

# Occurrence of High Risk Features of Breast Cancer in Young Females having Age $\leq 35$ Years

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## ABSTRACT

**Aim:** To evaluate the clinico-pathological and immuno-histo-chemical features of breast cancer in young females having age  $\leq 35$  years.

**Methods:** In this descriptive prospective study, we included the data of 60 BC female patients having age  $\leq 35$  years. The study period was Jan-2018 to Jan-2019. In all patients, histopathological tumor type, tumor staging and grading of tumors was done. Vascular invasion and extra-nodal involvement was also observed. Based on receptor expression the tumors were divided into luminal subtype A, luminal subtype B and triple negative cases.

**Results:** Out of 60, 80% patients presented with late stages (stage III or IV). Regarding histological typing, invasive ductal carcinoma with associated DCIS comedo type was found in 50 (83.3%) patients, invasive lobular in 4 (6.66%) patients, poorly differentiated in 4 (6.66%) patients and metaplastic Ca in 2 (3.33%) patients. Regarding molecular subtyping, there were 8 (13.3%) patients who were having luminal subtype A and 10 (16.7%) patients were having luminal subtype B class, and remaining 42 (70%) patients were triple negative.

**Conclusion:** Most of the young patients of breast cancer having age  $\leq 35$  years present with more aggressive clinicopathological features and have poor prognosis.

**Keywords:** Breast cancer, Young age, Histopathological features.

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## INTRODUCTION

Breast cancer (BC) is now designated as the most common carcinoma in females and about 0.5 million women deaths worldwide are due to BC.<sup>1</sup> In Pakistan BC incidence rate is 23%, and 16.1% deaths from cancer are due to BC<sup>2</sup>. Pakistan has been nominated to have highest rate of BC in the whole Asian continent<sup>3</sup>. BC is usually diagnosed in post-menopausal period, with a mean age of 50 years or more, but in recent years an increasing incidence of BC has been reported in young females<sup>4,5</sup>. However, no standardized definition of young age is still defined, some studies have used cut off value of 35 years, and some others 40 or 50 years<sup>6,7</sup>.

This increased incidence may be due to adaptation of behavioral factors such as changes in diet habits, exposure to exogenous hormones or first pregnancy in late age.<sup>8</sup> Family history also has significant association with BC diagnosis in young age, some studies have reported weak association of family history with BC and concluded that the cause in most cases is sporadic<sup>9</sup>.

The young women have severe disease and poor prognosis.<sup>10,11</sup> This is may be because of late diagnosis of BC in these females because of poor information about disease and therefore delay in medical check-up, absence of screening programs in young females, rapidly growing nature of tumors and dense breast parenchymal tissues, all these factors hinder the clinical diagnosis of BC and even during imaging evaluation. Therefore, diagnosis of BC in these females is highly based on imaging methods as compared to the clinical ones.

In present study we evaluated the clinico-pathological and immuno-histo-chemical features of breast cancer in young females, because very little work is published on

Pakistani women regarding clinic-pathological and immuno-histo-chemical features of BC in young females

## METHODS

In this descriptive prospective study, we included the data of 60 BC female patients having age  $\leq 35$  years. The study period was Jan-2018 to Jan-2019. Consent from patients was taken for collecting their personal data for study purpose. Hospital approval was also obtained.

In all patients, histopathological tumor type was defined using WHO classification of BC. Tumor staging was according to the 8<sup>th</sup> ed. of AJCC-classification, and grading of tumors was done using SBR grading classification system, while vascular invasion and extra-nodal involvement was observed on histological basis.

Progesterone and estrogen receptors were labelled positive if 10% cells showed nuclear expression. Her-2 expression was diagnosed using immunohistochemical techniques, by staining cytoplasmic membranes. Based on receptor expression the tumors were divided into luminal type A (PR +Ve, ER +Ve and Her-2 -Ve) and luminal type B lesions (PR -Ve, ER -Ve and Her-2 +/-Ve) and triple negative (PR -Ve, ER -Ve and Her-2 -Ve), and Her-2 enriched (ER-Ve, PR-Ve, Her-2 +Ve).

Because of descriptive nature of study, we only calculated mean  $\pm$  S.D. for continuous and percentages for qualitative variables. These calculations were performed through SPSS v23 software.

## RESULTS

All of study females were of age  $\leq 35$  years. Out of 60, 80% patients presented with late stages (stage III or IV). There

were 50 (83.3%) patients in whom high grade tumors were diagnosed (Table 1).

Regarding histological typing, invasive ductal carcinoma with associated DCIS comedo type was found in 50(83.3%) patients, invasive lobular in 4(6.66%) patients, poorly differentiated in 4 (6.66%) patients and metaplastic Ca in 2(3.33%) patients (Table 1).

Regarding molecular subtyping, there were 8(13.3%) patients who were having luminal subtype A and 10(16.7%) patients were having luminal subtype B class, and remaining 42(70%) patients were triple negative (Table 1).

Table 1. Data of study outcomes.

<b>BC Stage</b>	
Early (Stage I to II)	12 (20%)
Late (Stage III to IV)	48 (80%)
<b>SBR Grade</b>	
High Grade (G3)	50 (83.3%)
Low Grade (G1-G2)	10 (16.7%)
<b>Histological Type</b>	
<i>invasive ductal carcinoma with associated DCIS comedo type</i>	50 (83.3%)
<i>Invasive lobular</i>	4 (6.66%)
<i>Poorly Differentiated</i>	4 (6.66%)
<i>Metaplastic Ca</i>	2 (3.33%)
<b>Vascular Invasion</b>	44 (73.3%)
<b>Extra-nodal Involvement</b>	21 (35.0%)
<b>Molecular Subtype</b>	
<i>Luminal A</i>	08 (13.3%)
<i>Luminal B</i>	10 (16.7%)
<i>Triple Negative</i>	42 (70.0%)

## DISCUSSION

A dramatic increase in BC incidence has been observed more than any other cancer in past years worldwide. Still the causes of BC are not completely explored this may include; duration of estrogen exposure, alcohol intake, oral contraceptives, obesity, and hormone replacement therapy and family history of BC<sup>14</sup>.

Diagnosis of BC is much difficult in younger females as compared to older ones. Malignancy is more common at this age, and detection is also difficult in these patients<sup>15</sup>.

In present study, we used age cut-off value of 35 years to define young age. However, many other studies have used 40 years as cut-off value. We evaluated the histo-pathological and immune-histo-chemical aspects of breast carcinoma in young females.

We found Stage III and IV tumors in 80% patients, high grade tumors in 83.3% patients, invasive ductal carcinoma with associated DCIS comedo type was found in 50 (83.3%) patients, invasive lobular in 4(6.66%) patients, and poorly differentiated lesions in 4(6.66%) patients. Regarding molecular subtyping, there were 8(13.3%) patients who were having luminal subtype A and 10(16.7%) patients were having luminal subtype B class, and remaining 42 (70%) patients were triple negative

A similar study by Hwang et al. took young age as ≤35 years, and found stage III and IV stage tumors in 18.2% patients, and stage I-II tumor 81.8% patients. They reported Her-2 positive tumors in 55.8% cases, ER positive in 53.5% and PR positive in 44.2% and triple negative cases in only 30.2% patients. receptor expression in their study was different from our study<sup>16</sup>.

Another study conducted by Eugenio et al. on histo-pathology of BC in young (≤40 years) females, found SBR grade III tumors in 50.9% patients, vascular invasion in 2.5% cases, lymph-node invasion in 23.8% cases, perineural invasion in 7.4% cases, luminal subtype A in 13.9% patients, luminal subtype B in 42.6% patients and triple negative in 20.2% patients<sup>17</sup>

A study by Siauqi et al. found meta-stasis in 18.2% patients, stage III and IV tumors in 48.6% patients. They found vascular invasion in 38.1% patients. regarding SBR grading, grade III they reported in 31.4% patients, II in 61.1% and grade I in 7.4% patients. On molecular subtyping, luminal subtype A was found in 52.2% patients, Luminal subtype B in 24.4% patients and triple negative in 16.8% patients. More-over the authors compared young age patients with older ones and found more aggressive tumors, late diagnosis in higher number of young females as compared to older ones<sup>18</sup>.

Still no recommended guidelines have been published regarding screening of young females and to define young age in females for early BC detection, except in symptomatic or at high risk population<sup>19</sup>. Moreover, researches are needed to develop the approaches for BC prevention, predictors of early detection of BC in young aged females. Awareness programs should also be organized in young females to give them the awareness regarding BC.

## CONCLUSION

Most of the young patients of breast cancer having age ≤35 years present with more aggressive clinicopathological features and have poor prognosis.

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