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Original Article

Comparison between the Young and Elderly Diagnosed Patients of Carcinoma of the Breast

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ABSTRACT

Breast cancer presents a significant health challenge in Pakistan, marked by high incidence rates and specific cultural and societal barriers to early detection and treatment. **Objective:** To compare diagnosed cases of CA breast in younger and older patients in terms of mode of presentation, TNM stage at presentation, histological variety and hormonal status. **Methods:** In our prospective comparative study conducted at the Department of Surgery, Bahawal Victoria Hospital, Bahawalpur, we included a total of 220 breast cancer patients aged 20 years and above. Patients were stratified into two distinct age groups for comparison: younger patients (aged less than or equal to 35 years) and older patients (aged more than 35 years). Modes of presentation, histological types, and hormonal receptor statuses were compared between the both groups. **Results:** In a study of 220 breast cancer patients with a mean age of 42.97 years, younger patients (≤35 years) constituted 24%, while older patients (>35 years) made up 76%. The most common presentation was lump formation (78.18%), mainly in older patients. Ulceration was evenly distributed across age groups. Histologically, invasive ductal carcinoma Grade III was more frequent in older patients, whereas Ductal Carcinoma In Situ (DCIS) was exclusive to younger patients, underscoring distinct age-related disease patterns. **Conclusions:** Our study revealed significant age-related differences in breast cancer presentation among Pakistani patients. Older patients (>35 years) predominantly presented with lump formation, suggesting diagnostic delays, while all younger patients (≤35 years) had DCIS, indicating possible early detection or unique tumor biology. Additionally, older patients exhibited higher ER and PR positivity.

INTRODUCTION

Breast cancer remains a multifaceted disease with a significant global burden, as one of the most common forms of cancer in women. The international landscape reveals varying prevalence across different regions, with Western European countries exhibiting a higher incidence rate of breast cancer compared to Eastern Asian or African countries [1, 2]. In contrast, Asian countries, especially Pakistan, report alarmingly high rates despite the overall lower incidence [3]. For example, in 2020, it was estimated that 2.3 million females were diagnosed with breast cancer worldwide, with Pakistan showing a striking 1 in 9 women at risk of being diagnosed [4, 5]. Several factors contribute to breast cancer prevalence, including age, genetic, lifestyle, and environmental variables [6]. The disease mainly occurs in middle-aged and older women, with Western countries showing substantially greater survival rates due to early detection measures and better healthcare facilities; earlier epidemiological studies have further illuminated these regional differences, revealing a peak incidence between 40 to 50 years in Asian women, whereas the peak incidence was observed between 60 to 70 years in Western women [7]. Factors such as family history, hormonal imbalance, obesity, and alcohol consumption are recognized as crucial determinants, influencing the development of various presentations and pathological sub-types [8]. Breast cancer stages, numbered 0 - 4, define the extent to which cancer has spread, with higher numbers indicating wider spread. Stage 0 represents pre-

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cancer, while stages I - IV indicate invasive breast cancer requiring various treatments, including surgery, chemotherapy, hormonal therapy, biological therapy, and radiation[9]. Understanding the hormonal receptors such as ER, PR, and HER2 NEU and correlating them with the initial TNM staging helps to illuminate the complexity and treatment needs of the disease [10]. Breast cancer presents a significant health challenge in Pakistan, marked by high incidence rates and specific cultural and societal barriers to early detection and treatment. Notably, 1 in 9 Pakistani women is at risk of developing breast cancer during her lifetime, reflecting an urgent public health concern. The variations in incidence, risk factors, and presentations within Pakistan demand a focused and comprehensive study. Misconceptions and lack of awareness, often exacerbated by illiteracy, hinder early diagnosis and contribute to worsening prognosis. Moreover, understanding the relationships between variables like age, mode of presentation, histopathological variety, hormonal receptors, and staging within the Pakistani population can lead to more effective, personalized treatment strategies.

This research aimed to delve into these complexities specific to Pakistan, providing insights that could significantly impact prevention, early detection, and therapeutic approaches, ultimately contributing to the fight against breast cancer in the country.

METHODS

In our prospective comparative study conducted at the Department of Surgery, Bahawal Victoria Hospital, Bahawalpur, from August 02, 2022, to February 01, 2023, and approved by the CPSP with reference number CPSP/REU/SGR-2018-032-10124, we included a total of 220 breast cancer patients aged 20 years and above, selected using a non-probability sampling technique. Patients were stratified into two distinct age groups for comparison: younger patients (aged less than or equal to 35 years) and older patients (aged more than 35 years). This stratification was based on their age at the time of diagnosis, allowing for a focused comparative analysis between these two demographics. Our inclusion criteria targeted patients who were newly diagnosed with breast cancer during the study period, those who received treatment and followed up at the designated department, and those who provided informed consent. Essential for inclusion was that these patients had complete medical records, detailing the mode of presentation, TNM staging, histological type, and hormonal receptor status. The Operational Definitions were set as follows. Breast cancer refers to any case diagnosed as malignant neoplasm of the breast, as confirmed by histopathological examination. TNM Staging is the classification of cancer based on the size and extent of the primary tumor (T), involvement of regional lymph nodes (N), and presence of distant metastasis (M), as per the American Joint Committee on Cancer (AJCC) guidelines. Histological Type refers to the specific type of breast cancer as identified through histopathological analysis, including but not limited to invasive ductal carcinoma, invasive lobular carcinoma, and ductal carcinoma in situ (DCIS). Hormonal Receptor Status involves the determination of estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2) status in the tumor tissue, identified through immunohistochemistry or other relevant tests. Conversely, we excluded patients with a history of breast cancer or other malignancies prior to the study period, those with incomplete medical records, individuals unwilling or unable to provide consent, patients non-compliant with treatment or follow-up, and those diagnosed with metastatic breast cancer at the outset. This rigorous selection process ensured a representative and well-defined participant group for each age category. Upon breast cancer diagnosis, eligible patients aged 20 years and above were identified. The study's objectives, procedures, and confidentiality concerns were thoroughly explained to potential participants, followed by the collection of informed consent. Initial data collection involved gathering demographic information and specific breast cancer diagnosis details, including the mode of presentation, TNM staging, histological type, and hormonal receptor status, through a comprehensive review of medical records. Participants in both age groups were then followed up at regular intervals according to their treatment schedules. During each visit, updates on their treatment progress and any changes in health status were recorded. All data were meticulously entered into a secure, electronic database, ensuring the confidentiality and integrity of the information. This process was crucial in capturing the evolving clinical profile and treatment responses of the participants across both age groups, forming the foundation for an in-depth comparative analysis. We used SPSS version 24.0 to analyze all the data. We calculated the mean and standard deviation for age, and determined frequencies and percentages for the younger (≤35 years) and older (>35 years) age groups, modes of presentation, histological types, and hormonal receptor statuses. To compare these factors between the younger and older groups, we applied the Chi-square test or Fisher's Exact Test, as appropriate. We considered a p-value of less than 0.05 as statistically significant.

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RESULTS

Total 220 patients with breast cancer were selected. Mean age was 42.97 ± 13.26 years. Among 220 selected patients, the younger age group (≤35 Years) comprised 53 patients, accounting for 24% of the total. In contrast, the older age group (>35 Years) constituted a significantly larger proportion, with 167 patients representing 76% of the cohort. Table 1 reveals distinct patterns in the mode of presentation between the two age groups. Lump formation, the most common presentation, is significantly more prevalent in older patients (76.2%) compared to younger ones (23.8%). This could indicate a tendency for delayed detection or diagnosis in older age groups. Ulceration, representing an advanced symptom, is equally prevalent in both groups (50% each), suggesting similar progression rates regardless of age. Notably, nipple discharge and skin changes are exclusive to older patients, hinting at age-related biological differences in tumor behavior. The stark contrast in presentation types, underscored by a p-value of 0.000, underscores the necessity for age-specific clinical vigilance.

Table 1: Comparison of mode of presentation between both groups(n=220)

Mode of presentation	Age group		Total	p-value
	≤35 Years	>35 Years		
Lump	41(23.8%)	131(76.2%)	172(78.18%)	0.000
Ulcer	12(50.0%)	12(50.0%)	24(10.91%)	
Any other	0	24(100.0%)	24(10.91%)	
Total	53(24.1%)	167(75.9%)	220(100%)	

Table 2 illustrates a significant variation in histopathological types between the age groups. Invasive ductal carcinoma (IDC) Grade III, a more aggressive form, is predominant in older patients (68.8%) compared to younger ones (31.3%), implying a potential shift in tumor aggressiveness with age. Interestingly, younger patients show a 100% prevalence of DCIS (Ductal Carcinoma In Situ), a non-invasive form, indicating potential early detection or differing tumor biology. In contrast, IDC is notably higher in older patients (85.6%), suggesting an age-related increase in invasive forms. These findings, with a significant p-value of 0.000, highlight crucial age-related differences in breast cancer pathology.

Table 2 Comparison of histopathological variety between both groups(n=220)

Histopathological variety	Age group		Total	p-value
	≤35 Years	>35 Years		
Invasive ductal CA grade III	30(31.3%)	66(68.8%)	96(43.64%)	0.000
DCIS	6(100.0%)	0	6(2.73%)	
IDS	17(14.4%)	101(85.6%)	118(53.64%)	
Total	53(24.1%)	167(75.9%)	220(100%)	

Table 3 compares the hormonal receptor status across age groups. ER and PR positivity is considerably higher in older patients (ER: 68.8%, PR: 68.8%) compared to younger ones, indicating a possible link between hormonal receptor positivity and increasing age. This difference could influence treatment strategies, as hormonal therapies are more effective in ER/PR-positive cases. HER2 NEU positive status, however, shows no significant age-related difference, suggesting that HER2 NEU expression may be independent of age. These variations, particularly with significant p-values for ER and PR (0.011 and 0.029), underscore the complexity of hormonal influences in breast cancer.

Table 3: Comparison of hormonal status between both groups(n=220)

Hormonal Status	Age group		Total	p-value
	≤35 Years	>35 Years		
ER Status				
ER Positive	35(31.3%)	77(68.8%)	112(50.91%)	0.011
ER Negative	18(16.7%)	90(83.3%)	108(49.09%)	
PR Status				
PR Positive	30(31.3%)	66(68.8%)	96(43.64%)	0.029
PR Negative	23(18.5%)	101(81.5%)	124(56.36%)	
HER2 NEU Status				
Positive	17(19.1%)	72(80.9%)	89(40.45%)	0.154
Negative	36(27.5%)	95(72.5%)	131(59.55%)	

Table 4 details the TNM staging at presentation, providing insights into disease extent at diagnosis. Early stages like T1s N0 M0 are predominantly seen in younger patients, indicating potential early detection or slower progression in this group. Conversely, more advanced stages such as T4b N2 M1 are exclusive to older patients, reflecting possibly delayed diagnosis or faster progression in older age. The presence of diverse stages across both groups emphasizes the heterogeneity of breast cancer and the need for tailored diagnostic and therapeutic approaches.

Table 4: TNM stage at presentation

TNM stages	Age group		Total
	≤35 Years	>35 Years	
T1 N1 M0	0	6	6
T1s N0 M0	6	0	6
T2 N1 M0	12	36	48
T3 N0 M0	0	6	6
T3 N1 M0	12	12	24
T3 N2 M0	5	12	17
T3 N2 M1	0	5	5
T3 N3 M0	0	6	6
T4 N2 M1	6	0	6
T4a N2 M0	0	6	6
T4a N2 M1	0	12	12
T4b N1 M0	0	12	12
T4b N1 M1	0	6	6

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T4b N2 M0	0	18	18
T4b N2 M1	0	6	6
T4c N1 M0	6	0	6
T4c N1 M1	6	0	6
T4c N2 M0	0	6	6
T4c N2 M1	0	6	6
T4c N3 M0	0	6	6
T4d N2 M1	0	6	6
Total	**53**	**167**	**220**

DISCUSSION

In this study, the greater number of older patients (>35 years) compared to younger ones reflects the prevalent trends of breast cancer occurrence in Pakistan, where increased age is a significant risk factor. This selection was guided by the natural epidemiology of breast cancer, which shows a higher incidence and detection rate in older populations. Challenges in recruiting an adequate number of younger patients, given their lower incidence rate, contributed to this age disparity. Despite this, our statistical analysis has been carefully adjusted to account for these differences, ensuring the validity of our conclusions. This study's design paves the way for future research to further investigate age-related variations in breast cancer, ideally with more balanced age group representation. Our study's observation of a higher incidence of breast cancer in older Pakistani patients (>35 years) aligns with the findings of Zeeshan *et al.*, which also reported higher-grade tumors and more aggressive triple hormone receptor–negative phenotypes in younger patients [11]. However, unlike Zeeshan et al., who found a significant incidence of metastatic disease in younger patients, our study noted a prevalence of early-stage disease in this demographic. This discrepancy could suggest varying disease progression rates or differences in early detection effectiveness across regions. The study performed by Abdel-Razeq *et al.*, in developing countries echoes our findings in terms of the younger age at breast cancer diagnosis [12]. Both studies observed more aggressive pathological features in younger patients. However, unlike our study, Abdel-Razeq *et al.*, found older patients more likely to present with advanced-stage disease. This contrast highlights potential differences in healthcare access and screening practices between our study population and the reported cohort. Fernandopulle *et al.*, documented a high prevalence of invasive carcinomas in younger patients, which partially contrasts with our study's finding of 100% DCIS in this age group [13]. This difference might reflect variations in genetic predispositions, environmental factors, or diagnostic approaches between Singapore and Pakistan. The study of a large cohort in the National Cancer Database performed by Plichta *et al.*, showed younger women more likely to have higher-stage tumors and receive aggressive treatments, similar to our findings [14]. The high prevalence of HR+/HER2- tumors in older women in their study complements our observation of higher ER and PR positivity in this age group, suggesting age-related hormonal influences in tumor biology. Tzikas *et al.*, found more aggressive tumors and a higher Ki67 in younger patients with triple-negative breast cancer, a finding not entirely paralleled in our study [15]. While we did observe aggressive features in younger patients, the stark difference in Ki67 and histopathologic grade highlights potential biological or environmental factors influencing tumor aggressiveness that may vary between regions. Rudra *et al.*, identified higher rates of locoregional and distant recurrence in younger patients, aligning with our observation of aggressive disease features in this demographic [16]. This similarity underscores the need for vigilant monitoring and tailored treatment strategies for younger breast cancer patients, especially in underrepresented groups. Schaffar *et al.*, focusing on young women, found a high prevalence of luminal A and B molecular subtypes, which contrasts with our study's finding of a significant triple-negative disease in younger patients [17]. This contrast may be attributed to ethnic differences, as well as variations in environmental and lifestyle factors between Switzerland and Pakistan. Alwan *et al.*, highlighted significant differences between Iraqi and British breast cancer patients, with Iraqi women presenting younger and with more advanced stages, similar to our findings [18]. This similarity points to a broader trend in breast cancer presentation in developing countries, potentially influenced by socioeconomic and healthcare system factors. The study performed by Latif *et al.*, in Karachi, Pakistan, also found a higher prevalence of breast cancer in younger women presenting at advanced stages, aligning with our findings [19]. This consistency within the same country underscores the need for targeted breast cancer awareness and screening programs in younger Pakistani women. Moreover, recent findings underscore the complex relationship between menopausal hormone therapy (MHT) and breast cancer incidence in older women. Studies have revealed that while estrogen therapy alone may reduce breast cancer incidence for women with a prior hysterectomy, estrogen plus progestin therapy increases breast cancer risk, persisting over two decades. This highlights the need for a nuanced understanding of hormone therapy impacts in older women, which may also have implications for our study's observations in the older patient group [20].

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CONCLUSIONS

Our study underscores the nuanced variations in breast cancer presentation among Pakistani patients across different age groups. We observed a higher prevalence of breast cancer in the older age group (>35 years), predominantly presenting with lump formation, indicating potential delays in diagnosis. In contrast, younger patients (≤35 years) exhibited a 100% prevalence of Ductal Carcinoma *In Situ* (DCIS), suggesting earlier detection or distinct tumor biology. Notable differences were also evident in histopathological types and hormonal receptor status, with older patients showing higher ER and PR positivity. These findings emphasize the need for age-specific approaches in breast cancer diagnosis and treatment, highlighting the importance of tailored strategies to improve early detection, effective management, and outcomes in breast cancer care across varying age demographics.

Authors Contribution

Conceptualization: RK
Methodology: RK
Formal analysis: UJ
Writing-review and editing: RK, AUR

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

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