

Survival analysis of breast cancer women according to disease stage

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Objective: To predict the survival of breast cancer women with respect to stage of the disease in Punjab, Pakistan and evaluate the impact of the factors on the survival of breast cancer women.

Methodology: Medical records of the patients treated during 2009 were obtained from Mayo Hospital and INMOL. Date of diagnosis and stage of disease were confirmed. Patients were contacted on telephone and their follow up was completed by the end of 2013. A total of 563 patients were studied. Kaplan Meier method was applied for the survival analysis. Overall median survival and stage specific median survival was calculated.

Results: Majority of the patients were below 50 years of age. Stage III was the commonest. Two

hundred and four deaths were recorded and 359 patients were censored. At a follow up 5 years, median survival of 39 months was seen. Stage I and stage II patients had a median survival of 48 and 34 months, respectively, whereas, in stage III and stage IV a median survival of 26 months and 14 months, respectively.

Conclusion: Median survival of breast cancer patients, irrespective of stage was 39 months. Survival data for early breast cancer patients is not very encouraging. Whereas locally advanced and stage 4 patients had a reasonable survival. (Rawal Med J 201;41:77-80).

Key Words: Breast cancer, survival, stage of disease, Kaplan Meier.

INTRODUCTION

Breast cancer is the commonest cancer among the females of Pakistan.¹ Females' breast cancer is representing more than one third of females' cancers and about one fourth of all malignancies in the commonest cancer.² This is the most common cause of cancer death in women between ages of 42-59 years.³ Karachi Cancer Registry reported one of the highest incidences of breast cancer for any Asian population.⁴ Pakistani women have 50\100,000 incidence rate and neighboring country India with similar socio-cultural background have 19\100,000 incidence rate of breast cancer.⁵

Breast cancer patients with stage I and II had significant association with radiotherapy and chemotherapy while treatment surgery was associated with stage III and IV.⁶ In Pakistan, almost 80% patients are diagnosed in a very late stage so metastatic disease has also been associated with poor survival.⁷ Carcinoma breast is still a common problem presenting at a young to middle age group with invasive ductal carcinoma being the commonest variant with a high grade and a metastasis stage of presentation due to lack of

screening and awareness programs.⁸ Early detection of breast cancer improves the survival.⁹

Falsities of treatment are not available universally. For advanced cancer new adjuvant chemotherapy is not received. The outcome of patients in Pakistan is likely to be different from the treatments outcomes achieved abroad. The best measure of the success of a treatment is the prolongation overall survival. There are very few reports on the survival data of breast cancer in Pakistan due to the lack of regular follow up. Survival of the breast cancer patients can only be measured in institutions where long term follow up data is available. The aim of the study was to predict the survival of breast cancer women with respect to stage of the disease in Punjab, Pakistan and evaluate the impact of the factors on the survival of breast cancer women.

METHODOLOGY

This study used patients' records from the INMOL and Mayo Hospital, Lahore, Pakistan. The study includes women who were diagnosed with breast cancer between January 2009 and December 2009 and their follow up was completed up to the end of

2013. Those who did not come for their monthly follow-up, were contacted through the telephone. Death due to the breast cancer and all the survival up to the end of 2013 were considered as censored. Date of the diagnosis and the stage of the disease were confirmed from the pathological report and clinical observation. For the stage of the breast cancer, TNM Coding system was used. Ethical Clearance was obtained from the Ethics Committee of Hospitals.

During the study period, 663 women were diagnosed with breast cancer. Forty three women with bilateral tumors, 40 women with ductal carcinoma in situ and 17 with other previous cancer history were excluded from the study. Thus, the study population represented 563 women, who had primary invasive breast malignancy and who underwent breast surgery. All the women in had three treatment options as the surgery followed by the chemotherapy only, surgery followed by chemotherapy and then by radiation, surgery followed by radiation only by the treating physicians.

Non-parametric Kaplan Meier method was used to estimate the survival. Log rank test was used to determine the significance of the variables with 5% level of significance. Cox' regression model was used to find the association between every explanatory variable and outcome of the disease (survived or died). The results are presented as hazard ratios and 95% confidence intervals.^{10,11} Survival time was measured in months. Overall median survival and stage specific median survival was calculated. All the statistical analysis was conducted using SPSS-17.

RESULTS

Five hundred and sixty three breast cancer patients were included in the study and majority was from INMOL. Two hundred and four deaths were recorded and 359 patients were censored (Table-1). The study group consisted 50 patients of stage I (9%), 188 of stage II (33%), 201 of stage III (36%) and 124 of stage IV (22%). Stage III was the commonest. Age was between 16 and 70 years, however, most were below 50 years of age. The mean age of survivors was 46 years.

Table 1. Distribution of breast cancer patients according to stage and outcome.

Stage	Number	Number of Events (Died %)	Number of Censored (Survived %)
Stage I	50	13(26.0)	037(74.0)
Stage II	188	49(26.1)	139(73.9)
Stage III	201	69(34.3)	132(65.7)
Stage IV	124	73(58.9)	051(41.1)

Table 2. Survival time (months).

Stage	Medians of Survival Time			
	Estimate	Std. Error	95% Confidence Interval	
			Lower Bound	Upper Bound
Stage I	48	2.092	30.220	69.780
Stage II	34	1.592	29.879	36.121
Stage III	26	1.353	23.349	28.651
Stage IV	14	1.800	09.472	16.528
Overall	39	1.046	32.950	42.050

At a follow up 5 years, a median survival of 39 months was seen for all patients. Stage I and stage II patients had a median survival of 48 and 34 months, respectively, whereas, in stage III and stage IV a median survival of 26 months and 14 months was seen, respectively (Table 2, Fig. 1). In stage I and II, all patients received surgery, radiotherapy and chemotherapy. However, therapy with Tamoxifen was received by all the patients and very few post-menopausal patients received Arometer antibodies. Patients at stage 4 have lowest survival.

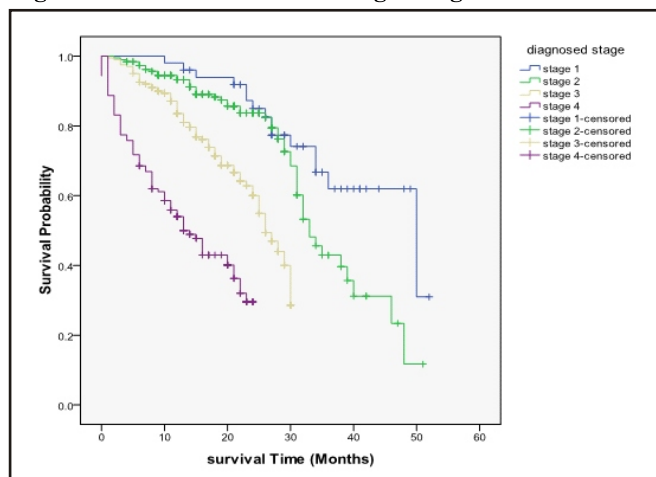
Table 3. Baseline characteristics of study population.

Characteristics	Expired N (%)	Survived N (%)	P
ER Status			
Negative	142(69.6)	205(57.2)	0.004
Positive	62(30.4)	154(42.8)	
Family History of Any Cancer			
Yes	74(36.3)	69(19.2)	0.235
No	118(57.8)	289(80.5)	
Do Not Know	12(5.9)	1(0.30)	
Family History of Breast Cancer			
Yes	111((54.4)	45(12.5)	0.009
No	87(42.6)	313(87.2)	
Do Not Know	6(2.94)	1(0.30)	
Menopausal Status			
Premenopausal	60(29.4)	182(50.7)	0.038
Perimenopausal	58(28.4)	43(12.0)	
Postmenopausal	86(42.2)	134(37.3)	

Table 4. Correlation of clinical stage with overall survival time.

Predictors	HR (95% CI)	P
Stage I		-
Stage II	1.043 (0.565-1.922)	0.897
Stage III	1.579 (0.873-2.857)	0.031
Stage IV	3.252 (1.797-5.884)	0.000

Estrogen Receptors status, Family history of breast cancer and postmenopausal status were statistically associated with the survival ($p < 0.05$), while no significant association was present for family history of any cancer with respect to breast cancer women (Table 3).

Fig 1. Survival function according to stage.

Women with stage II were 1.043 times as likely to die as women with stage I. Similarly, women with stage III and IV were 1.579 and 3.252 times more likely to die than women with stage I (Table 4). Stage III and stage IV had a significant impact on the survival time of breast cancer women.

DISCUSSION

Breast cancer in Pakistan is highest (69.1 per 100,000 persons) in Asia.^{2,12} A study from Punjab reported that the women with breast cancer were between 20 and 44 years with mean age 35.9 ± 5.2 and 70.9% were in the age group 35-44 years.¹³ Our results differ due to difference in duration, difference in study size and difference in locality. The stage frequencies of the current study is similar to a study, which reported that the stage of 1101

survivors was 9%, 37%, 39% and 15% of stage I, stage II, stage III and stage IV, respectively.¹⁴ A study of Sudan showed that the median overall 5-years survival was 40 months and the cumulative survival probability was 38%.¹⁵

This study showed that an overall 5 years median survival of 39 months, which is not satisfactory. Similarly, 43 and 33 months of median survival of stage I and II are not satisfactory. Five years survival rates are not very representative of actual cure rate which are better reflected in 10 to 15 years follow up. Locally advanced breast cancer at Jinnah Hospital Lahore was associated with poor survival and most patients relapsed by 5 years of treatment.⁷

In our study, the median survival of 43 and 33 months of stage I and II was lower indicating that treatment of early breast cancer was not optimal in our patients. Breast cancer patients received advanced surgery, radiotherapy and chemotherapy but do not afford to have monoclonal antibodies. In locally advanced breast cancer survival depends on different prognostic factors including age, menopause status, tumor stage, and histological grade, clinical response to new adjuvant therapy and estrogen receptor status.

In our series, median overall survival of 28 months was seen. This is most likely due to the lack of combined mortality approach in locally advanced cancer. Majority of patients with locally advanced cancer do not receive new adjuvant chemotherapy. Follow of the post menopause patients received aromatase and none received Trastuzumab therapy. On the other hand, in metastatic breast cancer, a median survival of 18 months is reasonable. Patients with bony metastasis alone tend to live longer. General patients who achieved a complete response live long 5 years. The median age of patients in a study was 45 years and most were premenopausal with receptor-negative disease in the developing countries,¹⁶ as in our study.

CONCLUSION

Median survival of breast cancer patients irrespective of stage was 39 months. Survival data for early breast cancer patients is not very encouraging. Locally advanced and stage 4 patients had a reasonable survival after the complete

treatment. We hypothesize that the survival of the women with the breast cancer is affected by delayed diagnosis due to cultural barriers, improper treatment and the low level of awareness about the breast cancer.

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