


Original Research Article

Clinical study of molecular hormonal receptor level status among carcinoma of breast in Karaikal population

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Abstract

Background: Breast cancer patients with the same stage of disease can have markedly different treatment responses and overall outcome. The strongest predictors for metastases (for example, lymph node status and histological grade) fail to classify accurately breast tumors according to their clinical behavior. The discordance in estrogen receptor (ER), progesterone receptor (PgR) and human epidermal growth factor receptor 2 (HER2) status between primary and recurrent breast cancer are being intensively investigated and a large amount of data have been produced.

Aim: To study the epidemiological and clinical profile of carcinoma breast with analysis of receptor status.

Materials and methods: A descriptive study of 40 cases of carcinoma breast with receptor analysis, in Vinayaka Missions Medical College, Karaikal, from June 2015- June 2016 was done. Detailed history, clinical examination, and investigations were done, after staging, patients were treated with a suitable type of mastectomy, chemotherapy, radiotherapy and hormonal therapy as indicated. Cases were followed up for one year, data thus obtained was analyzed and results compared.

Results: All our cases were unilateral- 26 (65%) right breast and 14(35%) left breast. Majority of the cases had lump measuring >5cm –30 (75%). 23 (57.5%) of cases had a tumor in the upper outer quadrant, followed by other locations. Most of the cases were stage III- 27 (67.5%), 3 (7.5%) had metastasis at the time of presentation. The predominant histological type was infiltrating ductal

carcinoma 31 (77.5%). There was a predominance of ER+/PR+24 (60%), followed by ER-/PR-, ER+/PR- then ER-/PR+.

Conclusion: Majority of the cases belonged to stage III, with a predominance of infiltrating ductal carcinoma. Reporting to the hospital in earlier stages of the disease is lacking in the study population and highlights the need for public education and screening methods. It also emphasizes to analyze hormone receptor status in patients, as receptor positive status significantly reduces recurrence if hormone therapy is initiated.

Key words

Breast carcinoma, Er (estrogen receptor), PR (progesterone receptor), Chemotherapy, Radiotherapy.

Introduction

Breast cancer is the most common female cancer worldwide representing nearly a quarter (25%) of all cancers with an estimated 1.67 million new cancer cases diagnosed in 2012. In India, the age-adjusted incidence rate of breast cancer is 25.8 per 100 000 with a mortality of 12.7 per 100 000. Earlier cervical cancer was most common cancer in Indian woman but now the incidence of breast cancer has surpassed cervical cancer and is leading cause of cancer death, although cervical cancer still remains most common in rural India [1]. Certain unknown factors, habits, and customs prevalent in the community are noted to lead to differences in the incidence of breast cancer. For most of this century, management of cancer breast was largely based on anecdotal experience and the results of retrospective studies. But today it is predicated largely on the basis of randomised prospective clinical trials. They have shown that screening, neo-adjuvant systemic therapy, and radiotherapy can reduce mortality from breast cancer. It is now an accepted fact that cancer breast is a local manifestation of a systemic disease and the need for the moment is a better understanding of the natural history of the carcinoma breast [2]. This may provide a framework for investigating new therapies which may translate into better outcomes. ER expression is generally low in normal breast epithelium, except for a small peak in the first week of the menstrual cycle. On average, 80% of atypical ductal hyperplasias are associated with ER overexpression. Approximately 75% of low-grade DCIS lesions express ER 2 ISRN Oncology compared to only

30% of the high-grade DCIS lesions. ER positivity is found in up to 60 to 70% of invasive breast cancers. Expression of ER in DCIS alone compared to contiguous DCIS associated with invasive carcinoma has been investigated in the past. One study showed that intraductal carcinoma associated with invasive cancer was more frequently ER-positive compared to DCIS without associated invasion. There was a strong concordance of ER/PgR expression in contiguous DCIS associated with invasive cancer (98%) with virtually all cases being ER/PgR positive [3, 4].

Materials and methods

This was a hospital-based, descriptive study of 40 cases of carcinoma breast admitted in Vinayaka Missions Medical College, Karaikal from June 2015- June 2016 age group of the patients were between 30-60 years.

Inclusion criteria – All proven cases of breast carcinoma.

Exclusion criteria – Male breast carcinoma.

Patients were identified through electronic searches of the hospital diagnostic and treatment databases. Data were retrospectively extracted from the charts of patients diagnosed with breast cancer. After confirmation of eligibility, the following data were extracted from the medical charts if available: age, breast cancer risk factors, menopausal status, tumor histological subtype, hormone receptor and HER2 status, tumor size, tumor grade, presence of positive lymph nodes, type of surgery (breast conservation or

mastectomy) and the type of adjuvant treatment including chemotherapy, radiation and endocrine therapy. Follow up information was collected with specific attention to dates of the last follow-up, disease recurrence or death from breast cancer or any other cause. Information was extracted by data managers of the medical oncology service under the supervision of a medical oncologist (JJC) using predesigned datasheets. All the cases underwent detailed history taking, complete clinical examination, and investigations. Routine blood investigations, renal function test, ECG, chest X-ray, FNAC, trucut biopsy, USG abdomen were done to stage the disease. In patients presenting with locally advanced breast disease or metastatic disease, investigations like CT abdomen, CT thorax, mammography of the opposite breast, pleural and ascitic fluid analysis was done wherever needed. The staging was done as per TNM classification. ER/ PR status was done in the operated specimen. After staging the disease, patients were treated accordingly with a suitable type of mastectomy (simple/ simple mastectomy with axillary clearance/ modified radical mastectomy) and chemotherapy, radiotherapy and hormonal therapy as indicated. Cases were followed up for one year for response, complications, recurrence or metastasis. The data and results thus obtained were analyzed and compared.

Results

In our study, the majority of the patients belonged to the age group between 41- 50 years (**Table - 1**), youngest patient was 30 years old and oldest was 63 years old. Out of 40 patients, 22 (55%) patients were postmenopausal, 18 (45%) were premenopausal. A positive family history with a first degree affected relative was there in 3 (7.5%) patients. Lump in the breast was the main presenting complaints of the patients 31 (77.5%).

Frequent complaints were Lump in the breast was the main presenting complaints of the

patients 31 (77.5%), followed by pain, skin changes, and ulceration (**Table - 2**).

Out of 24 patients (60%) of cases presented within 6 months of onset of symptoms, 12 (30%) within 2 months and the remaining within 1 year (**Table - 3**).

Table - 1: Age group among the study population.

| Age group (Years) | Number of cases | % |
|-------------------|-----------------|------|
| 21 – 30 | 2 | 5 |
| 31 – 40 | 6 | 15 |
| 41 – 50 | 21 | 52.5 |
| 51 – 60 | 10 | 25 |
| 61 – 70 | 1 | 2.5 |
| Total | 40 | 100 |

Table - 2: Represents the chief complaints which were faced frequently by the patients.

| Complaints | No. of cases | % |
|----------------------------|--------------|------|
| Lump | 31 | 77.5 |
| Lump with pain | 4 | 10 |
| Lump with skin changes | 3 | 7.5 |
| Lump with ulceration | 1 | 2.5 |
| Lump with nipple discharge | 1 | 2.5 |

Table - 3: Duration of symptoms among the patients.

| Duration | No. of cases | % |
|---------------|--------------|-----|
| 2 months | 12 | 30 |
| 3- 6 months | 24 | 60 |
| 7 – 12 months | 3 | 7.5 |
| < 2 years | 1 | 2.5 |

Table - 4: Various sites of tumour among the patients.

| Site of tumor | No. of cases | % |
|----------------------|--------------|------|
| Upper outer quadrant | 23 | 57.5 |
| Upper inner quadrant | 5 | 12.5 |
| Lower outer quadrant | 3 | 7.5 |
| Lower inner quadrant | 5 | 12.5 |
| Central | 4 | 10 |

Out of 40 cases, 26 (65%) had a lump in the right breast and 14 (35%) had a lump in the left breast. There were no bilateral cases in our study. In our study, majority of the tumors had an extension to more than one quadrant, the quadrant which was filled totally with a tumor was taken as the site of a tumor, 23 (57.5%) of cases had a tumor in the upper outer quadrant (**Table - 4**).

Table - 5: Size of tumor measured after clinical diagnosis evaluation.

| Size of tumor | No. of cases | % |
|---------------|--------------|----|
| < 2 cm | - | - |
| 2- 5 cm | 10 | 25 |
| >5 cm | 30 | 75 |

Table - 6: Staging level of breast carcinoma.

| Stage of the disease | No. of cases | % |
|----------------------|--------------|------|
| I | - | - |
| IIa | 4 | 10 |
| IIb | 6 | 15 |
| IIIa | 12 | 30 |
| IIIb | 15 | 37.5 |
| IV | 3 | 7.5 |

Table - 7: Histopathological type seen in breast carcinoma.

| Histopathological type | No. of cases | % |
|-------------------------------|--------------|------|
| Infiltrating ductal carcinoma | 31 | 77.5 |
| Medullary carcinoma | 6 | 15 |
| Lobular carcinoma | 3 | 7.5 |

Table - 8: Receptor type positivity and negativity among patients.

| Status | No. of cases | % |
|---------|--------------|----|
| ER+ PR+ | 24 | 60 |
| ER+ PR- | 4 | 10 |
| ER- PR+ | 2 | 5 |
| ER-PR- | 10 | 25 |

In our study, majority of the cases had lump measuring between 5 – 10 cm, with the largest size being 10 x 12 cm (**Table - 5**).

Staging of the cases revealed most of them being in stage III. 3(7.5%) had metastasis at the time of presentation (**Table - 6**).

Histopathological examination showed that majority of the cases were infiltrating ductal type 31 (77.5%) (**Table - 7**). ER/PR status in the operated specimen was as per **Table - 8**.

Discussion

HR status is an important prognostic and predictive factor in breast cancer. While most HR expressing breast cancers express the ER, a small minority express PgR but not ER, even after retesting. There remains uncertainty about whether the ER-/PgR+ phenotype is real or simply an analytic artifact. The ER-/PgR+ subgroup may represent false negative ER, which may result from failed binding of the ER by the antibody used for its detection. Such lack of binding may result from a conformational change of the ER, caused, [4, 8]. Alternatively, this subgroup may represent false positive PgR; anti-PgR antibodies may cross-react with other antigens. To avoid these false results, analysis of ER and PgR status with two independent antibodies is desirable as the epitopes recognized by different antibodies should be distinct. In our study, the average age of affliction was 46.02 years which are in concordance with the age of 45.8 years quoted by Haque, et al. [4]. He reported that breast cancer occurs a decade earlier in Indian women than westerns. A study by MacMahon B, et al. there was 70% postmenopausal women, whereas our study showed 55% postmenopausal group [5]. A positive family history with a first degree affected relative was there in 3 (7.5%) patients. Nulliparity is definitely a high-risk factor with relative risk of 1.1 – 2 according to Barbara S Hulka [6]. But our present study had only 3 (7.5%), nulliparous women. In the present study lump in the breast was the presenting complaint in 77.5%, but after retrospectively examining, all patients had a lump. In our study 26 (65%) had right sided and 14(35%) had left a sided lump. In Srivastava series 53% had pathology in the right

side, 45.8% in left and 1.2 % were bilateral [7]. Our study revealed that the upper outer quadrant 23 (57.5%) was the most commonly involved site for carcinoma breast, followed by lower inner quadrant 5 (12.5%). Marshall and Higginbothams in their study had incidence in the following order upper outer quadrant -60%, upper inner quadrant 12%, lower outer quadrant 10%, lower inner quadrant 6% [8]. Statistics show that the occurrence of carcinoma breast is higher in upper outer quadrant which is explained by the fact that there is more breast tissue. Our study showed all cases with the size of a tumor more than 2 cm, which is in concordance with the study by Gang, et al. [9]. This shows the late presentation to the hospital in our population. In our study there were no cases belonging to stage I, most of them had stage III 67.5%, followed by stage II- 25%.study by Gang, et al. [9] had the majority of cases in stage III – 31%, with equal distribution in other stages. In our study 77% were infiltrating ductal carcinoma (not otherwise specified), 15% were medullary and 7.5% lobular carcinoma. These results were comparable to Rosen series- 75% ductal carcinoma (10%) and Macdivit study with 78.10% infiltrating ductal carcinoma [11]. The ER/PR status in our study correlates with that of R. Kim, et al. and Dunnwald K L, et al., with a predominance of ER+/PR+ 60%, followed by ER-/PR-, ER+/PR- then ER-/PR+ [12,13]. Stage II cases were treated with MRM with axillary clearance, adjuvant chemotherapy and hormonal therapy for ER/PR+ cases. Stage IIb and III were given neoadjuvant chemotherapy followed by MRM with axillary node clearance and adjuvant chemotherapy and radiotherapy. Stage IV cases underwent Palliative chemotherapy, radiotherapy, toilet mastectomy for cases with skin ulceration and function. During follow up 4 cases had a recurrence, of which 2 had not taken tamoxifen, and 2 did not follow up for chemotherapy and radiotherapy. This shows that recurrence is much lesser in cases with ER/PR + with early breast cancer receiving hormone receptor blocker.

Conclusion

The study shows that despite significant improvement in the management of the disease in the last few decades, it requires reporting to the hospital in earlier stages of the disease, which is lacking in the study population. Majority of the cases belonged to stage III, with a predominance of infiltrating ductal carcinoma. The study emphasizes the need for public education and awareness regarding carcinoma breast. Simple and effective methods like self- breast examination and clinical breast examination should be popularised among people as mammography for screening may not be cost-effective for this region. The study also emphasizes to analyze hormone receptor status in patients, as receptor positive status significantly reduces recurrence if hormone therapy is initiated.

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