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CHARACTERIZATION OF BREAST CANCER SPECTRUM IN PAKISTANI FEMALES UNDER 40 YEARS

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Abstract

Objective: *To analyze the clinico-pathological characteristics, tumor biology, and risk factors of breast cancer in females under 40 years at a tertiary care hospital in Pakistan.*

Study Design: *Cross-sectional study.*

Place and Duration of Study: *The outpatient Department of General Surgery at Jinnah Postgraduate Medical Center in Karachi, from June 2024 to January 2025.*

Methodology: *A total of 144 female patients under the age of 40 who had histologically confirmed primary breast cancer were included. The study included patients with complete clinical and pathological data, such as demographic information, tumor size and stage, histological subtype, and receptor status.*

Results: *The study included 144 participants with a mean age of 33.7 years (±3.2). The majority of participants were between 35 and 40 years old (47.2%), followed by those aged 30 to 34 years (40.9%), and a smaller proportion aged 20 to 29 years (11.8%). Among the 144 participants, the majority of tumors were grade III (102 cases, 70.8%), followed by grade II (36 cases, 25.0%) and grade I (6 cases, 4.2%). Estrogen receptor (ER) positivity was observed in 106 cases (73.6%), progesterone receptor (PR) positivity was identified in 58 cases (40.2%). Regarding HER2/Neu status, 81 cases (56.2%) were HER2/Neu positive and 63 cases (43.8%) were HER2/Neu negative.*

Conclusion: *Breast cancer in young women often manifests through noticeable symptoms such as a prominent lump and associated discomfort. Our research revealed that 47% of the patients of BC were aged ≥35 years.*

INTRODUCTION:

Breast cancer remains the most prevalent malignancy among women worldwide, impacting more than 1.5 million women each year and representing the leading cause of cancer-related mortality in females globally.[1] In 2020 alone, there were approximately 19.3 million new cancer diagnoses and around 10 million fatalities.[2] Alarmingly, breast cancers constitute one in four cancer cases and one in six cancer deaths among women. This high incidence makes breast cancer the most common cancer type across the majority of countries worldwide, with 159 out of 185

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nations reporting significant cases, and causes of death from cancer recorded in 110 countries.[3]

In Pakistan, breast cancer affects a significant portion of women, with recent data showing an incidence rate of 14.5%, translating to approximately 25,928 new cases in 2020.[4] The mortality rate stands at 11.7%, resulting in about 13,725 deaths that year. The prevalence of breast malignancies is increasing, and currently, one out of every nine Pakistani women faces the risk of being diagnosed with this deadly disease during her lifetime.[5]

Enhanced awareness, increased mammographic screening, precise diagnoses, and a higher number of women receiving effective treatments have significantly contributed to lowering mortality rates across the Americas, Europe, and Australia.[6] However, the incidence of cancer continues to grow.[7] The rise in mortality rates, particularly in developing nations, is probably due to delayed diagnoses and restricted access to effective therapies and healthcare facilities, among other factors.[8]

Young women tend to be diagnosed with advanced-stage breast cancer more frequently, partly due to the absence of effective screening methods tailored for women at average risk in this age group.[9] Additionally, breast cancers in younger patients often exhibit more aggressive characteristics, such as being hormone receptor-negative, HER2-positive, and high grade.[10] The aim of present study was to analyze the clinico-pathological characteristics, tumor biology, and risk factors of breast cancer in females under 40 years at a tertiary care hospital in Pakistan.

Methods:

Study Design, Place and Duration of Study: This cross-sectional study was conducted in the outpatient Department of General Surgery at Jinnah Postgraduate Medical Center in Karachi, from June 2024 to January 2025.

Inclusion and Exclusion Criteria: The study included patients with complete clinical and pathological data, such as demographic information, tumor size and stage, histological subtype, and receptor status including estrogen (ER), progesterone (PR), and human epidermal growth factor receptor 2 (HER2). Patients with metastatic disease originating from non-breast primary tumors, as well as those lacking essential data—such as histology or receptor status—were excluded from the study.

Sample size: A total of 144 females were included who presented during the study period.

Study Protocol: A total of 144 female patients under the age of 40 who had histologically confirmed primary breast cancer were included. Informed consent was obtained from all participants prior to their inclusion.

Data Analysis: Data collection and analysis were conducted using SPSS Version 22. Quantitative variables such as age, and parity were summarized by calculating their means and standard deviations (Mean ± SD). For categorical variables—including tumor laterality, histological type, tumor grade, stage at diagnosis, ER/PR/HER2 receptor status, molecular subtype, and presence of—frequencies and corresponding percentages were determined.

RESULTS:

The study included 144 participants with a mean age of 33.7 years (±3.2). The majority of participants were between 35 and 40 years old (47.2%), followed by those aged 30 to 34 years (40.9%), and a smaller proportion aged 20 to 29 years (11.8%). Most participants resided in rural areas (61.1%), while 38.9% resided in urban areas. A family history of breast cancer was reported in 8.3% of the cases. The average parity was 2.3 (±1.7). Regarding lifestyle factors, 10.4% had a history of smoking, 31.2% had previously used hormonal therapy, and 3.5% had a history of prior breast biopsy. In terms of clinical tumor characteristics, the most common presenting symptom was a breast lump, observed in 95.1% of participants. Pain in the breast was reported by 12.5%, nipple discharge by 3.5%, skin retraction or dimpling by 6.2%, and axillary lymphadenopathy by 8.3%. The right breast was involved in 58.3% of cases, the left in 37.5%, and bilateral involvement was noted in 4.2% of the participants (Table 1).

Among the 144 participants, the majority of tumors were classified as grade III (102 cases, 70.8%), followed by grade II (36 cases, 25.0%),

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and grade I (6 cases, 4.2%). Estrogen receptor (ER) positivity was observed in 106 cases (73.6%), while 38 cases (26.4%) were ER negative. Progesterone receptor (PR) positivity was identified in 58 cases (40.2%), whereas 86 cases (59.8%) were PR negative. Regarding HER2/Neu status, 81 cases (56.2%) were HER2/Neu positive and 63 cases (43.8%) were HER2/Neu negative (Table 2).

Table 1. Baseline Characteristics (N=144).

Age	33.7±3.2
Age Range (%)	
20-29	17 (11.8%)
30-34	59 (40.9%)
35-40	68 (47.2%)
Residence (%)	
Urban	56 (38.9%)
Rural	88 (61.1%)
Family History of BC (%)	12 (8.3%)
Parity	2.3±1.7
Smoking History (%)	15 (10.4%)
History of Hormonal Therapy usage (%)	45 (31.2%)
History of Previous Breast Biopsy (%)	5 (3.5%)
Clinical and Tumor Characteristics (%)	
Breast Lump	103 (71.5%)
Pain in Breast	18 (12.5%)
Nipple Discharge	05 (3.5%)
Skin Retraction/Dimpling	09 (6.2%)
Axillary Lymphadenopathy	12 (8.3%)
Side Involved (%)	
Right	84 (58.3%)
Left	54 (37.5%)
Bilateral	06 (4.2%)

Table 2. Frequency of Tumor Characteristics (N=144).

Grade of Tumor (%)	
I	06 (4.2%)
II	36 (25.0%)
III	102 (70.8%)
ER (%)	
Positive	106 (73.6%)
Negative	38 (26.4%)
PR (%)	
Positive	58 (40.2%)
Negative	86 (59.8%)
HER2/Neu (%)	
Positive	81 (56.2%)
Negative	63 (43.8%)

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DISCUSSION:

Although breast cancer is uncommon among women in their teens and early twenties, it remains the most frequently diagnosed cancer in women under 35. In Western nations, approximately 4% of women under 40 are affected by breast cancer, with around 1,500 new cases detected each year in the UK among women aged 35 to 39.[11] The incidence rates of breast cancer tend to rise with age, with the sharpest increase occurring just before the age of 40.[12]

Current UK guidelines for breast cancer screening do not recommend routine checks for women under 40.[13] Consequently, women in this age group frequently present to breast clinics with symptoms. In one study, 98.2% of women under 40 reported concerns during self-examination, with 89.5% presenting with a palpable lump. Similarly, Agnese et al. found that among 163 women under 40 compared to 1,522 women over 40, younger patients were significantly more likely to present with a noticeable lump—70% versus 42% ($p < 0.0001$).[14] Foxcroft et al. reported that only 7% of the 239 women under 40 diagnosed with breast cancer were asymptomatic at diagnosis. In their study, the most common clinical finding was a distinct mass (72%) or an area of ill-defined thickening.[15]

In the present study, the majority of the patients had grade III tumors (70%), while 25.0% had grade II, and only 3.3% patients had grade I tumors. Similar results were reported by Alhaidary et al., who reported grade III tumors in 63.3% patients, grade II tumors in 25.8% patients, and grade I tumors in 3.3% patients. Regarding HER2 status, the authors reported HER2-positive status in 55.1% of patients and HER2-negative status in 44.9% of patients.1 A study by Kim et al. from South Korea reported HER2-positive status in only 25.1% of patients with breast cancer aged <40 years and HER2-negative status in 73.0%. The same study reported PR positive BC in 37.7% cases and PR negative BC in 62.3% patients, while ER positive BC was diagnosed in 28.7% patients and ER-negative in 71.3% patients.[16]

CONCLUSION:

Breast cancer in young women often manifests through noticeable symptoms such as a prominent lump and associated discomfort. Our research revealed that 47% of the patients were aged 35 years or older. Based on these findings, we suggest conducting additional studies to evaluate the practicality of implementing routine breast ultrasound screenings starting at age 35 for individuals without a family history of the disease.

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