

## Review Article

# Breast cancer survival studies in India: a review

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### ABSTRACT

Length of survival of cancer patients is an important indicator for knowing the outcome of treatment in any study. Epidemiological features and biological profile of breast cancer appear to be different in developing countries as compared to Western countries. Knowing the factors that influence survival rates among women with breast cancer may help define early detection actions, and improve treatment and care proposals in all the areas of health. Therefore, this study aims to identify, the publications defining the factors influencing survival for women with breast cancer in India. PUBMED database was searched from January 1990 to April 2016, using the key words Breast cancer, breast cancer outcome and Survival and their corresponding Mesh terms were used in combination with Boolean operators like OR, AND. Five year overall survival rate of breast cancer in India ranged from 40-62%. The results from 16 publications showed that survival of breast cancer varies widely depending on number of factors like age, stage at diagnosis, marital status, educational level, hormonal status, clinical extent of disease and treatment. The publications that make up this review present contributing factors that affect the survival rate of women with breast cancer in India. This information on survival studies can pinpoint the lacunae in treatment modalities and can guide us to do basic and translational research so the preventive strategies can be implemented.

**Keywords:** Survival rate, Breast cancer, India

### INTRODUCTION

Breast cancer is one of the most commonly diagnosed malignancies and the leading cause of cancer death in women over the world.<sup>1-2</sup> A varieties of risk factors for breast cancer have been well-established by epidemiologic studies. These include non-modifiable factors such as age, family history of cancer, benign breast disease, breast density and genetics, as well as modifiable exposures related to diet, physical inactivity, exogenous hormones and certain female reproductive factors.<sup>3-6</sup> Breast cancer is considered as a heterogeneous condition and so requires evaluation of as many clinical and pathological features as possible to allow for best prediction of survival.<sup>7</sup> Survival refers to the occurrence of a specific event of interest, starting from an initial time until a final time, for example, from the diagnosis of

breast cancer to the death.<sup>8</sup> The study of cause and effect relationships is a basis of research and measurement of survival time is necessary for evaluation of chronic diseases.<sup>9</sup> Length of survival of cancer patients is an important indicator for knowing the outcome of treatment in any study.<sup>9</sup>

Disease free survival and Overall survival are commonly used in breast cancer prognosis. A recent Lancet publication with global data showed age standardized net survival with breast cancer of 80% or more in 34 countries and an increase worldwide but had no data on factors influencing it.<sup>10</sup> Knowing the factors that influence survival rates among women with breast cancer may help define early detection actions, and improve treatment and care proposals in all the areas of health. Therefore, this study aims to identify, the publications

defining the factors influencing survival for women with breast cancer in India.

### **Data sources and searches**

The research question that gave rise to the study was: which factors influence survival among women with breast cancer studies in India? This paper is based on information gathered from a review of peer-reviewed publications on breast cancer survival studies in India. MEDLINE (<http://www.pubmed.com>) was searched from January 1990 to April 2016, using the keywords such as “breast cancer, survival rate, survival analysis, and their corresponding mesh terms were also used in combination with Boolean operators OR, AND.” We also examined bibliographies of included articles to identify additional references. The search strategy was limited to English language. Only journal article type was included.

### **Study selection**

#### **Inclusion criteria**

- Study designs eligible for inclusion in our review were randomized controlled trials, nonrandomized controlled trials and cohort studies conducted to evaluate the survival rate of women with breast cancer at five years or the disease-free survival rate at five years.
- Studies conducted in India only were included in the review.

#### **Exclusion criteria**

Studies not providing data on survival were evaluated and excluded from the review.

#### **Data extraction and analysis**

The title and abstract of each citation were screened first, and full report was screened second if necessary to select the relevant articles according to selection criteria. Full texts of these selected studies were retrieved and reviewed. A total of 16 studies were included in the review, and their findings have been presented. We extracted the following information from the full texts: First Author, the study design, study site, number of subjects, 5 year overall survival (OS) rate, relative survival (RS) and disease-free survival (DFS) and factors that affects survival rates. The data were entered into Microsoft Excel spreadsheets (Table 1).

## **DISCUSSION**

Many factors influence the survival of patients with breast cancer; they include patient factors, stage of disease, tumour biology, and cancer treatment. Population-based studies on breast cancer in India have showed five-year survival rates ranged from 42-48%, whereas hospital based studies across India shows 5 year

relative survival rate ranged from 40-45 %.<sup>11-15</sup> Five-year survival rates of more than 80% have been reported in many studies from the West and also from a developed Asian country in India.<sup>16,17</sup> The poor overall survival rate of breast cancer reflects delay in diagnosis, advanced stages of disease at presentation, and, probably, inadequate facilities for early diagnosis and treatment.<sup>18</sup>

### **Age at diagnosis**

Age is known to be an important factor that determines the prognosis. The epidemiological data encountered that the younger patients (<35 years) had better survival than older patients.<sup>19-23</sup> whereas in some studies younger age has been generally accepted as an independent adverse prognostic indicator of survival in breast cancer.<sup>24-27</sup> A review of the US National Cancer Database revealed that patients younger than 35 years had more advanced disease at diagnosis and a poorer 5-year survival rate than older premenopausal patients.<sup>28</sup> Similar findings have been reported in the past.<sup>29,30</sup>

### **Education status**

Relating the survival rate to education, studies have shown that women with higher education had better overall five-year survival rates as compared to illiterate.<sup>20-23</sup> Educational level can be taken as an indirect indicator of social class. Socio-economic status is an important factor in the survival of women with breast cancer.<sup>31</sup> In several populations, it has been reported that women in higher social classes have higher survival rates than those in lower social classes.<sup>32</sup> The lack of access to healthcare services may explain the direct relationship between the late stage diagnosis and educational levels.<sup>33</sup>

### **Religion**

India is a vast country with wide varying social, cultural and religious practices. Cultural dynamics and sociodemographic differences cross population subgroups modulate how biologic disease is expressed among different ethnic groups.<sup>16</sup> These interactions contribute to the observed variations in breast carcinoma incidence, mortality and survival. Yeole et al showed muslims had a better and christians a lower survival as compared to Hindus. The factors like life style of patient, level of exercise, early marriage, and other reproductive factors plays an important role in the survival rate of breast cancer patients.<sup>34</sup>

### **Marital status**

Indian women would not readily discuss issues concerning the breast with others. This is more pronounced in single women who may not have intimate partners and are less likely to discuss their breast symptoms with someone else immediately. This phenomenon is recognized as a contributory factor to delay in seeking help.<sup>31</sup> Gajlakshmi et al showed single

women in Madras displayed a twofold higher risk of dying than those who were married and living with their spouses; the 5-year observed survival rate among single women was 37.4% compared with 50% among those married and living with their spouses. Marital status may

again reflect socioeconomic differences and varying degree of family support and care contributing to differentials in access to health care and survival outcome.

**Table 1: Description of included studies qualitative synthesis.**

Author	Type of study	Study site	No. of patients studied	5 year survival rate	Factors influencing survival
Nair et al <sup>48</sup>	Retrospective-Hospital based	Kerala	449	OS 40%	Age, response to treatment, stage and regional nodal involvement
Nandakumar et al <sup>21</sup>	Retrospective-PBCR	Bangalore	1381	OS 42.3% and RS 46.8%	Clinical extent of disease and educational status
Gajalakshmi et al <sup>23</sup>	PBCR	Madras	1747	OS 48% and RS 51%.	Age, Marital status, education status and clinical extent of disease
Gajalakshmi et al <sup>49</sup>	Retropective-Hospital based	Chennai	67	RS for CBC 47%	Age at diagnosis, family history of cancer and stage
Yeole et al <sup>22</sup>	PBCR	Mumbai	2516	RS 46.2%	Age, Marital status, Religion, Education status, and clinical extent of disease
Dinshaw et al <sup>37</sup>	Retrospective-single institution	Mumbai	1022 EBC	OS 87% and DFS 76%	Lymphovascular emboli or invasion (LVI), nodal status and systemic adjuvant treatment.
Raina et al <sup>50</sup>	Retrospective-single institution	New Delhi	487 EBC	OS 73% and DFS 78%	Age, tumor size, nodal status, stage and number of positive lymph nodes
Deo SV et al <sup>51</sup>	Retrospective-single institution	New Delhi	902	DFS 82% and OS 88%	Tumor size, nodal involvement, ER/PR status, and Breast conservation therapy
Yadav BS et al <sup>52</sup>	Retrospective-single institution	Chandigarh	688	DFS 69% and OS 81 %	PMRT , menopausal status, tumor stage and pathological nodal status.
Yadav et al <sup>53</sup>	Retrospective-single institution	Chandigarh	141	LRR 6% and RFS 94%.	Tumor stage and pathological nodal stage , response to chemotherapy, type of surgery , extracapsular extension (ECE) and tamoxifen therapy.
Ganesh B et al <sup>9</sup>	Retropective-Hospital based	Mumbai	471	OS 67%	Age , Educational status and stage at diagnosis, treatment(Surgery)
Shanta et al <sup>54</sup>	Retrospective-hospital based	Chennai	1,117	DFS 75%	Nodal staging, nodal status and tumor sterility.
Raina V et al <sup>55</sup>	Retrospective-single institution	New Delhi	609 LABC patients	OS 58% and DFS 41%	clinical response to chemotherapy
Haroon Ali et al <sup>56</sup>	Retropective-Hospital based	Meerut city	285	OS 51%	Age, Religion, educational , laterality tumor size, treatment factors
Khadakban et al <sup>57</sup>	Retrospective review - Prospective database	Kerala	196 cases of MBC	Median OS 26.63 months (95 % CI – 16.69–36.57)	Age, ER/PR status, Her-2 neu status, site of metastases and level of metastatic suspicion.
Vettuparambil et al <sup>58</sup>	Retrospective-cohort study	Kerala	189	OS 71.4%.	Stage of the disease, axillary nodal status, and hormone-receptor status

\* OS-Overall survival, RS-Relative survival, DFS-Disease free survival , NACT-Neoadjuvant chemotherapy, MBC-Metastatic breast cancer, LABC- Locally advanced breast cancer, LRR-locoregional recurrence, PMRT-Post mastectomy radiation therapy, CBC-Contralateral breast cancer , ER/PR- Estrogen receptor/Progesterone receptor, EBC-Early Breast Cancer.

### Stage of disease

Stage of disease at diagnosis is a critical determinant in breast cancer survival. On average, 50% of breast cancer cases in India present at late stage (stage III and IV).<sup>17</sup>

Whereas in developed countries like the United states, only 12% of the breast cancer cases are diagnosed at an advanced stage.<sup>35</sup> Most of the Indian studies have showed an inverse relationship of stage-of disease with survival.<sup>20-23</sup> Late presentation is associated with advanced stages of tumor before treatment and poor

prognosis. This condition is now a leading cause of cancer deaths among Indian women.<sup>36</sup> The women present late because of the lack of knowledge and awareness.

**Clinical factors**

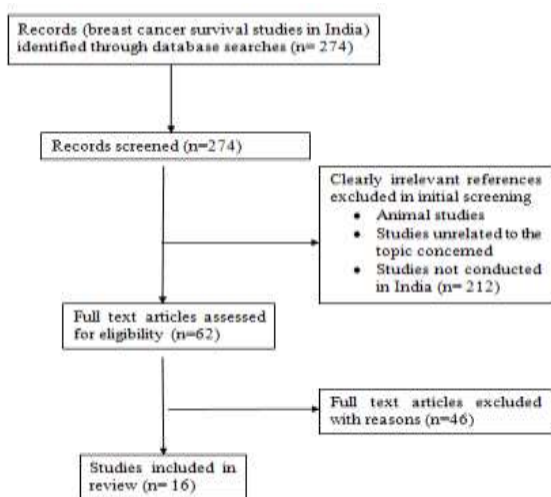
Tumour biology is likely the most important; secondly, the treatment options and the response to the treatment

(Figure 2). Breast cancer survival is driven by the variability of the patients and their tumours.<sup>37</sup>

Axillary nodal status, age, tumour size, pathologic grade, and hormone receptor status are the established prognostic and/or predictive factors for selection of adjuvant treatments.<sup>38-42</sup>

**Table 2: Factors influencing breast cancer survival.**

Patient Characteristics	Treatment	Histopathological Features	Receptor status
Age at Diagnosis	Surgery	Histologic subtype	Estrogen receptor
Education	Radiation	Axillary lymph node metastasis	Progesterone receptor
Marital status	Chemotherapy	Tumour size	Her2 neu receptor
Religion		Histological Grade	
		Lymphovascular invasion	



**Figure 1: Summary of evidence search and selection.**



**Figure 2: Overview of the factors that affect breast cancer survival.**

Breast cancer is commonly treated by various combinations of surgery, chemotherapy, radiation therapy, hormone therapy and targeted therapy via a multimodality approach. Selection of therapy is influenced by clinical and pathologic features that could predict their response to these therapies (Table 2). In the developed countries, breast cancer is treated using evidence-based recommendatory treatment schemes.<sup>37</sup> Treatment plan is individually devised for each patient with respect to the clinical manifestations, the extent of the process, and the morphology of the tumor. Hormone receptor status is an important prognostic and therapeutic tool in breast cancer.<sup>43-46</sup>

**CONCLUSION**

The publications that make up this review present contributing factors that affect the survival rate of women with breast cancer in India. This information on survival provides clinicians and researchers with opportunities to explore breast cancer trends, to measure progress against breast cancer, and to examine implications for breast cancer control in the context of associations with risk factors, prevention interventions, and the dissemination of advances in treatment. The survival studies can pinpoint the lacunae in treatment modalities and can guide us to do basic and translational research so the preventive strategies can be implemented.

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