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By
M.M. Sarfaraz Ali Khan, Imran Mohd. Ansari and
Anoop Kumar Jaiswal

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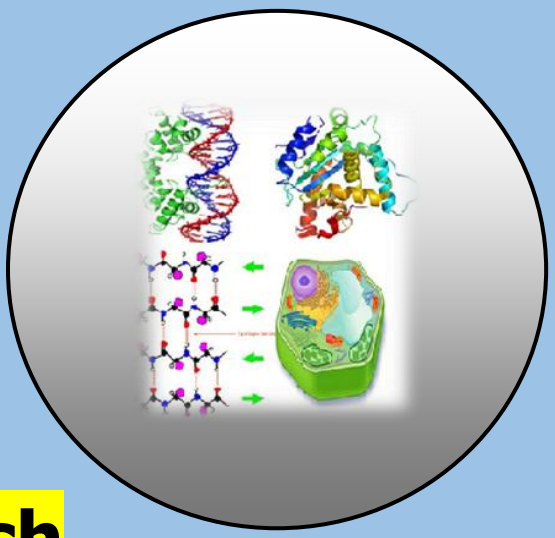

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**Dr. M.M.S.A. Khan, Dr. I.M. Ansari**
**http:// www.sasjournals.com**
**http:// www.jbcr.in**
**jbiolchemres@gmail.com**
**info@jbcr.in**

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# Metastasis in Carcinoma Breast: A Retrospective and Prospective Study

**M.M. Sarfaraz Ali Khan, Imran Mohd. Ansari and Anoop Kumar Jaiswal**

**Department of General Surgery IIMSR, Integral University, Lucknow, India**

## ABSTRACT

***Treatments for patient with breast cancer based are usually to reduced incidence of recurrence and metastases and those who already have metastatic disease to improve their life expectancy and quality of life. Retrospective studies suggest that discordance between primary and metastatic lesions leads to detrimental outcome. This prospective study investigated primary tumours and metastases in the same patient and assessed the impact of discordance on patient management and survival.***

***In our study patients who underwent surgery only, the chance of developing metastases 35.71% (5 of 14) was more in compare to patients who received hormone therapy after surgery 22.06% (15 of 68), risk of metastases further reduces when adjuvant chemotherapy were given after surgery 18.75% (12 of 64), when radiotherapy combined with chemotherapy after surgery risk of metastases was 17.65% (6 of 34). Thus the incidence of metastases in carcinoma breast reduced when adjuvant chemotherapy, neo-adjuvant chemotherapy, hormone therapy or radiotherapy added after surgery in comparison to patients who underwent surgery only.***

***Key words: Invasive lobular carcinoma, Invasive ductal carcinoma, Adjuvant chemotherapy, Neo- adjuvant chemotherapy, Retrospective study and Prospective study.***

## INTRODUCTION

The breast has always been symbol of women hood and it is the natural ornament gifted by god to women. Carcinoma of breast is common among Indian women and the incidence of carcinoma breast is surpassed only by carcinoma cervix amongst all cancer in India. For women the life time risk of developing breast cancer in U.S. is one in eight **(*Schwartz's Principles of Surgery*)**.

Currently, in India, the incidence of breast cancer has steadily increased over the years with as many as 100,000 new cases being detected every year. At a given time, there are as many as one million breast cancer patients in population. The lifetime risk of developing breast cancer is 1:30(incidence rate of 20/100,000) in urban India and 1:65 (incidence rate of 8.6/100,000) in rural India.Fewer than 10% of patient will present with metastatic disease but nearly 50% of newly diagnosed patient may eventually develop it in a classical study of untreated patient, the median survival of 2.7 year from the onset of symptoms **(BLOOM HJG, natural history of untreated breast cancer).**

The prognostic variables in breast cancer are still the gold standard:

***Tumour size***

***Axillary lymph node involvement***

***Lymph vascular invasion***

***Tumour grade and type***

## MATERIAL AND METHODS

Our study comprises of 242 cases of carcinoma breast from July 2011 to June 2014(Retrospective study) and July 2014 to June 2015 (Prospective study) presenting to the Department of surgery.

**Inclusion criteria**

1. All those cases presenting with breast lump proved by histological diagnosis as carcinoma breast had been included.
2. Those cases that could not be operated but presenting as a lump in breast proved as carcinoma breast after FNAC had also been included into study.

**METHODS**

Evaluation of the cases was made on the basis of two methods:

1. Retrospective study
2. Prospective study

In Retrospective study, the data was collected from the Bed Head Ticket of the patients, particular of patients, their clinical stage at the time of admission, treatment given; histopathology report and other investigation were noted from the Bed Head Ticket on Working Performa. Further the patient were written letter and a questionnaire was sent to them to comment on their wellbeing and complaint, if any.

In Prospective study the details were noted directly on Working Performa. The study was divided into three groups:

1. Early stage operable breast cancer
2. Locally advanced carcinoma breast
3. Patients already metastasised at the time of admission

Main consideration was given to:

*Stage of carcinoma breast at the time of admission.

*Treatment given in the form of neo adjuvant chemotherapy, curative surgery or palliative surgery, adjuvant chemotherapy, radiotherapy, and hormone therapy.

*Tissue histopathology report .

*Treatment of other systemic symptoms.

These cases further called upon at regular intervals for routine check-up and evaluated for complaints like cough with expectoration, bone pain, distension of abdomen, headache and vomiting etc. to find out the disease free survival and any metastasis if occurred (Table-1).

These patients were evaluated according to the need:

- Haemogram
- Biochemical investigation
- Liver function test
- Tumour marker
- Radiological investigation like X-ray chest, spine, pelvis, ribs etc.
- Ultrasonography
- CT scan

**Table1. On the basis of the site of metastases the distribution of the cases.**

| SITE | Invasive lobular carcinoma | Invasive ductal carcinoma |
|---|---|---|
| BONE | 7(77.7%) | 29(76.3%) |
| REGIONAL LYMPHNODE | 3(33.3%) | 32(84.2%) |
| LIVER | 3(33.3%) | 5(13.2%) |
| LUNGS | 3(33.3%) | 8(21.1%) |
| BRAIN | 2(22.2%) | 7(18.4%) |
| GASTROINTESTINAL TRACT | 4(44.4%) | 10(26.3%) |
| ASCITES | 3(33.3%) | 8(21.1%) |
| PERITONEUM | 3(33.3%) | 6(15.8%) |
| OVARY | 3(33.3%) | 5(13.2%) |
| TOTAL | 9 | 38 |

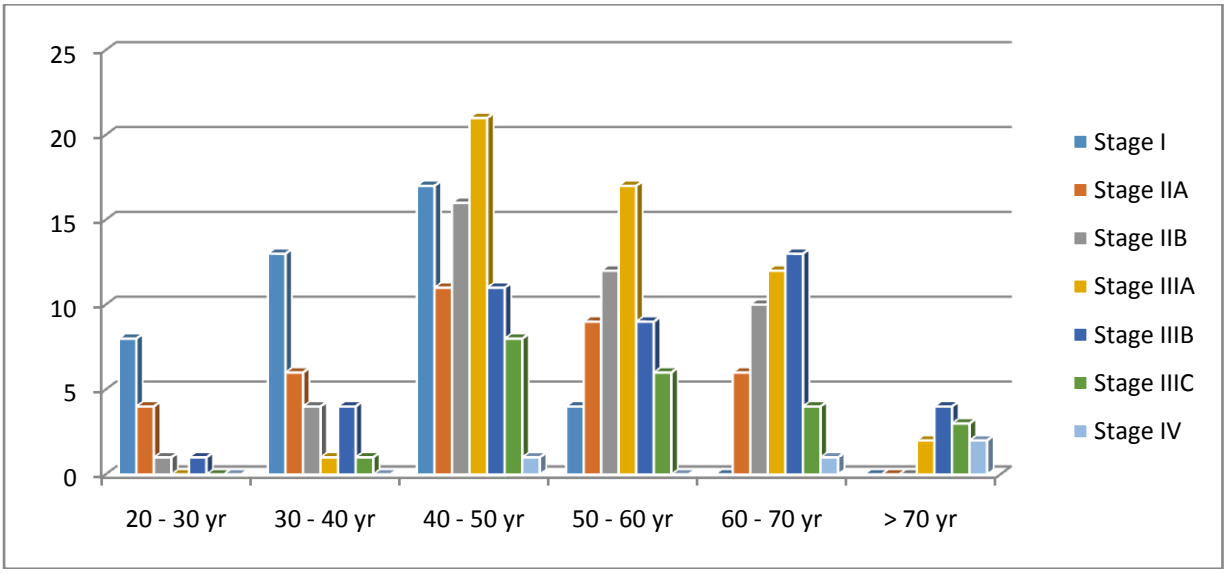


**Figure1.Distribution of Patients of Carcinoma Breast According to Age Group and Tumour Stage.**

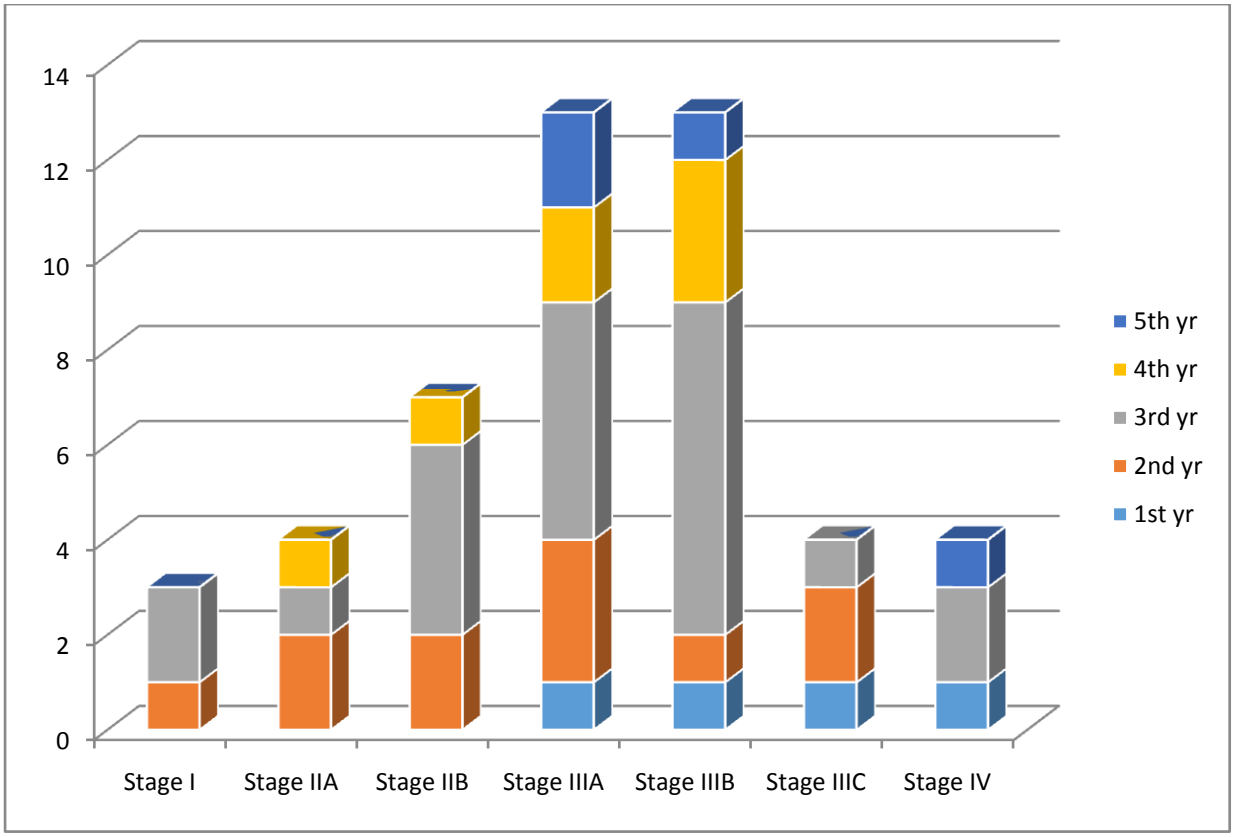


**Figure 2.Metastases in Relation to Stage of Carcinoma Breast and their Follow up.**

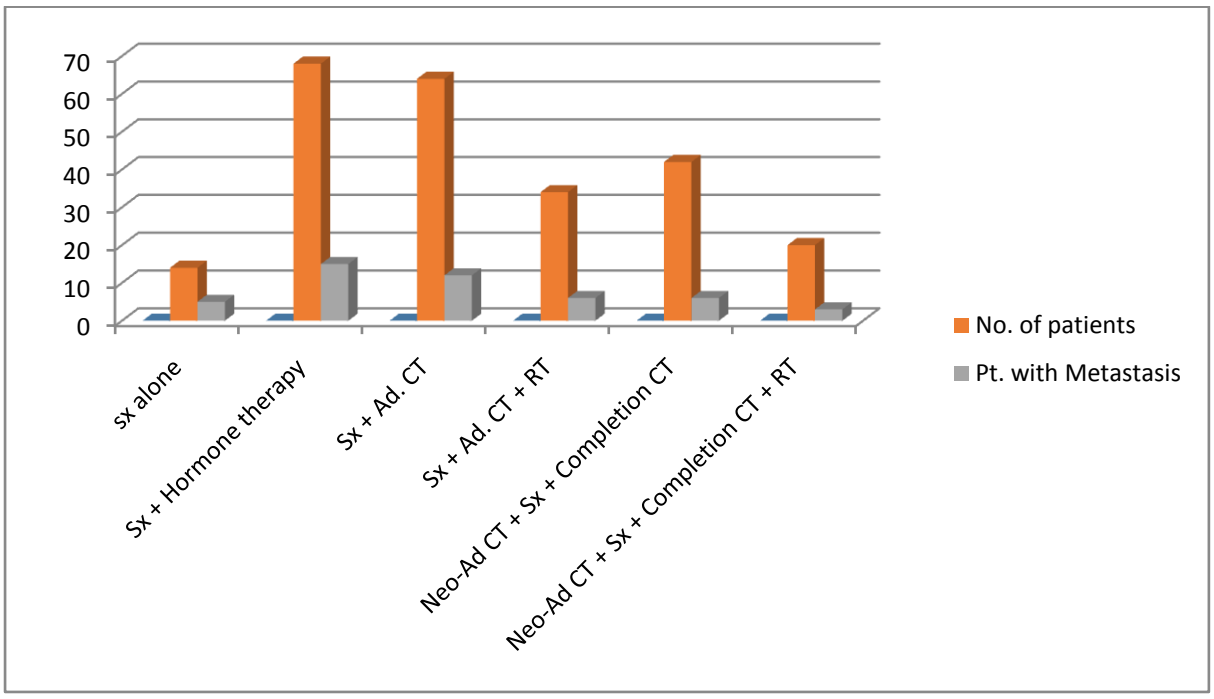


**Figure 3.Metastases in Relation to Modality of Treatment.**

## DISCUSSION

According to **Fig 1** metastases in carcinoma breast most common in age group 50-60 years 16(24.56%) cases followed by age group 60-70years 14(21.74%) cases then age group 40-50 years 12(18.82%), 30-40 years 3(10.03%) cases and there is only one case of metastases in age group 20-30years(7.14%).

The **table 1**(Carty et al., 1995) shows that Infiltration ductal carcinoma carries an increased rate of metastases, being 22.09% as compared to 14.81% of lobular carcinoma. Metastases in lobular carcinoma more commonly occurred to the gastro intestinal tract as compared to infiltration ductal carcinoma. At other sites the distribution of metastases was Bone(Coleman and Rubens 1987) (77.7%vs76.3%), ovary (33.3%vs13.2%), liver (33.3%vs 13.2%), lungs (33.3%vs 47.4%) and brain (Cady et al., 1997) (22.2%vs 18.2%). Overall, the metastases to bone was most common (76.59%), followed by liver (44.7%), lung (23.4%), ascites (23.4%), brain (19.2%), gastrointestinal tract (19.2%) and ovary (17

In our study patients who underwent surgery only chance of developing metastases 35.71% (5 of 14) was more in compare to patients who received hormone therapy after surgery 22.06% (15 of 68), risk of metastases further reduces when adjuvant chemotherapy were given after surgery 18.75% (12 of 64), when radiotherapy combined with chemotherapy after surgery risk of metastases was 17.65% (6 of 34). **Almost similar results of NSABP (National Surgical Adjuvant Breast and Bowel Project-University of Pittsburgh) B-17 and NSABP B-24 at 7 years of follow-up**, the total ipsilateral and contralateral breast cancer recurrence rate was 30% for excision alone, 17% for excision with radiation therapy, and 10% for excision, irradiation, and tamoxifen. Adjuvant chemotherapy(Chu and De Vita, 2003) reduces the risk of metastases. In stage I and II when surgery and adjuvant chemotherapy are the mode of treatment the risk of developing metastases is reduced to 18.75% from 35.71% in patients who underwent surgery only. In stage III or locally advanced disease the risk of developing metastases is 16.67% which is reduced to 15.0% if radiotherapy is added**(Fig 3).**Neo adjuvant (anterior) chemotherapy as a treatment modality reduces the incidence of metastases. In our study addition of neo adjuvant chemotherapy before surgery reduced the incidence of metastases from 18.75% to16.67% and further reduced to 15.00% in patients who had received radiotherapy after surgery. Similar observations were reported by **Nemeto** *et al* 1980.

**Table 2. Metastases of Different Organs in Carcinoma Breast.**

| **Site of metastases** | **3rd month** | **6th month** | **1st year** | **2nd year** | **3rd year** | **4th year** | **5th year** |
|---|---|---|---|---|---|---|---|
| BONE | 0 | 1 | 0 | 8 | 18 | 6 | 3 |
| REGIONAL LYMPHNODE | 0 | 1 | 2 | 10 | 14 | 6 | 2 |
| LIVER | 0 | 0 | 0 | 7 | 9 | 3 | 2 |
| LUNGS | 0 | 0 | 0 | 10 | 7 | 4 | 0 |
| BRAIN | 0 | 0 | 0 | 4 | 3 | 1 | 1 |
| GASTROINTESTINAL TRACT | 0 | 0 | 0 | 3 | 5 | 1 | 0 |
| ASCITES | 0 | 0 | 0 | 4 | 5 | 1 | 1 |
| PERITONEUM | 0 | 0 | 0 | 3 | 6 | 0 | 0 |
| OVARY | 0 | 0 | 0 | 3 | 4 | 1 | 0 |

Thus the incidence of metastases in carcinoma breast reduced when adjuvant chemotherapy, neo-adjuvant chemotherapy, hormone therapy or radiotherapy added after surgery in comparison to patients who underwent surgery only. Overall best results were achieved when neo-adjuvant chemotherapy given prior to surgery and adjuvant chemotherapy with radiotherapy given after surgery(Ciezki and Mackils, 1995). Similar observation were reported by **Fisher B. *et al,*** 2001.

In our study most of the bone metastases (75%) in breast carcinoma developed within three year of follow up and belongs to stage III (Table-2). Majority of Regional metastases in lymph nodes developed in stage II and I in 2nd and 3rd year of follow up. Liver and lung metastases also developed in 2nd and 3rd year of follow up in post mastectomy patients) **(Fig 2)**.

The patients who treated with surgery alone or with hormone therapy after mastectomy had more chance to developed metastases in compared to patients who received adjuvant chemotherapy and radiotherapy after mastectomy.

**FACTORS ASSOCIATED WITH METASTASIS IN BREAST CARCINOMA**

- PATIENT AGE(Albain et al., 1994)
- NODAL STATUS(Cady et al., 1997)
- STAGE OF THE PRIMARY TUMOR
- ESTROGEN AND PROGESTERONE RECEPTORS(Alanko et al., 1985)
- HISTOLOGICAL FEATURES AND NUCLEAR GRADE(Battifora et al., 1993)
- MOLECULER RECEPTOR

## CONCLUSIONS

- During the management of patients with carcinoma breast admitted to this hospital from July 2014 to June 2015,the following conclusions was drawn regarding its correlation with the clinical status and its effect on the outcome of the patients.
- Metastasis was lowest in the age group 20-30 years(Albain et al., 1994).
- Most common age of presentation with Carcinoma breast was between 40 to 50 years (Albain et al., 1994).
- There was no significant difference in the incidence of metastasis in the age group 40 to 50 years and 50 to 60 years(Albain et al., 1994).
- Incidence of carcinoma breast and metastases increases with age(Albain et al., 1994).
- Higher tumour stage was associated with increased risk of metastasis.
- Patients with positive ER/PR receptor status had lower risk of developing metastasis as compared to patients with negative ER/PR receptor status(Alano et al., 1985).
- Higher tumour grade was associated with increased risk of metastasis.
- Lympho-vascular embolization is associated with increased risk of developing metastasis.
- Incidence of metastasis is lower in patients having infiltrative lobular carcinoma as compared to infiltrative ductal carcinoma.
- Most common sites of metastasis were bones, liver, lungs and brain.

- Metastasis of infiltrative lobular carcinoma occur more commonly to gastrointestinal tract, genitourinary region where as infiltrative ductal carcinoma occur more commonly to liver and lungs. Metastases to bones are same in both histological types.
- Most of the metastasis occurred within three years of follow up.
- The risk of developing metastasis is higher in patients who undergone surgery only in comparison to patients who receive chemotherapy or radiotherapy after surgery(Alberts et al., 1997, Bartelink et al., 1993 and Battifora et al., 1993)
- Neo.-adjuvant (anterior) chemotherapy when given before surgery as a treatment modality reduces the incidence of metastases(Bria et al., 2006, Brodie et al., 1986 and Buzdar and Cuzick, 2006)
- Adjuvant chemotherapy reduces the risk of metastases. When surgery and adjuvant chemotherapy are the mode of treatment the risk of developing metastases is reduced to 18.75% from 35.71% in patients who underwent surgery only(Bonadonna et al., 1976).

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**Corresponding author: Dr. M.M. S.A. Khan, Department of General Surgery IIMSR, Integral University, Lucknow, India**
**Dr. Imran Mohd. Ansari, Department of General Surgery IIMSR, Integral University, Lucknow, India**
**Mobile No.: 08081167275**
**Email:dr.m.m.s.a.khan@gmail.com/ drimranafreen@gmail.com**