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ORIGINAL ARTICLE

Survival Rate in Cancer Cervix Patients in a Regional Cancer Centre of South India: A Retrospective Analysis

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Abstract

Context Carcinoma Cervix is one of the leading prevalent cancers in India especially in rural population and causes a significant mortality. WHO has launched many projects for prevention, screening and treatment plans. Even after many projects, Cervical Cancer persists as a heavy burden public health problem in rural India.

Aims To calculate survival of cancer cervix patients in a rural population-based RCC and to discuss the factors affecting it.

Methods and Material A hospital-based gathering of retrospective data of the patients diagnosed with carcinoma cervix over 5 years from January 2013 to December 2017 (single institution analysis). We included 751 patient's data from our cancer registry for analysis. Data related to demographics, treatment and follow up records were taken and statistical analysis done.

Results The survival rates were 64.0%, 50.0%, 36.9% and 17.5% for Stage I, Stage II, Stage III and Stage IV, respectively. The best survival outcomes were for those treated with only surgery. Involvement of nodes had poor survival than those with no involvement. Various patient-related factors like Religion, Education and Marital status are found to be non-significant factors even-though they have survival differences. STAGE of the disease emerged as a significant prognostic factor.

Conclusion Our study concluded that higher stage and nodal involvement had poor outcomes and also lower survival compared to Western and Indian literature. We should also address all the socio-economic factors that affects survival. Randomized prospective studies are needed to evaluate the effect of socio-economic factors on survival.

Keywords Cervical cancer · Rural · Socio-economic · Stage · Survival

Introduction

According to GLOBOCAN 2020, nearly 604,100 new cases of Cervical Cancer are diagnosed every year and around 341,831 patients die due to the disease every year [1]. In India around 1.2 lakh new cases of cervical cancer are diagnosed every year which accounts for one-fifth of the global burden [2]. Around 77,000 people die every year due to cervical cancer in India. It accounts for 9.5% of all cancers diagnosed in India every year [2].

It is one of the leading cancers in women and also a leading cause of mortality especially in rural populations. This is because the majority of the rural population are unaware of screening methods and HPV vaccination, poor sexual practices, poor access to health care, and late diagnosis leading to treatment failure. Elderly people and people with low socio-economic status are vulnerable groups for developing cervical cancer but it is still controversial how they interact with these factors and which of these factors have a huge impact on screening, diagnosis, and survival of patients [3]. Various risk factors commonly encountered in the rural population are early age marriage, early age of sexual intercourse, poor sexual practices and multiple sexual partners, early age pregnancy, etc., and all these lead to increased risk of HPV infection among them which in turn leads to increased risk of

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cervical cancer. 70% to 75% of cervical cancers are due to high-risk HPV subtypes 16 and 18. Several cofactors have been identified that may contribute to the development of HPV carcinogenesis. These include smoking, high parity, and coinfection with other sexually transmitted diseases. The development of HPV vaccines is based on this strong causative factor and association between high-risk HPV subtypes and cervical carcinoma. So, in 2014, WHO concluded that immunologic evidence was sufficient to recommend a schedule of two doses administered with at least a 6-month interval to girls younger than 15 years old. Even after WHO recommendations and multiple health projects, the existence and clinical use of HPV vaccination in rural populations is subtle and doesn't change the rates of cervical cancer in rural populations.

Squamous cell cancer is the predominant subtype followed by adenocarcinoma. Other histological subtypes are rare constituting less than 3%. The prognosis of rural patients tends to be poorer than urban population. The two important reasons for this are lack of access to standard health care and advanced-stage diagnosis. This inequality in cancer survival between and within countries is largely due to the differences in awareness about sexual practices and risk of cervical cancer, availability of screening practices, socio-economic and cultural factors, and accessibility to tertiary cancer institutes, diagnosis, and treatment [4]. Late-stage diagnosis and delay in treatment of cervical cancer results in poor survival outcomes in low-resource settings, even though it is a preventable one [5]. We all know the FIGO stage directly correlates with prognosis. So early diagnosis is important in improving the survival of the patient.

Considering all these factors, we did a retrospective analysis of all cancer cervix patients in our institute by collecting data from our cancer registry. We describe in this study the incidence, demographics related to patient and tumor factors, and survival outcomes.

Methods

Study Population and Data Collection

A hospital-based gathering of retrospective data of the patients diagnosed with Cancer Cervix from a Regional Cancer Centre of South India over 5 years from January 2013 to December 2017 (data taken from our cancer registry). Most of our patients are from rural population-around 90%.

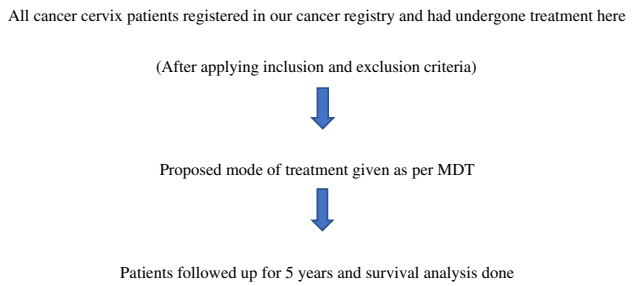
Inclusion Criteria

- Any age
- Diagnosed as Carcinoma cervix of any stage
- with HPE and imaging done.
- should be registered in our cancer registry and treated in our institute.
- must be complaint and willing for regular follow up as per protocol
- all patients will be included in study irrespective of the mode of treatment

Exclusion Criteria

- Patients diagnosed in our institute and not willing for further treatment here.
- Patients not under proper follow up and unable to trace the contact.

Nearly 1083 patients are registered in our registry but only around 751 patients are eligible for our analysis. Patients fulfilling the inclusion criteria will be recruited in our analysis. All data regarding clinical history, histo-pathological report, stage of disease, and imaging findings are taken. All patients received the proposed line of treatment based on Stage, Performance status, and Multi-Disciplinary Team decision. Patients followed up for 5 years post-therapy to calculate the overall survival.



Follow Up Protocol

- Every 3 to 6 months for the first 2 years
- Every 6 to 12 months for 3 to 5 years
- Imaging as needed
- Laboratory assessment (Complete Blood count, Blood Urea and Creatinine) as indicated based on symptoms or examination findings suspicious for recurrence
- Patient education regarding symptoms of recurrence and periodic self-examinations

Statistical Analysis

Patients who did not complete their treatment, patients who went for treatment somewhere else after diagnosis but

registered in our cancer registry, and patients who didn't turn in for follow-up or were not willing for follow-up are excluded from our analysis. We only included 751 patients in our analysis after applying inclusion and exclusion criteria. Demographics related to patient and tumor factors such as Age, Marital status, Education, performance status, Histo-Pathological report, stage (FIGO 2018), and type of treatment given are recorded and analysis done. Follow-up records of all patients were taken and survival analysis was done using the Kaplan–Meier method and SPSS software to calculate OS which is our endpoint.

Results

751 Cancer Cervix cases are included in our analysis. The most common age group affected are 40–60 years. Characteristics of Age distribution, Marital status, Religion, and Education are illustrated in Table 1. It clearly explains that around 24% of our treated population is widowed, which causes various difficulties in undergoing treatment and follow-up and there indirectly affects survival. Similarly, Education of the patient can affect survival indirectly through cultural and sexual practices, attitudes, beliefs, and the importance of all forms of treatment and adherence to follow-up.

Table 1 Distribution of patients general characteristics

	Number	Percentage (%)
Age in years		
21–40	90	11.9
41–60	473	62.9
61–80	186	24.7
> 80	2	0.27
Marital status		
Married	560	74.57
Unmarried	3	0.4
Widowed	182	24.23
Separated	6	0.8
Religion		
Christian	19	2.5
Hindu	720	95.8
Muslim	12	1.6
Education		
Illiterate	380	50.60
Primary school	108	14.38
Middle school	57	7.5
Secondary school	17	2.26
Degree holder	4	0.5
Unknown	185	24.6

Squamous cell carcinoma is the most common histology which constitutes about 88.9% of cases followed by adenocarcinoma- 9.7%, small cell carcinoma-0.26%, and other rare histologies-1.19%.

The most common Stage of presentation in our analysis is II B (n = 196, 26%) followed by III C1 (n = 148, 19.7%) and III B (n = 137, 18.2%). The detailed distribution of individual stages is represented in Table 2. But as a whole, FIGO stage 3 patients are higher (n = 385, 51.3%) compared to stage 2 patients (n = 228, 30.4%) concerning the stage-wise distribution of cervical cancer patients. Locally advanced cases are most-commoner in our institution which in turn affects overall survival.

Patients were treated based on their performance status, Stage at presentation, and as per MDT decision. Patients have undergone either single-modality treatment or multimodality treatment. Concurrent Chemo-Radiation is the most common treatment given since the majority of cases are locally advanced cases (n = 460, 61.3%) followed by radiotherapy alone (n = 217, 28.9%). Surgery with or without adjuvant treatment is given for 52 patients (6.92%). Kaplan–Meier analysis (Fig. 1) based on various modalities of treatment given shows that patients treated with surgery alone have the highest survival (early cases) followed by surgery with or without adjuvant treatment (early cases with high-risk features) followed by concurrent chemoradiation (locally advanced cases). Patients treated with chemotherapy alone have the least survival (metastatic disease). This concluded that treatment based on stage is the independent prognostic factor for survival.

Survival drops as the stage increases. But in our analysis, a notable difference is, survival is low for all stages (stage 1 -64%, stage 2–50%, stage 3–36.9%, stage 4–17.5%-Table 3) compared to a standard study from TATA memorial hospital, India (stage 1– 83.5%, stage 2–80.6%, stage 3–66%, stage 4–37.1%). Also, survival from our institute is low

Table 2 Individual stage-wise distribution of cases

Stage	Frequency	Percent (%)
IA1	2	0.3
IA2	4	0.5
IB1	26	3.4
IB2	43	5.7
IIA	32	4.2
IIB	196	26.1
III A	13	1.7
III B	137	18.2
III C1	148	19.7
III C2	87	11.5
IV A	29	3.8
IV B	34	4.5
Total	751	100

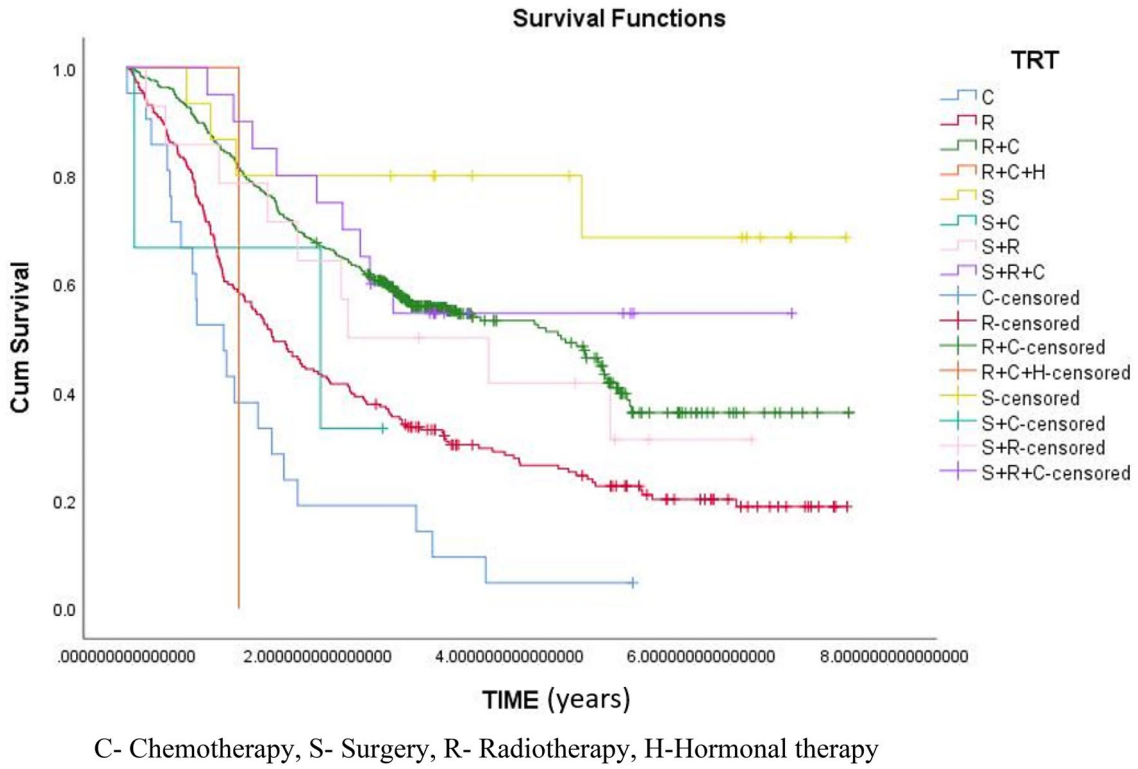


Fig. 1 Kaplan–Meier analysis–survival based on individual treatment modalities. C-Chemotherapy, S-Surgery, R-Radiotherapy, H-Hormonal therapy

Table 3 Survival rate based on stage of disease

Stage	Total of patients	No of events	Remaining alive	Survival percentage (%)
Stage 1	75	27	48	64.0
Stage 2	228	114	114	50.0
Stage 3	385	243	142	36.9
Stage 4	63	52	11	17.5
Overall	751	436	315	41.9

compared to Western literature-SEER data (stage 1–92%, stage 2- 84%, stage 3–58%, stage 4–18%). This difference in survival can be attributed to various other factors like socio-economic status, the patient's geography (rural or urban), the patient's general condition and nutrition, adherence to treatment protocol and follow up and finally advances in treatment modalities. All these factors lack in many of the rural population-based cancer centers in our country leading to diminished survival rates compared to standard literature. Figure 2, Kaplan–Meier curves on survival demonstrating significant survival differences based on stage. This again confirms stage of the disease is the most independent predictor for survival. Our findings are similar to a study conducted by Ganesh Balasubramaniam et al [6].

Multivariate analysis for overall survival of Education, Religion, Marital status, and FIGO stage was done (Table 4). With regards to the education and marital status of patients, there is no significant survival difference but the FIGO stage (p-value < 0.008) and histological subtype (p-value $= 0.04$) have significant survival differences. From our analysis, the FIGO stage and Histological sub-type are significant prognostic factors for survival.

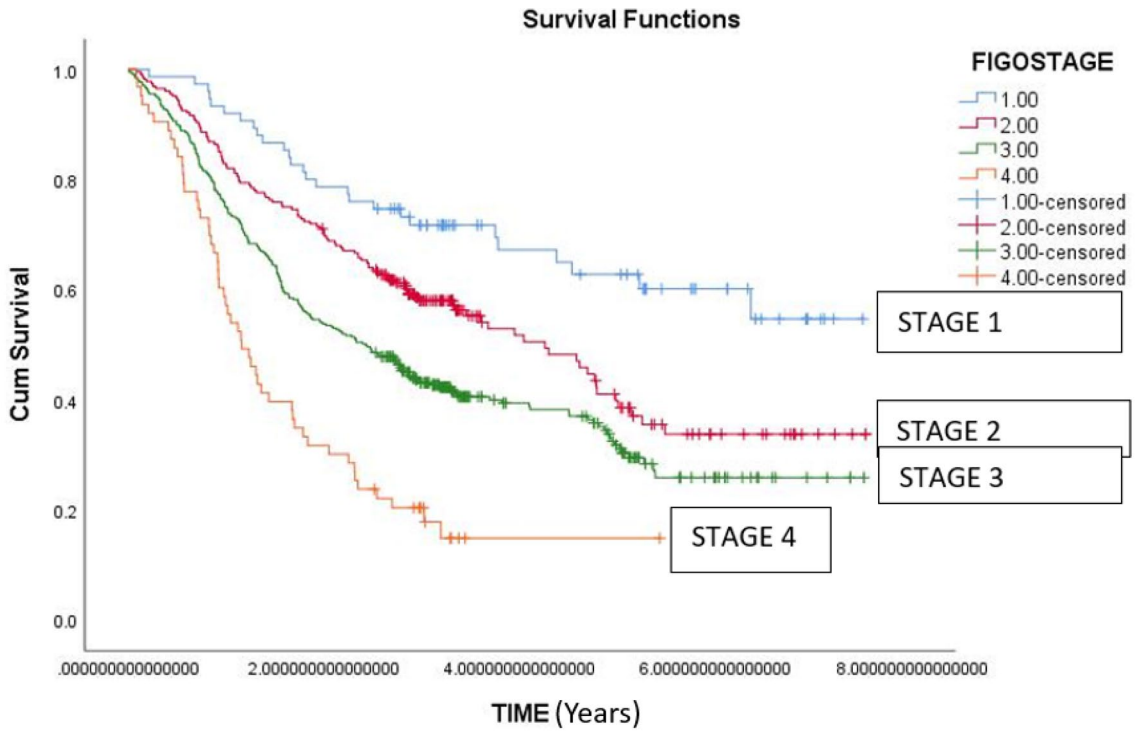


Fig. 2 Kaplan–Meier analysis–survival based on figo stage

Table 4 Multi-variate analysis for survival

Various factors	5-year survival	*P*-value
Education		
Illiterate	40.70%	0.1
Literate	43%	
Religion		
Hindu	40%	
Christian	44.80%	0.2
Muslim	43.10%	
Marital status		
Married	43.90%	
Widowed	39.30%	0.82
Unmarried	42.20%	
Histological sub-type		
Squamous	45.70%	0.04
Adeno	38.10%	
Figo stage	41.90%	< 0.008

Discussion

Cervical Cancer is more common in Rural places of our country than in urban and western populations [7]. There have been variations in Cervical cancer based on location and treatment facilities available and that affects Health infrastructure Nationally and also globally. In-equality in Cervical Cancer survival is attributed due to various geographic, cultural, medical, genetic, and socioeconomic factors [8–10]. Few Western literatures showed there is no association between socioeconomic status and Cervical cancer survival [11]. But one South Indian study from Kerala showed socio-economic factors can affect Cervical cancer survival [12]. In a real-life scenario, one's socioeconomic status and factors can improve or decline during a timeline which makes us difficult in conducting a prospective study to find an association between socio-economic factors and survival. Also, these factors vary from place to place and cannot be uniform and standard which also makes the situation difficult to do a multi-centric study. What indirectly affect survival by delay in diagnosis and treatment are the cultural beliefs, sexual practices, health consciousness, nutrition, and access to health care [12]. These socio-economic factors also affect the percentage of dropout patients during treatment and loss of follow-up during surveillance.

Survival of cancer cervix has been reported way back in 1998 with an overall 5-year survival of about 51% [13]. In our study, the observed 5-year survival rates by stage of disease were 64.0%, 50.0%, 37%, and 17.5% for Stage I, Stage

II, Stage III, and Stage IV, respectively. A globally released survival data- SURVCAN from different countries depicted India has poorer 5-year survival rates compared to other Asian countries [4, 14]. The survival rates also differ within India among various population registries (35.7%, 46.4%, 34.5%, and 59.6% in Barshi, Mumbai, Bhopal, and Chennai, respectively) [4]. Our survival analysis is compared to previous studies from India [6, 12, 13, 15–17]. The difference in survival can be attributed to various other factors like socio-economic status, Education, Nutrition, patient's geography (rural or urban), treatment adherence and follow-up protocol, new advances in therapy, and other causes of non-cancer-related deaths as confounding factors.

Even though multivariate analysis in our study doesn't show significant survival differences based on Education, Religion, and Marital status, it does show non-significant survival differences. These factors have been proven to affect Survival in cancer cervix in previous studies but most of them are similar to retrospective analysis like us [6, 12]. To make it a matter of concern, prospective randomized controlled trials are needed to find the exact role of these factors in affecting survival.

The incidence of cervical cancer has been decreasing in India for the past three decades [18]. But to decrease its impact on public health, information, education, and communication activities are needed for the community [18]. To improve survival in these rural population, awareness regarding screening and implementing screening programs, awareness regarding HPV vaccination, following good cultural and sexual practices, improving their socio-economic status, improving nutrition, and addressing all social factors helps in preventing the disease, early detection of cancer with curative treatment and proper follow up which in turn improves the overall survival rate.

Conclusion

Cancer cervix survival differs within various parts of the country and also differs between countries. To get uniform survival across the globe, concentrating not only on the treatment part is adequate but also to concentrate and address the socio-economic factors, especially in rural populations which indirectly affect survival. Without this measure, there will always be inequality of overall survival in our country which in turn affects the efficiency of the health system.

Authors Contributions SUD, PSR and TDB was involved in data collection, design, manuscript editing and manuscript review the manuscript, SUD, PSR, TDB and AK were involved in definition of intellectual content, literature search, clinical studies, experimental studies, data acquisition, data analysis, manuscript preparation the manuscript, PSR, TDB and AK was involved in statistical analysis.

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Declarations

Conflict of interest The authors declare that there are NO conflicts of interest. The authors whose names are listed immediately below certify that they have NO affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

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