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**Original article**

# Retrospective record based descriptive study assessing breast cancer occurrence and its management among females at tertiary care center in Goa

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**Abstract**

Current study is aimed at summarizing the current knowledge about breast cancer, its epidemiology, classification, prognostic markers and available treatment modalities. Mean age of study participants was 55.54 +/- 11.82 yrs, Roughly 60% study population belong to 41 – 60 years of age. Infiltrating duct carcinoma was the most common type, with ER +ve PR+ve HER2u – ve as most common molecular pattern. Around 50% patients presented with TNM stage 2b at the time of diagnosis.

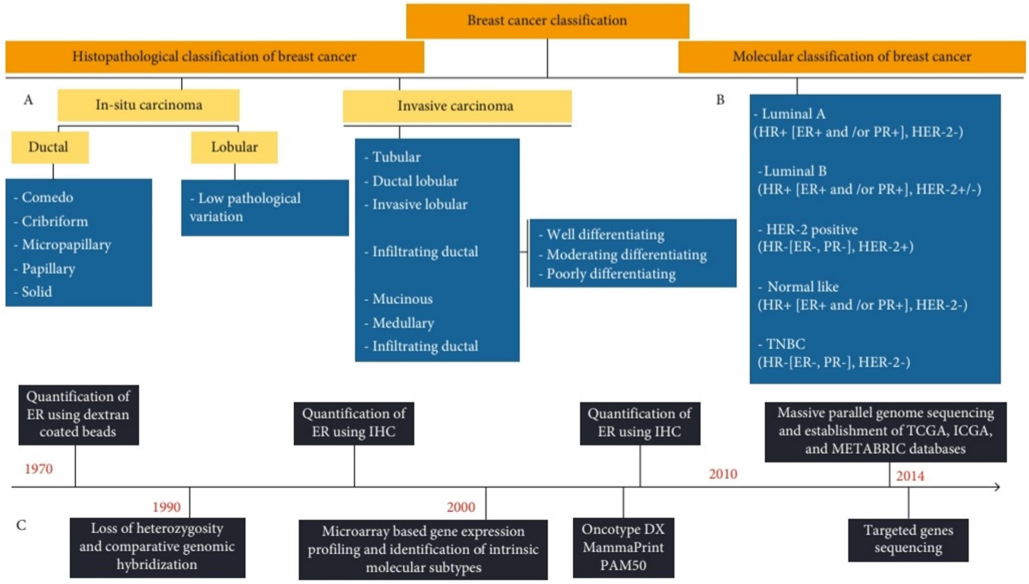
Neoadjuvant therapy received by ~ 20% patients following which patient underwent surgery. Roughly 85% patients underwent modified radical mastectomy and 5 % underwent breast conservation surgery , as choice of breast conservation surgery is limited by its contraindications and willingness of female for continues follow up also fear of recurrence in elderly fefemales. Different combination of adjuvant management was given depending on stage and molecular subtype.

**Introduction:**

According to a study the risk of 7.0% (95% confidence interval: 5.2, 9.1) in womenwho married at age 30 or older, relative to women who married at a younger age (~20 year), whereas the corresponding risk was 1.4% (95% confidence interval: 1.1, 1.8) when marriage age was less than 30 but the first childbirth age is 30 or more. [17] Late age at marriage and childbirth leads to lack of breast tissue differentiation, more exposure to nonoestrogenic mutagens, and genotoxicity by estrogen. [18] Menopause after 50 years of age puts the women at prolonged estrogen exposure. [19,20.] A meta-analysis study observed that early pregnancy and longer breastfeeding duration reduce ER (Estrogen receptor) positive and ER negative breast cancer risk . [21, 22.] It was observed that postmenopausal women with ≥5.0BMI (Body Mass Index) and ≥90 cm abdominal circumference were more likely to develop breast cancer. [23, 24] It results from the activity and accumulation of polycyclic aromatic hydrocarbons (PAH) in breast fat tissue. In the breast fat tissue, PAH interacts with the cellular oestrogen receptor to enhance the risk of development of breast cancer. [25] Besides, another study noted that obese women with breast cancer have worse disease-free an overall survival than non obese women with breast cancer. [26] Moreover, a study found that moderate alcohol consumption of >35-44 grams/day increases 46% (95% CI =1:33-1.61) risk for breast moderate[27, 28] In breast tissue, higher dose of alcohol is metabolized to acetaldehyde by alcohol dehydrogenase enzyme. Accumulated acetaldehyde can bind to proteins and DNA and interferes with the antioxidative defense system, DNA synthesis, and repair system by downregulating BRCA1

(BReast CAncer gene1). [29, 30] Hormonal contraception formulations contain lower doses of estrogen, but its use for long time can also put the women at high breast cancer risk (RR=1.20; 95% CI=1.14-1.26). [31]

## CLASSIFICATION OF BREAST CANCER




### Prognostic Biomarkers

1. Estrogen Receptor

Nearly 70–75% of invasive breast carcinomas are characterized by significantly enhanced ER expression. [32, 33] According to current practice measurement of ER expression on both—primary invasive tumors and recurrent lesions is mandatory to decide who will most benefit from the implementation of the endocrine therapy mainly selective estrogen receptor modulators, pure estrogen receptor downregulators, or third-generation aromatase inhibitors. [34] ER expression might also constitute a predictive factor of significantly better clinical outcomes. [35] ER expression can also be utilisedm as a diagnostic biomarker of breast cancer in cases of familial risk. [36] Besides, Konan et al. reported that ERα-36 expression could constitute one of the potential targets of PR-positive cancers and a prognostic marker at the same time. [37]

2. Progesterone Receptor

PR is highly expressed in >50% patients with ER-positive while very rarely in ER-negative breast cancer.However, PR expression is regulated by ER and physiological values of PR inform about the functional ER pathway. [38] However, both ER and PR are abundantly expressed and are both considered as diagnostic and prognostic biomarkers of breast cancer (especially ER-positive ones) [39] Greater PR expression is positively associated with the overall survival, time to recurrence, and time to treatment failure or progression while lowered PR levels are considered more aggressive course of the disease as well as poorer recurrence and prognosis. [40,41]

3. Human Epidermal Growth Factor Receptor 2

The expression of human epidermal growth factor receptor 2 (HER2) is seen in approximately 15–25% of breast cancers. HER2 overexpression is one of the earliest events during breast carcinogenesis. [42] Besides, HER2 increases the detection rate of metastatic or recurrent breast cancers from 50% to more than 80%. [43] Serum HER2 levels are considered to be a promising real-time marker of tumor presence or recurrence. [44] Overexpression of HER2 also correlates with a significantly shorter disease-free period and alsohistologic type, pathologic state of cancer, and a number of axillary nodes with metastaticcancerous cells. [45]

**STUDY METHODOLOGY:**

Management

**LOCAL THERAPY**

1) BREAST CONSERVATION THERAPY AND MASTECTOMY

Breast-conserving therapy (BCT) and mastectomy are both well-established local therapies for invasive breast cancer. Multiple randomized clinical trials with follow-up of up to 20 years have demonstrated that BCT is safe and has survival outcomes equivalent to mastectomy in stage I and II breast cancer. [46,47.] It is now understood that local control is not solely a function of disease burden and extent of surgery, but varies with tumor molecular subtype and administration of systemic therapy. [48]

Rates of local recurrence differ significantly among breast cancer subtypes, regardless of whether patients are treated with mastectomy or BCT. Local recurrence rates are highest among patients with hormone receptor (HR) negative, HER2 negative cancers ("triple negative"), and lowest among patients with HR positive, HER2 negative cancers. [49,50.] This understanding eliminates the rationale for treating biologically aggressive cancers with mastectomy, and the majority of patients with stage I and II disease are candidates for BCT. [51]

**Staging and management of the axilla**

The axillary nodes are the initial site of metastases in the majority of breast cancer patients, and approximately 25% of those with a normal physical exam will have nodal metastases.

The sentinel node predicts the status of the remaining axillary nodes in > 95% of cases in the hands of experienced surgeons, and the risk of an isolated axillary recurrence after a negative sentinel node biopsy is < 1%. [52,53.] Completion ALND was routinely performed for any positive axillary nodes found on sentinel node biopsy, even though approximately 50-70% of patients with positive sentinel nodes had no additional positive nodes on completion ALND. [54, 55]

2) RADIOTHERAPY

Postmastectomy radiation (PMRT) is a well-established component of breast cancer treatment in patients with advanced disease. The most important predictor of LRR after mastectomy is the extent of axillary nodal disease. Patients with 4 or more positive axillary lymph nodes have a 25% or greater risk of developing an LRR. [56]

Tumor size ≥ 5 cm is also associated with an increased risk of chest wall recurrence of > 20%. [57] For this reason, PMRT has been considered standard in these patients for many years. At 5 years the LRR rate was 3.2% in the PMRT group versus 4.3% in the group not receiving radiation . [58.]

PMRT includes the treatment of the chestwall and often the supra−/infraclavicular lymph nodes as well as the internal mammary nodes Recently, a metaanalysis of 14 trials with about 13,500 patients on individual patient data by the Early Breast Cancer Trialists'

Collaborative Group (EBCTCG) was presented at the San Antonio Breast Cancer Symposium (SABCS) in December 2018 . Adding regional nodal irradiation ( RNI) to chest wall or breast irradiation showed an improvement in any recurrences (−2.9%) and breast cancer death (− 4.0%). the absolute benefit of RNI in breast cancer mortality was the largest in the subgroup of patients with > 4 positive lymph nodes. [59]

Axillary radiotherapy

The AxRT started within 12 weeks after the sentinel lymph node biopsy (SNB) and

included axillary lymph node levels I-III and the medial supraclavicular level. Regarding side effects, the endpoint lymphedema by clinical observation and/or treatment after 5 years was significantly lower after AxRT as compared to ALND (14.6% versus 29.4%,

$p < 0.0001$). [60]

**SYSTEMIC THERAPY**

1) NEOADJUVANT CHEMOTHERAPY

Neoadjuvant chemotherapy initially utilized as a way of rendering locally advanced, inoperable breast cancer resectable. More recently, Neoadjuvant chemotherapy has been used in operable tumors to downstage disease in the breast and axilla with the intention of facilitating breast conservation and, in some instances, avoiding Axillary LN dissection. The oncologic safety and equivalent survival outcomes of Neoadjuvant chemotherapy have been studied in several randomized trials. [61, 62]

**RESULTS :**

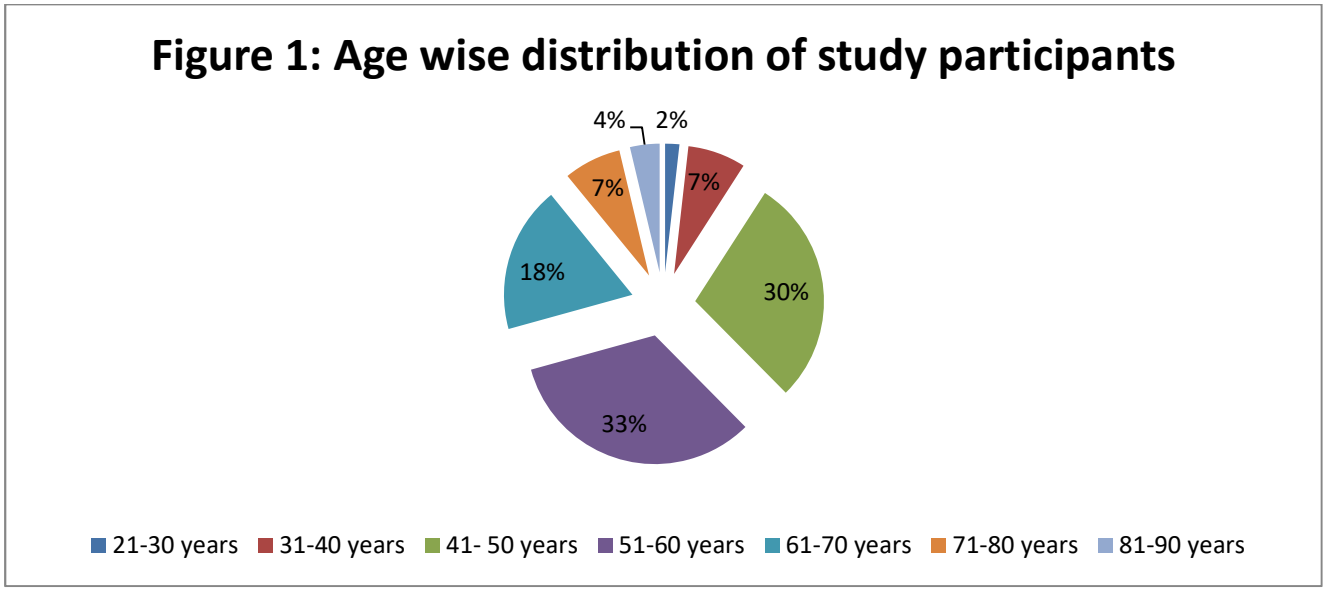
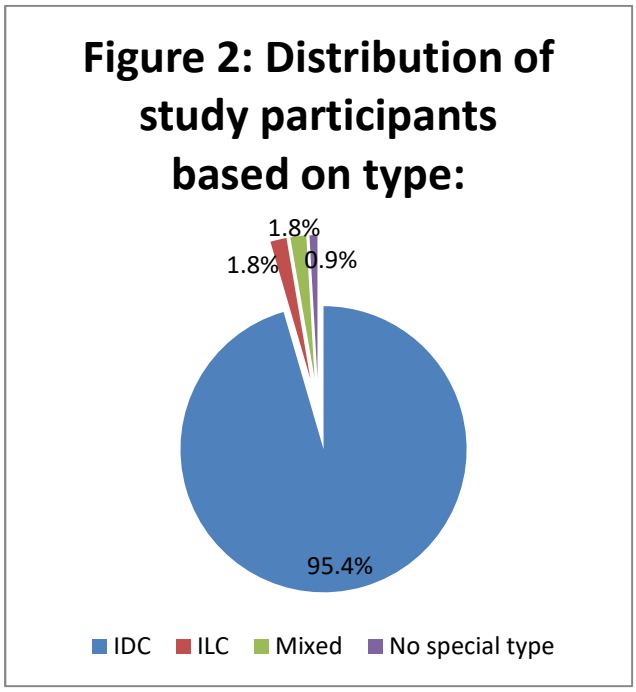



**Figure 1 - shows age wise distribution of study participants. There were 1.8%, 7.3%, 28.5%, 33.1%, 18.4%, 7.2% and 3.7% study participants in the age group of 21-30 years, 31-40 years, 41- 50 years, 51-60 years, 61-70 years, 71-80 years and 81-90 years respectively. The mean age of study participants was 55.54 ± 11.82 years with minimum 30 years and maximum 82 years of age.**



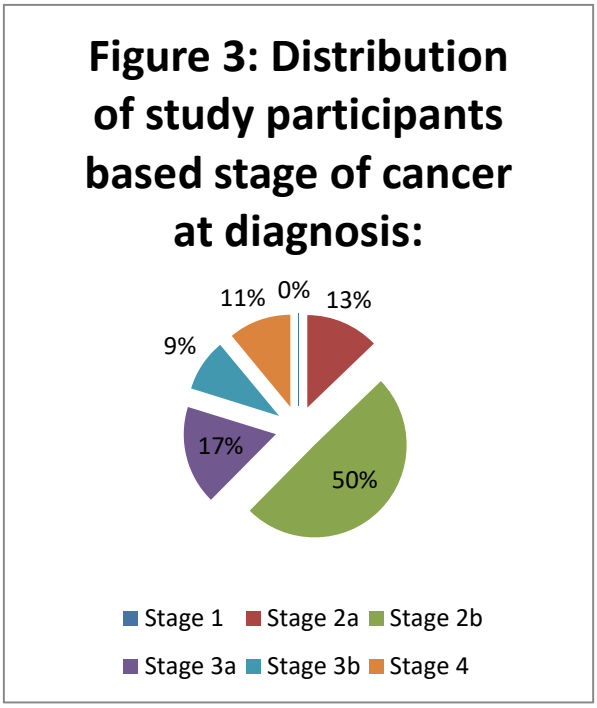




**Figure 2- shows distribution of study participants based on type. There were 95.4% participants with IDC type and 1.8% participants each with ILC and mixed type.**

**Figure 3 - shows distribution of study participants based on grade. There were 48.6% participants with grade 2 cancer and 51.4% participants with grade 3 cancer**

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**Figure 4: Distribution of study participants based on Estrogen Receptor biomarker:**

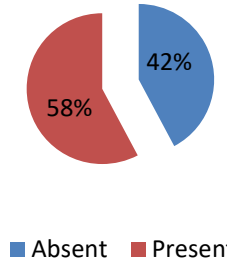


**Figure 5: Distribution of study participants based on Progesterone Receptor biomarker:**

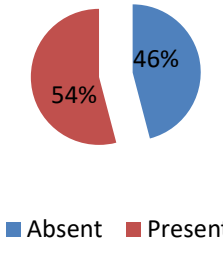


**Figure 6: Distribution of study participants based on Human Epidermal Growth Factor Receptor 2:**

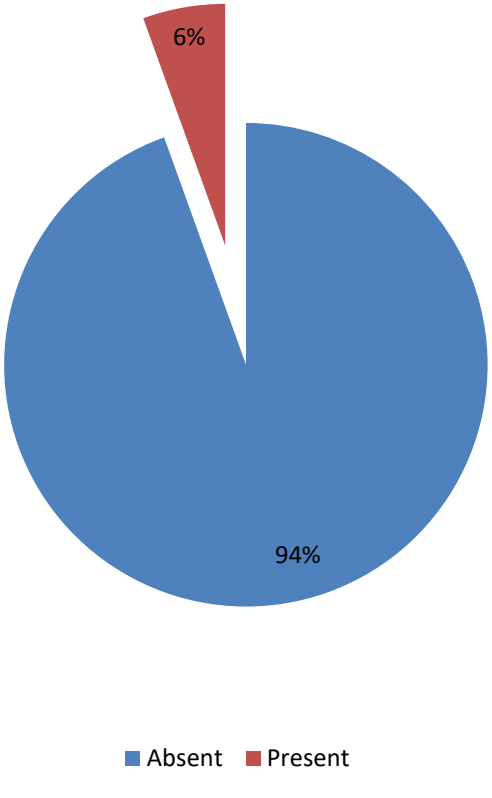


**Figure 4 -shows distribution of study participants based on Estrogen Receptor biomarker. There were 57.8% participants in which Estrogen Receptor biomarker was present while in 42.2% it was absent.**

**Figure 5 - shows distribution of study participants based on Progesterone Receptor biomarker. There were 54.1% participants in which Progesterone Receptor biomarker was present while in 42.2% it was absent.**

**Figure 6- shows distribution of study participants based on Human Epidermal Growth Factor Receptor 2. HER2 was found positive among 5.5% participants while it was absent in 94.5% participants.**

**Hence ER , PR positive with her2 negative is most common molecular pattern.**

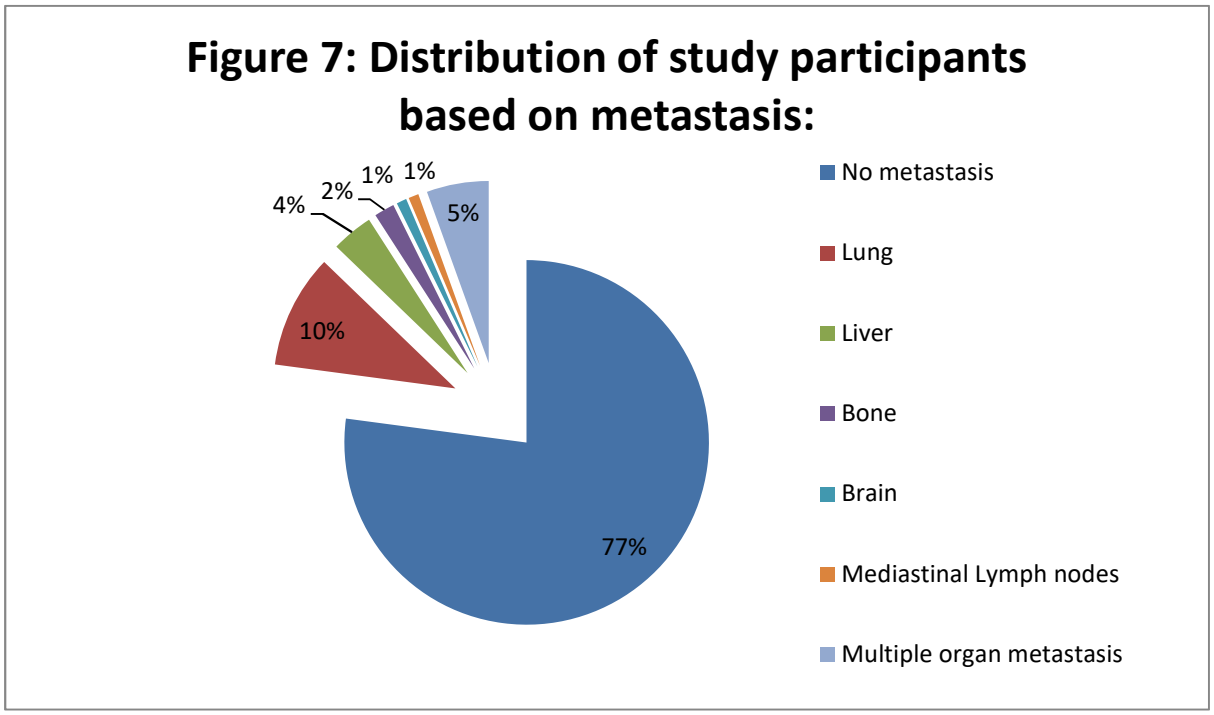


**Figure 7 shows distribution of study participants based on metastasis. There were 77.1%, 10.1%, 3.7%, 1.8%, 0.9%, 0.9%, 5.5% participants with no metastasis, lung metastasis, liver metastasis, bone metastasis, brain metastasis, mediastinal lymph nodes metastasis and multiple organ metastasis respectively.**

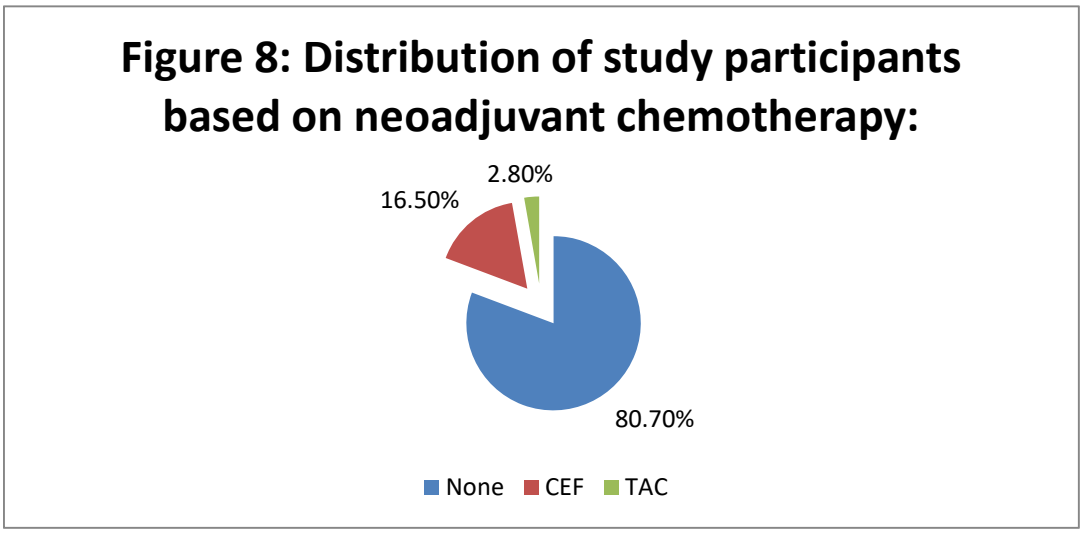


**Figure 8 - shows distribution of study participants based on neoadjuvant chemotherapy. There were 16.5% and 2.8% participants given CEF and TAC as neoadjuvant chemotherapy respectively while 80.7% were not given.**

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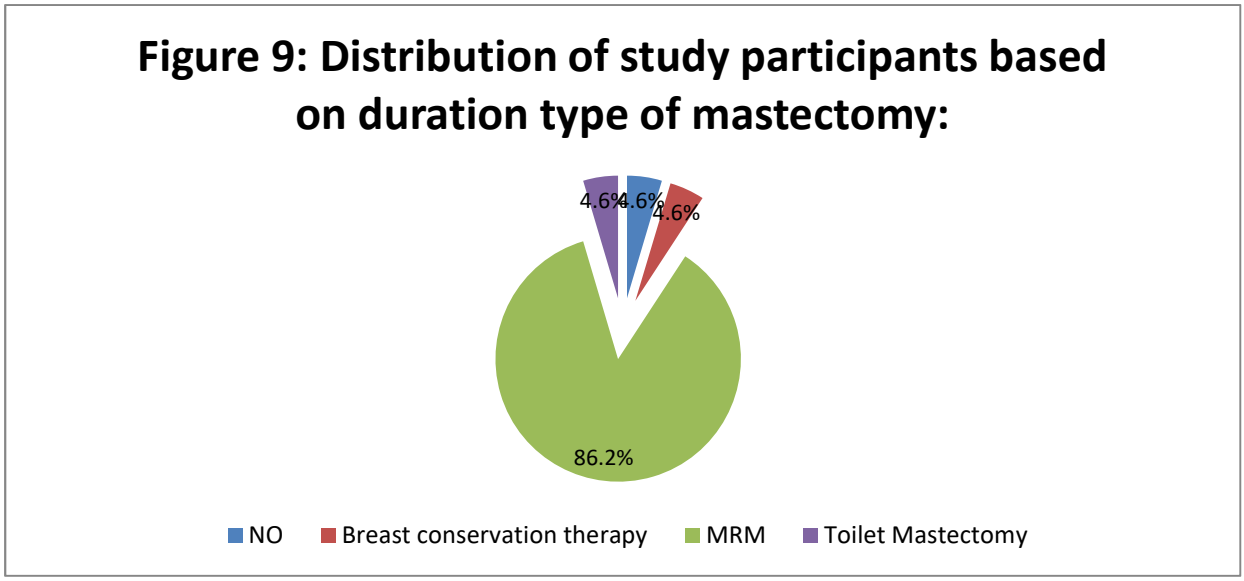


**Figure 9 shows distribution of study participants based on type of mastectomy. No mastectomy was done in 4.6% participants while 86.2% participants underwent MRM , 4.6% patients underwent breast conservation surgery and 4.6% participants underwent total mastectomy.**

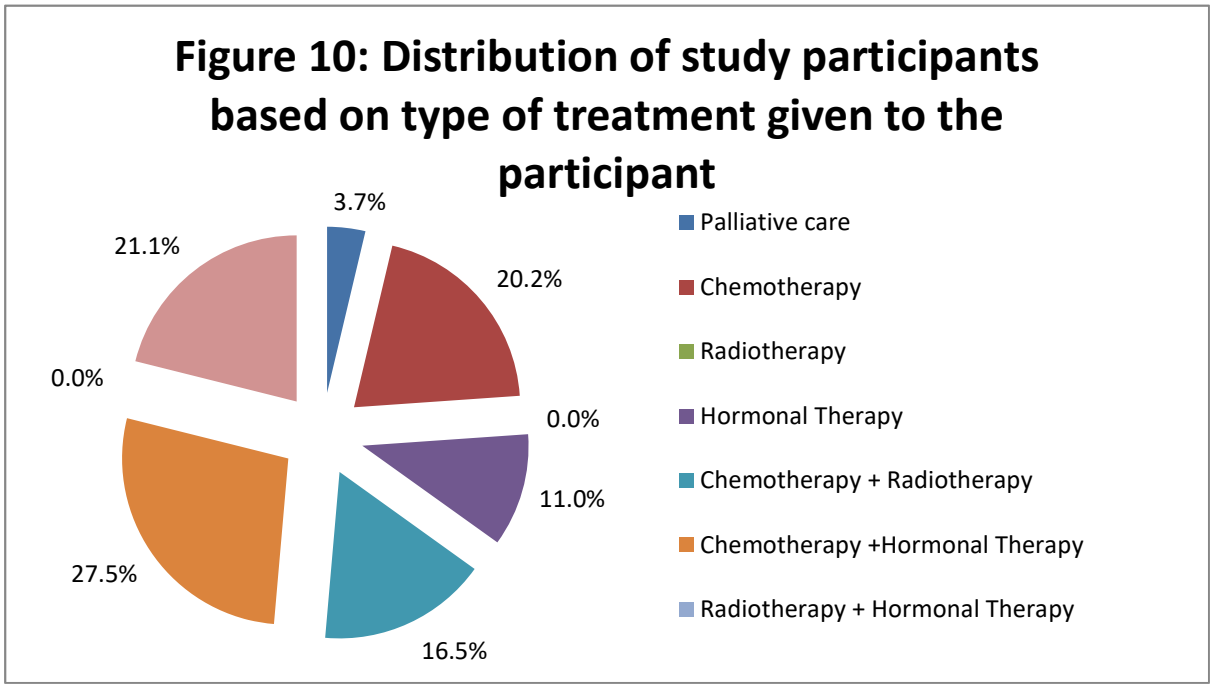


**Table 16 shows distribution of study participants based on type of treatment given to the participants. There were 3.7%, 20.2%, 0%, 11%, 16.5%, 27.5%, 0% and 21.1% participants who underwent palliative care, chemotherapy, radiotherapy, hormonal therapy, chemotherapy + radiotherapy, chemotherapy +hormonal therapy, radiotherapy + hormonal therapy, chemotherapy + radiotherapy + hormonal therapy respectively.**

**Discussion:**

In 2018, approximately 6.8 million women across the world were living with breast cancer. But the information in cancer registries is incomplete, it is not documented that how many women have metastatic spread and are now cancer free, as only incidence or mortality is being registered in cancer registries [1,2]. Globalization and growing economy may further exacerbate breast cancer incidence in developing (64% to 95) and developed (32% to 56%) countries by 2040. [3,4] In urban India, high breast cancer incidence reported was in the age group of 40–49 years, while in rural areas, it was between 65 and 69 years. [5] A study from northern India population documented that 26% of patients detected with breast cancer were less than 35 years of age. [6]

International Breast Cancer Burden.

Recently, the GLOBOCAN 2020 data by the IARC (International Agency for Research on Cancer) reported worst breast cancer incidence and prevalence in 185 countries. [3] Breast cancer is the leading most commonly diagnosed cancer with a total of 2.3 million new cases (11.7%) of breast cancer. [3] Further, as per estimated the number of new breast cancer cases and deaths in US were 0.28 million and 0.04 million, respectively. [7] As an estimation, one in 4 women has breast cancer, and one in 8 women died due to breast cancer disease. [3] According to the American Cancer Society, global cancer burden would be 28.4 million cases by 2040, which is ~47% raise compared to 2020 cancer burden. [8] Women in older age have high breast cancer incidence. In 2018, 6,45,000 vs. 1·4 million breast cancer cases and 130,000 vs. 490,000 deaths were reported in the premenopausal and postmenopausal group, respectively. [3] It is reported that countries with high human development index (HDI) has the highest premenopausal (30.6/100,000) and postmenopausal (253.6/100,000) breast cancer incidence, [9] while countries with low and medium HDI had the lowest premenopausal (8.5/100,000) and postmenopausal mortality (53.3/100,000). [10] Insufficiency to approach for early diagnosis and effective treatment remains a crucial factor for higher breast cancer mortality in developing countries. [9]

National Breast Cancer Burden.

Breast cancer remains the fast-growing cancer in India after crossing cervical cancer. National Cancer Registry Program in 2018 estimated ~1,62,468 new breast cancer cases and ~87,090 deaths due to breast cancer in India. [11, 12] Annual percentage change in the incidence of breast cancer ranged from 0.46% to 2.56% which crossed cervical cancer in 2012. According to a survey carried out by the ICMR (Indian Council of Medical Research) New Delhi, breast cancer incidence has almost doubled from 1982 to 2005. [13] It is noted that breast cancer is more common in the younger population and has poor prognosis in India compared to the Western world. [14] The survival rate in India is very poor due to the detection of disease at an advanced disease stage. Usually, 60% of women present with TMN (tumor size, metastasis, and lymph node) stage III with 80% lymph node positivity and only 1.4% presents with stage I. [16] The mean breast cancer tumor size reported in India is 3.56cm and ranged from <2cm in 18.2%, 2-5cm in 65.1%, and >5cm in 16.7% cases, [15] whereas in USA, 64% of patients present with local disease, 28% with regional spread, and 6% with distant spread of disease. The late presentation of the disease is influenced by socioeconomic status, level of education, marital status, and residence. [6] Nhh Considering breast cancer subtypes distribution, TNBC is the more common and highly prevalent subtype in Indian women and accounts about 20-43% of total breast cancer patients. [16] A meta-analysis study found a higher prevalence of TNBC subtype in India compared to in Western populations. Different risk factors, primarily including lifestyle, deprivation status, obesity, family history, high mitotic indices, and BRCA1 mutations, might be associated with increased incidence of TNBC in the Indian population.

[14] HER-2 positive subtype is also observed to be highly prevalent in young Indian women. On the contrary Luminal A subtype in younger Indian women is lowest compared to other races. [16]

**CONCLUSION**

Current study is aimed at summarizing the current knowledge about breast cancer, its epidemiology, classification, prognostic markers and available treatment modalities. Mean age of study participants was 55.54 +/- 11.82 yrs, Roughly 60% study population belong to 41 – 60 years of age. Infiltrating duct carcinoma was the most common type, with ER +ve PR+ve HER2u – ve as most common molecular pattern. Around 50% patients presented with TNM stage 2b at the time of diagnosis.

Neoadjuvant therapy received by ~ 20% patients following which patient underwent surgery. Roughly 85% patients underwent modified radical mastectomy and 5 % underwent breast conservation surgery , as choice of breast conservation surgery is limited by its contraindications and willingness of female for continues follow up also fear of recurrence in elderly fefemales. Different combination of adjuvant management were given depending on stage and molecular subtype.

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