rates in developing countries reflect lack of awareness, inadequate screening facilities, the advanced stages of disease at presentation and inadequate treatment due to poor patient compliance, financial constraints and inadequate treatment facilities.

This study was conducted to determine the survival rates and prognostic factors in cervical cancer patients. The observations from the present study will provide useful inputs for policy makers so that efforts can be directed towards universalization of cervical cancer detection and treatment.

METHODS

This combined prospective and retrospective study was conducted for a period of one year during January 2012 – December 2012 in a tertiary care cancer hospital at Mysuru. Institutional Ethics Committee approval and required permission from hospital authorities were obtained prior to the start of the study. The study subjects were 380 newly diagnosed cervical cancer patients during the period 1st January 2006- 31st December 2007. Patients who were registered prior to the study period and already on treatment were excluded from the study. Survival status of the patient at five years was assessed by follow up either through telephone, house visits and review of follow up details in the hospital registry taking feasibility factor into account.

A pre tested structured questionnaire was used to collect data regarding socio-demographic profile, details of reproductive factors, clinical features, diagnosis, treatment details and survival status of the patients. The socio demographic profile consisted of name, age, residential address, locality, religion, marital status, education and socio economic status. The modified B.G. Prasad's Classification was used to assess the socio economic status. ⁴Reproductive factors included age at marriage, age at first sexual intercourse, age at first pregnancy, parity and age at menopause. Symptoms of cervical cancer and its duration, performance status at presentation, history of reproductive tract and sexually transmitted infections were obtained. Diagnosis details included date and method of diagnosis, histology and International Federation of Gynaecology and Obstetrics (FIGO) staging.⁵ The survival status of the patient was assessed at the end of five years after diagnosis.

Data thus obtained was coded and entered into Microsoft Excel worksheet. This was analyzed using SPSS version 18. Survival analysis was done using the Kaplan Meier method. The Log rank test and Breslow test were used to test the statistical significance. Cox proportional hazards regression model was used to find the prognostic factors associated with cervical cancer.

RESULTS

In the present study consisting of 380 cervical cancer patients, 183 (48.1%) were alive, 147 (38.7%) were dead and 50 (13.2%) were lost to follow up by the end of 5 years. To find out the association of various factors influencing survival in cervical cancer patients, 330 patients were included since 50 were lost to follow up. Loss to follow up was due to migration of the patients, inability to trace the address and change in telephone numbers.

The survival rate was 53.8% among patients aged < 35 years when followed up for five years. 65.8% and 56.8% of the patients survived in the 35-49 and 50-64 years age group. Whereas among patients aged more than 65 years the survival was only 30.9%. The median survival time (14 months) was the highest among patients in the age group of 50- 64 years. Patients aged < 35 years as well as patients aged > 65 years had a median survival time of 6 months (Table1), (Figure 1).

Nulliparous women had a median survival time of 18 months whereas women who had given birth to >4 children had a median survival time of 12 months. Patients who had the habit of chewing tobacco had a median survival time of 8 months compared to 12 months in non chewers (Table 1).

Patients who were active at the time of presentation to the hospital had a median survival time of 14 months. The median survival time was only 3 months among the bedridden patients (Table 1), (Figure 2).

Patients who were diagnosed at an early stage had a better survival compared to those patients who were diagnosed at a later stage. The survival was 84%, 80%, 71.7%, 58.8%, 45.7% and 8.1% among patients belonging to stage I, IIA, IIB, IIIA, IIIB and stage IV respectively. Patients in stage I had a median survival of 35 months and patients in stage IV survived only for 4 months (Table 1), (Figure 3).

Patients who took treatment for < 4 weeks survived only for 8 months and those who took treatment for > 6 weeks had a median survival time of 22 months (Table 1), (Figure 4).

Cox proportional hazards regression model was used to find the independent predictors of survival. Age at diagnosis (hazard ratio = 2.17, p = 0.05), performance status at presentation (hazard ratio = 0.21, p = 0.001), staging (hazard ratio = 0.55, p = 0.001) and treatment

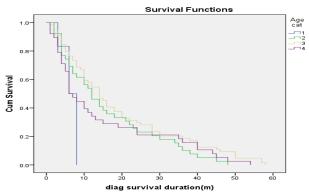
Table 1: Factors determining survival in cervical cancer patients and median survival time.

Factor	Median survival time (months)	Std. Error	95% CI	Log rank test	
				X^2	p value
Age (years)					
< 35	6	1.225	3.60 - 8.40		0.029
35-49	12	2.075	7.93 - 16.07		
50- 64	14	1.815	10.44 –17.56	9.041	
>65	6	1.156	3.74 - 8.27	J.U+1	
overall	11	1.010	9.02 – 12.98		
Education					
Illiterate	12	1.314	9.42 - 14.58		0.887
Primary school	3	1.414	.23 - 5.77		
Middle school	10	4.000	2.16 – 17.84	1 1 47	
High school	10	1.651	6.76 – 13.24	1.147	
Overall	11	1.010	9.02 – 12.98		
Parity					
Nulliparous	18	7.856	2.60 - 33.40		0.84
1-2	11	1.990	7.10 – 14.90		
3-4	10	1.573	6.92 - 13.08	0.833	
>4	12	2.209	7.67 – 16.33		
Overall	11	1.010	9.02 - 12.98		
Tobacco chewing*					
Yes	8	2.143	3.80 - 12.20		0.036
No	12	1.458	9.14 -14.86	4.413*	
Overall	11	1.010	9.02 - 12.98	7.713	
Presentation statu	\mathbf{s}				
Active	14	1.368	11.32 –16.68		0.001
Bedridden	3	0.577	1.87 – 4.13		
Overall	11	1.010	9.02 – 12.98	54.179	
Staging					
I	35	16.500	2.66 – 67.34		0.001
IIA	8	1.095	5.85 – 10.15		
IIB	14	2.639	8.83 – 19.17		
IIIA	8	2.619	2.87 – 13.13	22.064	
IIIB	14	1.384	11.29 –16.71	33.064	
IV	4	.398	3.22 -4.78		
Overall	11	1.010	9.02 – 12.98		
Treatment duration	on (weeks)				
< 4	8	1.996	4.09 – 11.91		0.004
4-6	14	2.644	8.82 - 19.18		
>6	22	6.573	9.12 - 34.88	10.813	
Overall	14	1.470	11.12 –16.88		

^{*}was used for breslow test

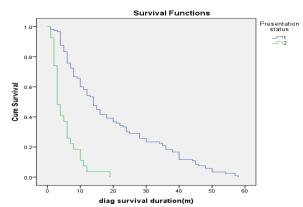
Table 2: Independent predictors of survival for cervical cancer.

Factor	β coefficient	Hazard ratio	p value	95% CI
Age (years)			0.05	
<35	0 .77	2.17	0.09	0.89 - 5.24
35- 49	-0.07	0.95	0.77	0.60 - 1.47
50- 64	-0.34	0.71	0.10	0.47 - 1.07
Education			0.90	
Illiterate	-0.65	0.52	0.52	0.07 - 3.79
Primary school	-0.43	0.65	0.69	0.08 - 5.26
Middle school	-0.65	0.52	0.53	0.07 - 3.96
High school	-0.80	0.45	0.45	0.06 - 3.51
Parity			0.86	
Nulliparous	-0.08	0.93	0.85	0.42 - 2.07
1-2	0.16	1.17	0.47	0.76 - 1.80
3-4	0.11	1.12	0.58	0.75 - 1.68
Menopause (years)			0.29	
< 40	0.27	1.31	0.56	0.53 - 3.24
40 - 45	-0.10	0.91	0.81	0.40 - 2.06
Tobacco Chewing	0.27	1.31	0.17	0.89 - 1.92
Performance status	-1.54	0.21	0.001	0.14 - 0.34
Staging			0.001	
I	-1.46	0.23	0.01	0.08 - 0.66
IIA	-0.60	0.55	0.26	0.21 - 1.41
IIB	-1.23	0.29	0.001	0.17 - 0.50
IIIA	-1.06	0.35	0.01	0.15 - 0.79
IIIB	-0.93	0.40	0.001	0.26 - 0.60
Treatment duration(weeks)			0.008	
<4	0.67	1.96	0.18	0.74 - 5.18
4-6	-0.08	0.92	0.86	0.37 - 2.28



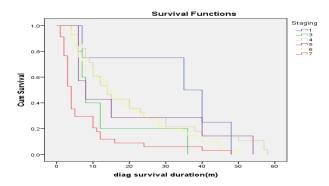
Age category: 1- <35 years; 2- 35 to 49 years; 3- 50-64 years; 4- >65 years.

Figure 1: Age at diagnosis and diagnosis survival duration.



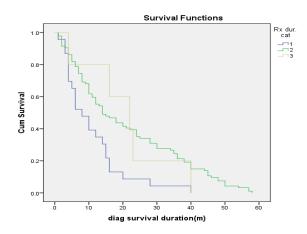
Performance status: 1: Active; 2: Bedridden.

Figure 2: Performance status at presentation and diagnosis survival duration.



Staging: 1- stage I; 3-stage IIA; 4-stage IIB; 5-stage IIIA; 6-stage IIIB; 7-stage IV

Figure 3: Staging and diagnosis survival duration.



Treatment duration: 1-<4 weeks; 2-4 to 6weeks; 3->6 weeks.

Figure 4: Treatment duration and diagnosis survival duration.

duration in weeks (hazard ratio = 1.96, p < 0.01) were the independent predictors of survival (Table 2).

DISCUSSION

Cervical cancer is an important cause of morbidity and mortality among women. Survival studies indicate the overall performance of a group of patients after diagnosis or treatment. The present study was undertaken to determine the survival rates and prognostic factors for cervical cancer in Mysuru.

The 5 year survival rate for cervical cancer was 48.1% in the present study. The overall 5-year relative survival during 2003 -2009 for 18 Surveillance Epidemiology End Result (SEER) geographic areas was 67.9%. In studies conducted in 23 Population Based Cancer Registries (PBCR) worldwide, the 5-year Age Standardized Relative Survival (ASRS) ranged from 63–79% for cervical cancer in China, Singapore, South Korea and Turkey. The 5 year age standardized relative survival in India was 46(34-60), Gambia -22 and Uganda -13. Survival was highest in Hong Kong, South Korea, Singapore, and Turkey where

health services are well developed. Survival was intermediate in Costa Rica, mainland China, Thailand, India, Saudi Arabia, Pakistan, and Philippines, where cancer health services are moderately developed with diagnostic and treatment facilities centred in urban areas. Survival was lowest in The Gambia and Uganda, with poorly developed health services. The large variations in survival within populations in regions of China, India, and Thailand reflect varying levels of development of cancer health services, particularly in urban versus rural areas. In India, marked differences in survival for most cancers were noted between rural (Barshi), semi-urban (Karunagappally), or small urban (Bhopal) registries, whereas differences were small between the metropolitan cities of Chennai and Mumbai, where more developed and accessible health-care services are available.

In the present study, the 5 year survival rate was 53.8%, 65.8%, 56.8% and 30.9% respectively in <35years, 35-49 years, 50-64 years, >65 years age group respectively. In a hospital based study in Kerala, the five year survival was 33.4%, 46.7%, 48.3% and 61% among patients aged <35 years, 35-49 years, 50-64 years and >65 years respectively. As per the population based Osaka Cancer Registry data during 1993- 1996, the relative 5 year survival was 88.6% in <30 years, 78.1% in 30-54 years, 67.7% in 55-64 years and 54.4% in >65 years.9 In Gambia, the age specific relative survival was 26.4%, 20.2%, 22.5%, 13.2% and zero respectively in <45 years, 45-54 years, 55-64 years, 65-74 years and >75 years. 10 The age specific relative survival was 63.4%, 59.9%, 55.8%, 58% and 69.4% respectively in <45 years, 45-54 years, 55-64 years, 65-74 years and >75 years in Chennai. 11 The age specific relative survival was 61.1%, 48.6%, 32.7%, 24% and 20.9% respectively in <45 years, 45-54 years, 55-64 years, 65-74 years and >75 years in Mumbai. 12 As the age at diagnosis was delayed, the survival rate of cervical cancer patients was lesser.

In the present study, illiterate patients had lesser survival compared with literate patients. Similarly, in a study done by Sankaranarayanan et al. the five year survival was 45.2% among the illiterates. The contributing factors are low standards of hygiene, coitus or marriage at an early age, early age at first pregnancy, multiparity. The risk of cervical cancer increases with early age at first pregnancy^{13,14} and number of births. ^{13,15,16}

The present study showed a survival rate of 84%, 80%, 71.7%, 58.8%, 45.7% and 8.1% among patients belonging to stage I, IIA, IIB, IIIA, IIIB and stage IV respectively. In a study done in Kerala, 69%, 61.5%, 52.8%, 43%, 28% and 0% survived in stage IB, IIA, IIB, IIIB, IVA and IVB respectively. 8

Age at diagnosis, performance status at presentation, staging and treatment duration were the independent predictors of survival in the present study. In a study conducted in Kerala, socioeconomic status, performance

status and the clinical stage of the disease were the independent predictors of survival. 8

CONCLUSION

The 5 year survival rate for cervical cancer was 48.1%. Age at diagnosis, performance status at presentation, staging and duration of treatment were the prognostic factors for cervical cancer. Emphasis should be on creating awareness regarding cervical cancer from the adolescent age group through school health programmes; providing screening facilities; accessible and affordable diagnostic and treatment facilities form the level of primary health care.

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Ethical approval: The study was approved by the

Institutional Ethics Committee

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