DETERMINANTS OF SURVIVAL AMONG PATIENTS WITH CERVICAL CANCER: A HOSPITAL BASED STUDY

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ABSTRACT

Introduction: Cervical cancer is the fourth most common cancer among women worldwide and India contributes largest proportion to it. As per Globacon 2012 there were 1,23,000 cases and 67,000 deaths due to cervical cancer in India. Studies directed towards identifying the factors determining survival will help policy makers in designing the strategies for prolonging the life of these patients. Objective of the study was to assess the factors determining survival among patients with cervical cancer.

Methodology: This combined prospective and retrospective study was conducted during January 2012- December 2012 (One year) among all the newly diagnosed cases of cervical cancer 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.

Results: Among 380 patients included in the study, overall five year survival rate was found to be 48.1%, 38.7% had lost their life and 13.2 % lost to follow up. Age at diagnosis, education, performance status at presentation, staging (p = 0.001), parity, tobacco chewing (p< 0.01) and age at menopause (p = 0.05) were significantly associated with survival.

Conclusion: Five year survival rate for cervical cancer was found to be 48.1%. Various factors determining survival were potentially modifiable.

Key words: Cervical cancer, survival, modifiable factor, followup

INTRODUCTION

Cervical cancer is an important cause of morbidity and mortality among women. It is the fourth most common cancer among women world wide.[1] There were 5,28,000 cases and 2,66,000 deaths due to cervical cancer in 2012. The burden of cervical cancer is high in developing countries, where screening programmes are not well established or are minimally effective. In India, there were 1,23,000 cases and 67,000 deaths due to cervical cancer in 2012.[1]

Cervical cancer is more common among women living in poor conditions, with low income levels and lack of education. 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, more number of sexual partners, high parity, smoking, use of oral contraceptives, tobacco chewing, immunosuppressed states such as HIV infection.[2-5]

Survival refers to the life of a person after diagnosis of the disease. Survival analysis from Population Based Cancer Registries (PBCR) indicates that the mean age of diagnosis in India is 50 years. The five year age standardized relative survival in India was 46%. Marked difference in survival was noted in the urban and rural registries due to presence of cancer health services mainly in the cities. The low survival rate in India indicates lack of awareness, inadequate screening facilities, diagnosis of the cancer in the advanced stages and lack of access to affordable treatment. [6-8]

This study was conducted to assess the factors which determine the survival rates in cervical cancer patients. Studies directed to identify these factors help policy makers in designing the strategies for prolonging the life of these patients.

METHODS

This combined prospective and retrospective study was conducted in a tertiary care cancer hospital at Mysore city for a period of one year during January 2012 – December 2012. Approval from Institutional Ethics Committee and required permission from hospital authorities were obtained prior to the start of the study. The study was conducted among all the 380 newly diagnosed cancer cervix patients during the period 1st January 2006- 31st December 2007. Patients of cancer cervix 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.

Details related to socio-demographic profile, details of reproductive factors, clinical features, diagnosis and treatment details and survival status were collected in a pre tested structured questionnaire.

Table 1: Socio-demographic characteristics and association with survival in cervical cancer

Factor	5 year survival			χ^2	p value
	Survived (n=183)	Died (n=147)	Total (n=330)		
Age (years)					
<35	7 (53.8)	6 (46.2)	13	18.5	**0.001**
35- 49	75 (65.8)	39 (34.2)	114	d.f =3	
50- 64	84 (56.8)	64 (43.2)	148		
>65	17 (30.9)	38 (69.1)	55		
Religion					
Hindu	165(54.1)	140(45.9)	305	4.13*	0.224
Muslim	14(73.7)	5(26.3)	19	d.f = 3	
Christian	2(100)	0(0)	2		
Buddhist	2(50)	2(50)	4		
Locality					
Rural	128(54.7)	106(45.3)	234	0.19	0.667
Urban	55(57.3)	41(42.7)	96	d.f = 1	
Education					
Illiterate	98 (46.9)	111 (53.1)	209	23.13*	**0.001**
Primary School	30 (78.9)	8 (21.1)	38	d.f = 6	
Middle School	19 (54.3)	16 (45.7)	35		
High School	32 (74.4)	11 (25.6)	43		
Pre University	2 (66.7)	1 (33.3)	3		
Degree	1 (100)	0 (.0)	1		
Post graduate	1 (100)	0 (.0)	1		
Socio Economic Status					
I	9 (69.2)	4 (30.8)	13	4.02	0.403
II	33 (62.3)	20 (37.7)	53	d.f = 4	
III	64(54.2)	54 (45.8)	118		
IV	49 (57)	37 (43)	86		
V	28 (46.7)	32 (53.3)	60		
Marital status					
Unmarried	0(0)	1(100)	1	3.79*	0.240
Married	121(58.7)	85(41.3)	206	d.f = 3	
Separated	1(33.3)	2(66.7)	3		
Widow	61(50.8)	59(49.2)	120		

* Fisher's Exact Test

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.[9]

Reproductive factors such as age at marriage, age at first sexual intercourse, age at first pregnancy, parity, history of oral contraceptive pill (OCP) use and duration of usage, age at menopause were obtained. Clinical history included details of symptoms and its duration, performance status at presentation, history of reproductive tract and sexually transmitted infections. Diagnosis and treatment details included date and method of diagnosis, histology and FIGO staging,[10] date of starting treatment, type of treatment taken and duration of treatment, side effects and complications following treatment. 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. Chi square test was used to test the association between various factors and survival. Independent sample 't' test was used to compare between the means and standard deviations. The differences and associations were interpreted to be statistically significant at $P<0.05$.

Table 2: Various factors associated with survival in cervical cancer

Factor	5 year survival			χ^2	p value
	Survived (n=183)	Died (n=147)	Total (n=330)		
Age at marriage (years)#					
< 15	5 (38.46)	8 (61.54)	13	5.71*	0.116
15-20	133 (54.73)	110 (45.27)	243	d.f = 3	
21-25	40 (58.82)	28 (41.18)	68		
>25	5 (100)	0 (.0)	5		
Age at first sexual intercourse (years)#					
< 15	5 (38.46)	8 (61.54)	13	5.71*	0.116
15-20	133 (54.73)	110 (45.27)	243	d.f. = 3	
21-25	40 (58.82)	28 (41.18)	68		
>25	5 (100)	0 (.0)	5		
Age at first pregnancy (years)@					
15-20	117 (53.7)	101 (46.3)	218	2.49*	0.498
21-25	45 (63.4)	26 (36.6)	71	d.f = 3	
26-30	18 (60)	12 (40)	30		
>30	1 (50)	1 (50)	2		
Parity					
Nulliparous	2 (22.2)	7(77.8)	9	13. 5*	**0.003**
1-2	57 (56.4)	44 (43.6)	101	d.f = 3	
3-4	92 (63.9)	52 (36.1)	144		
>4	32 (42.1)	44 (57.9)	76		
Age at menopause (years)$					
<40	0 (.0)	3 (100)	3	6.92*	**0.05**
40-45	40 (43)	53 (57)	93	d.f = 3	
46-50	60 (56.6)	46 (43.4)	106		
>50	4 (66.7)	2 (33.3)	6		
OCP use					
Yes	105 (64.8)	57 (35.2)	162	11.29	**0.001**
No	78 (46.4)	90 (53.6)	168	d.f = 1	
Tobacco chewing					
Yes	21 (36.8)	36 (63.2)	57	9.66	**0.002**
No	162 (59.3)	111 (40.7)	273	d.f = 1	
Performance status at presentation					
Active	183 (60.4)	120 (39.6)	303	36.61	**0.001**
Bedridden	0 (.0)	27 (100)	27	d.f = 1	
Staging					
I	21 (84)	4 (16)	25	63.52	**0.001**
IIA	20 (80)	5 (20)	25	d.f = 5	
IIB	71 (71.7)	28 (28.3)	99		
IIIA	10 (58.8)	7 (41.2)	17		
IIIB	58 (45.7)	69 (54.3)	127		
IV	3 (8.1)	34 (91.9)	37		

* Fisher's Exact test; ; #Data for one died subject was not included due to incomplete data;
@Total for survived is 181 and died is 140; $Total for survived is 104 and died is 104

RESULTS

Among the 380 patients included in the study, 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. Since 50 patients were lost to follow up, 330 patients were included for finding out the association of various factors with cervical cancer. Loss to follow up was due to migration of the patients, inability to trace the address, change in telephone numbers. 114 (44.8%) were in the age group of 50 – 64 years. Most of the patients were Hindus (92.4%), from rural areas (70.9%), illiterates (63.3%) and belonged to class III socio economic status (35.8%) and married (62.4%). (Table 1)

In the present study, majority of patients were Hindus but 54.1% survived for 5 years. Survival was higher in urban (57.3%) than rural residents (54.7%). Only 46% illiterate patients had survived (p = 0.001). Survival in class I socio economic status was 69.2% where as in class V it was 46.7%. 64.8% patients using OCP survived compared to 46.4% non users (p = 0.001). Tobacco chewing was associated with a lower survival rate of 36.8% (p < 0.01). Patients who were active at the time of presentation to hospital had a survival of 60.4% (p = 0.001). 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 (p = 0.001) (Table 1, 2).

Survival was highest in 35 – 49 years age group (65.8%) and least in > 65 years age group (30.9%). The mean age at diagnosis was greater among the patients who died (55.45 + 13.13) compared to those who survived (49.69 + 10.74) from cervical cancer. This difference was statistically significant (p = 0.001). Survival was 100% among patients who married after 25 years of age and 38.46% among the patients who were married at < 15 years of age. Patients who had their first pregnancy at an early age had a lower survival compared to those who had their first pregnancy after the age of 20 years. Patients with parity >4 had a lower survival (42.1%) compared to those who had parity 1- 2 (56.4%). This was statistically significant (p < 0.01). None of the patients who had their menopause at age < 40 years survived. But survival was 66.7% among the patients who had their menopause after 50 years of age (p = 0.05) (table 2, 3).

In the present study survival was better in patients diagnosed at a younger age, from urban areas, higher socioeconomic status and those who were married. Survival was low among the illiterate patients. Early age at marriage, early age at first pregnancy, more number of children and early menopause were associated with lower survival rates. Survival was better in patients using OCP. Survival was poor in patients who had the habit of chewing tobacco. Survival was better in patients who were active at the time of presentation. Stage of cervical cancer was significant in determining survival.

Table 3: Comparison of various quantitative variables between subjects who survived and died in five years

Factor*	Survived (Mean±SD)	Died (Mean±SD)	p value
Age at diagnosis	49.69±10.74	55.45±13.13	0.001
Age at marriage	18.52±2.94	18.02±2.92	0.126
Age at first sexual intercourse	18.52±2.94	18.02±2.92	0.126
Age at 1st pregnancy	20.20±3.71	19.49±3.63	0.085
Parity	3.24±1.55	3.59±1.97	0.071
Age at menopause	46.18±2.53	45.48±2.90	0.064

*all figures in years

DISCUSSION

Studies from 23 PBCR s worldwide show 5 year survival of 63–79% for cervical cancer in China, Singapore, South Korea and Turkey. Five year survival in India was 46(34-60), Gambia -22 and Uganda -13. [6] The overall 5-year relative survival for 2003-2009 from 18 Surveillance Epidemiology End Result (SEER) geographic areas in U.S.A was 67.9%.[11]The survival was 42.2% in the Mumbai Cancer Registry during 1992- 1999.[12]In Hospital Based Cancer Registry (HBCR), Trivandrum, Kerala, overall 5 year survival rate was 47.4%. [13]The survival rate in cervical cancer patients in the Chennai PBCR during 1990 – 1999 was 54%. [14]

The mean age at diagnosis was greater among the patients who died (55.45 + 13.13) compared to those who survived (49.69 + 10.74) from cervical cancer. As per the data from HBCR s, cervical cancer is found more commonly in women aged between 40 and 54 yrs.[13] As per the SEER, the median age at diagnosis for cancer of the cervix uteri was 49 years of age.[11] 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.[13] The age specific relative survival was 63.4%, 59.9%, 55.8%, 58% and 69.4% respectively in < 45 years, 45-54 years, 55-64years, 65-

74 years and > 75 years in Chennai.[14]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] The age at diagnosis in our study was later compared to the above studies. This indicates that there is a lack of awareness about the disease, no proper screening facilities to diagnose the disease at an early age.

Study done by V.Patil et al. in Nagpur stated that illiteracy was significantly associated with the risk of cervical cancer.[7]In a study done by Sankaranarayanan et al. the five year survival was 45.2% among the illiterates.[13]This finding was similar to the present study.

The survival was highest among patients in class I (69.2%) and lowest among patients belonging to class V (46.7%).In a study done by Sankaranarayanan et al. the five year survival was 43.6% in the low socio economic groups and 85.6% in patients belonging to the higher socio economic status.[13]

Early age at marriage implies early age at first pregnancy and the possibilities of having more number of children. Most of the patients had their first sexual intercourse at an early age predisposing to HPV infection and development of cervical cancer. The risk of invasive cervical cancer increased with younger age at first intercourse.[2, 4] Most of the patients had their first pregnancy at 15- 20 years of age. The risk of carcinoma cervix increased with early age at first birth.[2, 4]The risk of cervical cancer increased with the number of births.[2, 7,16]

In the present study, survival was better among the patients who had used oral contraceptive pills (64.8%) and this was statistically significant. There was a strong positive association between OCP use and the risk of cervical cancer.[2, 4, 17, 18]So, this study suggests that oral contraceptive pills have a protective effect on cervical cancer.

Stage at presentation was the strongest factor in the prediction of five-year survival; 86% in stage I survived compared with 58 % in stage II , 31% in stage III and 0 in stage IV.[19]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.[13]

CONCLUSION

Age at diagnosis, education, performance status at presentation, staging, parity, tobacco chewing and age at menopause were associated with survival. As many of the factors affecting survival are modifiable, efforts have to be made early through educational intervention regarding the risk factors for cervical cancer to the adolescent age groups through School Health Programme, community awareness through women Self Help Groups /Mahila Mandals and also through mass media to the general public. Efforts should be made to provide accessible and affordable diagnostic and treatment facilities for cervical cancer at least from the taluka level as a decentralization effort.

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