Comprehensive Review on Cost Analysis in Various Stages of Breast Cancer

Ajay, Moghal Roshni, Kesav, Sriram Alagappan*

*Department of Pharmacy Practice, SRM College of Pharmacy, SRMIST, Katankulathur, Tamilnadu, India.

Corresponding author: **Sriram Alagappan**

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Abstract

Breast cancer is the most common type of cancer in women. In 2020, there were 13,24,413 new cases, 8,51,678 deaths and 27,20,251 cases of common breast cancer in India. In 2020, 2.3 million women were diagnosed with breast cancer and 685,000 died worldwide. As of the end of 2020, 7.8 million women alive had been diagnosed with breast cancer in the past five years. Female gender is the strongest risk factor for breast cancer. About 0.5 to 1% of breast cancers occur in men. The treatment of breast cancer in men follows the same management principles as in women. Economic burden is a real and emerging problem for breast cancer patients among worldwide. Direct medical cost associated with breast cancer was substantial.

Key words: Breast cancer, Direct and Indirect costs, Breast cancer stages, Treatment.

Introduction

Cancer is a disease with a significant burden in terms of incidence, prevalence, mortality and morbidity. Breast cancer is the abnormal, uncontrolled growth of malignant tissue[1]. Breast cancer is a heterogeneous disease first described by the ancient Egyptians more than 3,500 years ago. The first case of breast cancer comes from the surgical papyrus of Edwin Smith (Egyptian period 2500-3000 BC)[2]. Breast cancer is the second most common cancer and the leading cause of death related to cancer in women around the world. Although there has been an improvement in overall survival rates for breast cancer, there are still variations between countries and regions. Limited screening, diagnosis, and treatment may be contributing factors[3]. If not controlled, tumors will spread throughout the body and cause death.

Breast cancer cells start inside the milk ducts and milk-producing lobules of the breast. The earliest form (local) is not life-threatening. Cancer cells can spread to nearby breast tissue (invasive). This creates lumps that cause clumping or thickening. Invasive cancer can spread to nearby lymph nodes or other organs (metastasize). In 2020, 2.3 million women were diagnosed with breast cancer and 685,000 died worldwide. As of the end of 2020, 7.8 million women alive had been diagnosed with breast cancer in the past five years. Female gender is the strongest risk factor for breast cancer. About 0.5 to 1% of breast cancers occur in men. The treatment of breast cancer in men follows the same management principles as in women. We know that there are many factors that increase the risk of breast cancer. Factors associated with increased or decreased risk of breast

cancer include personal and family history (genetic predisposition, personal history of breast cancer, ductal or lobular carcinoma in situ, benign breast disease, endogenous hormone levels, menstrual cycle and bone mineral density), reproductive factors. risk factors (pregnancy, use of fertility drugs, breastfeeding, hormonal birth control and postmenopausal hormones), environmental factors (radiation, exposure to diethylstilbesterol, environmental pollution and occupational exposure) and other risk factors (tobacco use, obesity, physical activity, diet and alcohol consumption)[2] About half of all breast cancers develop in women with no identifiable risk factors for breast cancer other than sex (female) and age (over 40). Breast cancer requires expensive treatment.Current breast cancer treatment depends on disease characteristics (stage, grade, HER-2ER receptor status, RP) and patient characteristics (age and menopausal status). The total cost of breast cancer treatment includes direct costs for examination, treatment costs, surgical intervention, radiotherapy costs, consultation costs and palliative care, as well as indirect costs of the disease taking into account losses. on productivity and premature mortality. Non-medical direct costs such as transportation and non-medical costs related to cancer management. Indirect costs represent opportunity costs, including loss of income due to cancer-related illness and treatment[1]. In this article, the cost of treating breast cancer at different stages in different countries is discussed.

Epidemiology

According to WHO, malignant tumors represent the greatest global burden on women, with an estimated cancer burden of 265.6 million YLL across all ages, 182.8 million (68.8%) YLL are due to premature deaths from cancer worldwide in 2020, of which 124.3 million (68.0%) are preventable and 58.5 million (32.0%) are treatable[4]. Breast cancer is the most common type of cancer in women.In 2020, there were 13,24,413 new cases, 8,51,678 deaths and 27,20,251 cases of common breast cancer in India. 1,86,598 new cases and 85,787 deaths from breast cancer in African countries, 2,10,100 new cases and 57,984 deaths. in Latin America and Caribbean countries, 2,81,591 new cases and 48,407 deaths due to BC in North America, 10,26,171 new cases and 3,46,009 deaths due to BC in Asian countries, 5, 31,086 new cases and 1,41,765 deaths BC in European countries, 25,873 new cases and 5,044 deaths BC in Oceaniacountries.In addition to being the most common disease, breast cancer is also the leading cause of cancer death in women worldwide. Globally, breast cancer is responsible for 684,996 deaths, with an age-adjusted rate of 13.6/100,0007. Although incidence is highest in developed areas, countries in Asia and Africa accounted for 63% of all deaths in 2020[5]. Most women develop breast cancer in a country with high income will survive; The opposite is true for women in most low-income countries and many middle-income countries[6].In 2020, the breast cancer mortality-incidence ratio (MIR), considered a proxy for five-year survival, was 0.30 globally. Given the clinical severity of breast cancer, in areas with developed health systems (Hong Kong, Singapore, Turkey), the 5-year survival rate is 89.6% for localized cancer. and 75.4% for regional cancers[6]. In less developed countries (Costa Rica, India, Philippines, Saudi Arabia, Thailand), survival rates are 76.3% and 47.4% for localized and regional breast cancer, respectively[6].

Breast cancer stating system

The breast cancer staging system, called the TNM system, is overseen by the American Joint Committee on Cancer (AJCC). This is to ensure that cancerisexplainedconsistentlyby all doctors and treatment facilities. Previously, the stage number was calculated based on onlyher three clinical features: T, N, and M.

- The size of the cancerous tumor and whether it has spreadto nearby tissues (T)
- Whetherthecancer is in the lymph nodes (N)
- The cancer isin other parts of the body otherthan the breast (M)

T, N, and thefollowingnumberorletter M explaineachcharacteristicin more detail.Ahighernumbermeans the cancer is more advanced.

Stage 0: Alsocalled carcinoma in situ.This means that cancer cells are present but have not spread because theyworediagnosedearly.Alsocalled non-invasive (Tis, N0, M0).

Stage I: The cancer is very small and does not spread tothe lymph nodes or a small amount Spreadsto nearby lymph nodes

IA: SizeCancer is small insize and does not spread to lymph nodes (T1, N0, M0).

IB: Cancer size from 0.2 mm to 2 mm is found in lymph nodes (breast tumor isundetectable or smaller than 20). mm)(T0 or T1, N1mi, M0).

Stage II: In this stage,the tumor is larger than inStage 1 and may have spread to nearby lymph nodesverylittle.

IIA: Undetectable, the tumor has spread to 1 to 3 lymph nodes but not to other parts of the body(T0, N1, M0), or the tumor is 20 mm Thedisease has spread to 1 to 3lymphnodes.Three lymph nodes havebeenspread(T1, N1, M0) or the tumor is 20 mm to 50 mm insize and has not spread to any lymph nodes(T2, N0, M0).

IIB: Tumor size is 20 The tumor is larger than 50 mm but has not spread to lymph nodes(T3, N0, M0).

Stage III: In this stage,thetumoris larger than inStage 2 and has spread tomultiple lymph nodes or tissues around the lymph nodes.

IIIA: Tumor of any size has spread to 4 to 9 axillary or internal mammary lymph nodes. Has not spread to other parts of the body (T0, T1, T2, or T3,N2, M0). At this stage,thetumor may be larger than 50 mm andmayhave spread to 1 to 3 axillary lymph nodes (T3, N1, M0).

IIIB: Ifthe tumor has spread to the chest wall or causes swelling or ulceration in the chest,inflammatoryBC is diagnosed. It may or may not have spread to up to 9 axillary or internal breast lymph nodes. Not spread to other parts of the body (T4; N0, N1 or N2; M0).

IIIC: Tumor of any size that has spread to 10 or more axillary lymph nodes. Has not spread to other parts of the body (T, N3, M0).

Stage IV (metastatic): The tumor isof any size and has spread to other organs, including:BreastBones, lungs, brain, liver, excised lymph nodes or chest wall (T, N, M1). Also called de novo metastatic breast cancer.

BC stage wise treatment

Stage 0: At this stage, in most cases, women can choose betweenbreastconserving surgery (BCS) and a simple mastectomy. However,insomecases,mastectomymaybe a better option. Once BCS is performed, it is usually followed by radiation therapy. This reduces the chance thatthe cancer will come back in the same breast. IftheareaofDCISisverylarge,asimple mastectomy (removal of the entire breast) may benecessary.

Stage I: In BC stage 1, treatment usually includes:

- **Surgery:** BCS (sometimes called partialmastectomy or lumpectomy), mastectomy.
- **Radiation:**Radiotherapy (tamoxifen, aromatase inhibitors) is the standard treatment for BC stage 1.Thisdepends on factors such as age, typeofcancer,and size ofthetumor
- **Hormone therapy:**Hormone therapy is effective if BC is estrogenand progesterone positive.

- **Chemotherapy:** This depends on the size of the tumor, thelikelihoodthatthe cancer hasspread, and the status of the tumor'shormonereceptors.
- **Targeted therapy:** This type of treatment is recommended for peoplewhoare HER2 positive. Targeted drugs such as transtuzumab, pertuzumab, abemaciclib.

Stage II

- **Surgery:** Same as stages 1 and 2. Both lumpectomy and mastectomy are options at this stage.
- **Radiation:** Radiation therapy is recommended after mastectomy to help destroy remaining cells and prevent metastasis.
- **Chemotherapy:** Depends on the type of cancer. Can be recommended before and after surgery.
- **Hormone therapy:** Hormone therapyisused if the cancer haspositive hormone receptors.Can be started before surgery but recommended to continue for 5 years.
- **Targeted therapy:** usuallyused if HER2 is positive.
- **Immunotherapy:** women with triple negative breast cancer mayreceive immunotherapy, pembrolizumab.Used before and after surgery.

Stage III

- **Neoadjuvant therapy:** Neoadjuvant chemotherapy was usedat this stage. This means chemotherapy is given before surgery to increase the effectivenessofthetreatment.
- **Surgery:** Mastectomy is almost always an option at this stage because the tumor is large and has spread into or growingclosetothetissue.
- **Radiotherapy:** Radiotherapy is also recommended at this stage.
- **Hormone therapy:** Aswith other stages,dependingonyourHER2statusandhormonereceptorstatus, hormone therapy may be recommended.

Stage IV

- **Hormone therapy:** To slow the growth of cancer cells or,mayhelpyoustoporstop. IfHER2ispositive,chemotherapy is usually given in combination with trastuzumab and pertuzumab.
- **Chemotherapy:** This therapy destroyscancercells in the body.
- **Immunotherapy:** Intriple-negativeBCpatients, immunotherapy drugscan be used in combination with chemotherapy.May help boostthe immune response againstcancercells.
- **Surgery and radiation:** In the most advanced stages of BC, surgery and radiation are only recommended incertaincircumstances.
- **Pain management:** If thepainis severe in thelaterstagesof BC, your doctor may prescribe medication to makethe pain bearable.

Direct and indirect cost of breast cancer treatment in various country

Study	Country	Currency	Study type	Direct cost	Indirect cost
Maneeta Jain etal.(2016)[7]	India	INR	Cross-sectional descriptive	826,639,662	21,594,507.97
Antoaneta etal.(2021)[8]	Bulgaria	BGN	Retrospective	19,634,509.67	1,442,299.45
Wendy max et.al (2008)[9]	California	USD	Cost analysis	1,909,058	1,500,913
John J. Barron etal.(2007)[10]	US	USD	Retrospective	4,421 PM (BC Pt) 3,352 PM (control pt)	-
Joachim Marti et.al (2015)[11]	UK	Euro	Cost of illness	249.5 PM	70.8 PM
Michal Seweryn et.al (2022)[12]	Poland	Euro	Retrospective	209,527.3 (2017) 228,398.4 (2018) 224,284.3 (2019)	305,371.4 (2017) 332,998.2 (2018) 344,648.5 (2019)
Saverio mennini et.al (2021)[13]	Italy	Euro	Retrospective	300 million	-
Young Ae Kim etal. (2015)[14]	Korea	USD	Retrospective	719.18 million (2007) 1016.58 million (2010)	3339.09 million (2007) 465.70 million (2010)
FarideSadat Jalali etal.(2023)[15]	Southern Iran	USD	Cross sectional	170,126,212.2	229,647,39.3
AbolhasanAfkar etal. (2021)[16]	Iran	USD	Cost of illness	10,050 (private) 3960 (public)	1870 (private) 22,350 (public)
Rezende etal. (2021)[17]	Brazilian	International Dollars	Cost of illness	314.4 million	-
Hasan Rohani etal. (2022)[18]	Afghanistan	USD	Cross sectional	241,849.68	-

Discussion

As precision medicine and pharmacy have advanced in recent years, an increasing number of cutting-edge anticancer medications, including immune checkpoint inhibitors, antibody–drug conjugates, and gene treatments, have received international approval.Furthermore, the expenses associated with cancer treatment are a significant factor in determining the cost-effectiveness of research on BC therapies or preventive measures. Nevertheless, the average expenditures associated with treatment at various phases did not disclose patient heterogeneity. Data at the patient level, such as socioeconomic status, medical history, and available

treatments, enable cost comparisons between patient subgroups and the discovery of cost predictors.In order to further reduce healthcare costs, certain nations may also have implemented restrictions that restrict the kinds of pharmaceuticals that are available as well as the introduction of new technology. Furthermore, patients in these nations can be used to waiting in lines for surgery, diagnostic scans, or other procedures in order to manage supplies.

Conclusion

Economic burden is a real and emerging problem for breast cancer patients among worldwide. Direct medical cost associated with breast cancer was substantial. The highest cost was considered for stage IV breast cancer and more than 30% of the patients were diagnosed with the disease in stage IV. Roughly one third of the costs were linked to systemic anticancer therapy and the rest came from hospitalization and ED services.These results confirm the necessity for efficient therapies to lower the use of expensive services.

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