Original Article

Breast carcinoma in young females below the age of 35 years - histopathological and prognostic significance

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Keywords:
Breast; Ductal carcinoma; Prognosis; Young age

ABSTRACT

INTRODUCTION
Breast cancers rarely occur in young women. About 2% of the patients with breast cancer are < 35 years.¹ Breast cancer at young age has been reported to have a more aggressive behavior and unfavorable prognosis compared to the older patients.¹²

The aim of this study was to evaluate the implication and prognostic significance of diagnosis of breast carcinoma below the age of 35 in comparison to the age over 35 in Pokhara valley, Nepal.

MATERIALS AND METHODS
This was a retrospective and prospective study done from the period of January 2000 to September 2011. All the patients who were diagnosed as breast carcinoma and underwent mastectomy were included. All cases were reviewed and the relevant clinical data were collated and the
Table 1: Distribution of cases according to age

<table>
<thead>
<tr>
<th>Age group</th>
<th>Number of cases</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>20 – 25</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>&gt;25 – 30</td>
<td>9</td>
<td>23(16%)</td>
</tr>
<tr>
<td>&gt;30 – 35</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>&gt;35 – 40</td>
<td>23</td>
<td></td>
</tr>
<tr>
<td>&gt;40 – 45</td>
<td>46</td>
<td></td>
</tr>
<tr>
<td>&gt;45 – 50</td>
<td>41</td>
<td></td>
</tr>
<tr>
<td>&gt;50</td>
<td>15</td>
<td></td>
</tr>
</tbody>
</table>

Table 2: Histological types in all cases

<table>
<thead>
<tr>
<th>Types Of Carcinoma</th>
<th>Below 35 (n=23)</th>
<th>Above 35 (n=125)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ductal</td>
<td>20 (87%)</td>
<td>113 (90%)</td>
</tr>
<tr>
<td>Lobular</td>
<td>1 (4%)</td>
<td>3 (2%)</td>
</tr>
<tr>
<td>Medullary</td>
<td>2 (8%)</td>
<td>3 (2%)</td>
</tr>
<tr>
<td>Metaplastic</td>
<td>-</td>
<td>2 (1.6%)</td>
</tr>
<tr>
<td>Secretory</td>
<td>-</td>
<td>1 (0.8%)</td>
</tr>
<tr>
<td>Apocrine</td>
<td>-</td>
<td>1 (0.8%)</td>
</tr>
<tr>
<td>Papillary</td>
<td>-</td>
<td>1 (0.8%)</td>
</tr>
<tr>
<td>Mucinous</td>
<td>-</td>
<td>1 (0.8%)</td>
</tr>
</tbody>
</table>

Table 3: Tumor size (T) and nodal status (N) in all cases below and above 35 years of age

<table>
<thead>
<tr>
<th>Tumor &amp; Lymph node</th>
<th>Below 35 (n=23)</th>
<th>Above 35 (n=125)</th>
</tr>
</thead>
<tbody>
<tr>
<td>T0</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>T1 ≤2 cm</td>
<td>16 (70%)</td>
<td>54 (43%)</td>
</tr>
<tr>
<td>T2 &gt;2 cm and ≤5 cm</td>
<td>6 (26%)</td>
<td>44 (35%)</td>
</tr>
<tr>
<td>T3 &gt;5 cm</td>
<td>1 (4%)</td>
<td>20 (16%)</td>
</tr>
<tr>
<td>T4 Chest wall / skin invasion</td>
<td>-</td>
<td>7 (6%)</td>
</tr>
<tr>
<td>N0 No regional node</td>
<td>12 (52%)</td>
<td>45 (36%)</td>
</tr>
<tr>
<td>N1 Movable ipsilateral axillary node</td>
<td>11 (48%)</td>
<td>80 (64%)</td>
</tr>
</tbody>
</table>

Table 4: TNM staging of all cases

<table>
<thead>
<tr>
<th>TNM Stage</th>
<th>Below 35 (n=23)</th>
<th>Above 35 (n=125)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>9 (39%)</td>
<td>34 (27%)</td>
</tr>
<tr>
<td>II</td>
<td>12 (52%)</td>
<td>50 (40%)</td>
</tr>
<tr>
<td>III</td>
<td>2 (9%)</td>
<td>41 (33%)</td>
</tr>
</tbody>
</table>

Table 5: Microscopic findings of tumors in both age groups

<table>
<thead>
<tr>
<th>HISTOLOGICAL FINDING</th>
<th>Below 35 (n=23)</th>
<th>Above 35 (n=125)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tumor emboli</td>
<td>15 (65%)</td>
<td>83 (66%)</td>
</tr>
<tr>
<td>Dermal / nipple invasion</td>
<td>-</td>
<td>10 (8%)</td>
</tr>
<tr>
<td>Stromal inflammation</td>
<td>18 (78%)</td>
<td>108 (86%)</td>
</tr>
<tr>
<td>Necrosis</td>
<td>18 (78%)</td>
<td>90 (72%)</td>
</tr>
</tbody>
</table>

Table 6: Bloom Richardson Grading of all cases

<table>
<thead>
<tr>
<th>Grade</th>
<th>Below 35 (n=23)</th>
<th>Above 35 (n=125)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>6 (26%)</td>
<td>63 (50%)</td>
</tr>
<tr>
<td>2</td>
<td>8 (35%)</td>
<td>46 (37%)</td>
</tr>
<tr>
<td>3</td>
<td>9 (39%)</td>
<td>16 (13%)</td>
</tr>
</tbody>
</table>

Histopathology slides were reviewed by two pathologists independently. Patients were grouped in two age groups as below and above 35 years. All data including family history, clinical presentations, pathological type and grade, TNM stages were compared. Follow up data with data on recurrence were analyzed. Exclusion criteria included (a) the patients who were diagnosed as Stage IV and did not undergo mastectomy and (b) patients who were diagnosed as breast carcinoma on fine needle aspiration cytology but were lost to follow up.

RESULT

Out of total 148 mastectomy specimens, 125 cases (84%) were above 35 years and 23 cases (16%) were below 35 years (Table 1). Ductal carcinoma was the most common tumor in both age groups. Table 2 enumerates all the histological subtypes in both age groups. Tumor size and regional node involvement are shown in Table 3. Majority of the patients in younger age group presented in T1 stage (70% vs 43%) and 48% of younger patients had nodal metastasis in contrast to 64% in older age groups with nodal metastasis. Among those patients with nodal metastasis, older patients had lesser number of nodes. In younger patients with positive lymph nodes (11 cases), 6 cases (54.5%) had ≥4 lymph nodes involved; whereas among the older patients with positive lymph nodes (80 cases), 54 (67.5%) had ≤3 lymph node metastasis.

TNM stages in both age groups are compared in Table 4. In the microscopic findings, tumor emboli, stromal inflammation and necrosis were seen in both age groups but dermal/ nipple invasion (T4) was more common in older age groups as shown in Table 5. According to Modified Bloom Richardson grading (Table 6), grade 3 (fig. 1) was the commonest below 35 years age group (39%) followed by grade 2 (35%; fig. 2). In contrast, older age group showed lower grade with 50% being grade 1 (fig. 3) followed by grade 2 (37%). More positive family history (39% vs. 9.6%) and higher recurrence rate (87% vs. 74%) among the followed up cases were seen in younger age group.

DISCUSSION

Breast cancer in adolescence and early adulthood is a rare condition.\(^1\) The estimated incidence is less than 0.1 per 100,000 women below the age of 20 years, increasing to 1.4 for women 20–24 years, 8.1 for women 25–29 years and 24.8 for women 30–34 years old.\(^2\) In our study 4.05% women were of 20-25 years, 6.08% women were of 26-30 years and 5.4% were of 31-35 years were having breast cancer. Childhood breast cancer accounts for less than 1% of childhood cancers and less than 0.1% of all breast cancers.\(^3\)\(^-\)\(^5\)

Breast masses in young women are mostly benign.\(^6\)\(^-\)\(^8\) A population-based study over a period of 70 years confirms...
that breast carcinoma in young women is rare and more often caused by metastases or stromal malignancy such as malignant phyllodes tumor. Breast masses in adolescence demonstrates that fibroadenomas are the most common breast masses whereas malignancy was rare and more often caused by metastases or stromal malignancy such as malignant phyllodes tumor. Breast carcinoma accounted for only 0.02% in surgically removed breast masses in girls and young women. In a review of 357 patients aged 25 years or younger with a breast mass, 0.8% were benign phyllodes tumor, 0.3% had a breast carcinoma, and the rest had benign disease.

In another study of 178 breast masses in patients aged 20 years or younger, no carcinomas were found. Dehner et al found only one case of breast cancer in a review of 374 breast masses in patients younger than 20 years of age. In our study there was no malignant case in younger than 20 years as the youngest patient with cancer was of 22 years-old.

Breast cancer occurring in very young patients are reported to have an aggressive biological behavior leading to a unfavourable prognosis. 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. Similar findings have been reported in the past. More positive axillary lymph nodes and higher incidence of local recurrences were detected in younger compared with older patients. According to Ashley S et al, breast cancers in young age group tend to be larger when diagnosed and have a longer history of a palpable mass than tumours diagnosed in older women. However in our study, the tumor size in the younger group was smaller in size than the older group. T1 tumor was more frequently found in younger group (70% vs 43%) resulting in lower TNM stage in younger age group.

Immuno-markers and genetic studies also confirm that the breast carcinoma in young is different subset. Younger patients usually have ER/PR negative tumor and, those with ER-positive tumors had a significantly worse prognosis than those with ER-negative tumors. There are specific subsets of young women who have a potential high-risk of developing breast cancer at a young age based on a genetic predisposition or having previously received irradiation. Women diagnosed with breast cancer at the age of <35 years are likely to have germ-line BRCA1 or BRCA2 mutations in up to 15–30% of cases. These mutations are more frequently associated with higher histological grade, lack of ERs, perivascular invasion and high proliferation rate. The percentages of overexpression of HER2/neu in very
young’ and ‘less young’ women were similar in the study
done by Colleoni et al. 1

A study of more than 1 million women with breast cancer
recorded in the American College of Surgeons Cancer
Database between 1998 and 2005 demonstrated that women
younger than 40 years of age were more likely to present
with more advanced (stage III or IV) disease (20% vs.
13.5%), and they were more likely to have infiltrating ductal
carcinoma (76.9 vs. 67.9). 22

In our 11 years study, 16% of all mastectomy cases were
of < 35 years of age. Lymph node metastasis was seen
more frequently in older age group (older 64% vs. younger
48%) but in those cases with nodal metastasis, younger
patients showed more predilections to increased number of
nodal involvement. In both groups TNM stage II was
the commonest, but Stage I is seen to be more common in
younger age group. Older age group showed more number of
skin infiltration (10 cases, 8%) resulting in T4 stage
(fig.4). But, on the contrary, histological grade clearly
shows a more aggressive tumor in younger group.

The triple test (palpation, ultrasound examination and core
needle biopsy) is currently considered the gold standard
for evaluation of breast masses in women younger than 30
years. 18 Excisional biopsy is now reserved for the patient
in whom the core needle is non-diagnostic; when there is
discordance in pathological findings, physical examination,
and radiologic appearance. There is growing evidence that
core needle biopsy is not routinely required in evaluation
of breast masses in young women, except where metastatic
disease is suspected. 6,18

Poorer survival, in young patients, could be related to
reduced screening, more aggressive disease, and delayed
diagnosis. 23 Corpron CA et al found that delayed diagnosis
in young women results from delayed presentation and
biopsy, similar to other reports. 23 Younger women still have
significantly poorer survival even after adjusting for stage,
histology and grade. 24 Prevention and early detection are
vitally important in these women. At present, definitive
data on effective screening and prevention of breast cancer
in very young women are lacking, but there are a number of
ongoing trials which would provide some evidence on
which to base future recommendations. 18

CONCLUSION

In our study we found that younger patients presented
with higher grade, more positive family history and more
recurrence rate. However, tumor size and TNM stage was
lower in younger age group. So, age should be considered as
an important factor in assessment of the prognosis and more
regular follow up should be carried out after mastectomy
in younger patients. Further studies including hormonal
markers like ER/PR and genetic studies in this group of
population may give more insight in future.

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