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ORIGINAL ARTICLE

Age-specific patterns and molecular subtypes of breast cancer in a tertiary care hospital in Pakistan

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ABSTRACT

Objectives: To estimate age-specific incidence patterns and trends in breast cancer molecular subtypes in a local hospital-based population.

Methods: This retrospective cross-sectional study was conducted at Akbar Niazi Teaching Hospital, Islamabad, from August 2022 to August 2024. One hundred women aged ≥20 years with biopsy-proven breast cancer were included through convenience sampling. Male patients, lobular carcinoma, phyllodes tumors, sarcoma/lymphoma, and cases with missing age data were excluded. Demographic, clinical, pathological, and treatment data were extracted from hospital records. Tumors were classified into luminal A, luminal B, human epidermal growth factor receptor-2 (HER2)-enriched, and triple-negative subtypes using immunohistochemistry and fluorescence in situ hybridization where required. Statistical analysis was performed using SPSS v25. Chi-square test assessed associations between age groups and tumor subtypes, while linear regression estimated age-related incidence trends.

Results: Mean age was 50.5 ± 12.0 years (range: 20-75). Breast cancer occurred in 47% of women aged ≤50 years and 53% in those >50 years. Luminal A was the most frequent subtype (55%), followed by triple-negative (25%), luminal B (15%), and HER2-enriched tumors (5%). Hormone receptor status showed no significant association with age ($p>0.05$). A significant association was observed between age groups and molecular subtypes ($p=0.043$), driven primarily by the luminal A subtype after Bonferroni correction. Age was not an independent predictor of breast cancer on regression analysis.

Conclusion: Nearly half of breast cancer cases occurred in women aged ≤50 years. Luminal A was the predominant subtype and showed significant age-related variation, emphasizing the need for age-stratified screening and subtype-focused management strategies.

Keywords: Breast Neoplasms (MeSH); Receptors, Estrogen (MeSH); Receptors, Progesterone (MeSH); Triple Negative Breast Neoplasms (MeSH); Biomarkers, Tumor (MeSH); Neoplasm Staging (MeSH).

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INTRODUCTION

Breast cancer is the most common malignancy affecting women worldwide.[1] In high-income countries, advancing age has traditionally been the strongest risk factor, with incidence and mortality increasing with age.[2] However, since the early 2000s, both incidence and breast cancer-related mortality have declined in many developed nations, largely due to early detection and improved treatment strategies.[3] Globally, demographic changes alone were projected to result in approximately 2.4 million new breast cancer cases in 2018, accounting for nearly one-quarter of all cancers among women.[4] Although breast cancer incidence remains lower in Asia compared with Western countries, recent decades have seen a rapid and substantial rise in Asia's contribution to the global breast cancer burden.[5]

In Pakistan, the burden of breast cancer has risen substantially, with approximately one in nine women now facing a lifetime risk of developing the disease.[6] Among Asian countries, Pakistan reports one of the highest age-standardized incidence rates of breast cancer.[7] Alarmingly, breast cancer–related mortality remains high, largely due to late-stage presentation and delayed referral to appropriate healthcare facilities.[8] The introduction of advanced screening strategies and expansion of screening age limits have uncovered marked differences in age-adjusted incidence rates.[4] In Western populations, breast cancer incidence increases sharply before menopause and continues to rise more gradually thereafter, with the most pronounced increase observed among women aged 50 years and above.[9]

Conversely, evidence from developing regions indicates that a substantial proportion of breast cancer cases (approximately 47.3%) occur in premenopausal women, highlighting a younger age at onset compared with Western populations.[10] Across Asia, the peak incidence typically occurs between 40 and 59 years of age, with reported peaks at 50-59 years in India, 40-49 years in Korea, and 45-54 years in Japan.[10-12] In contrast, data from Sri Lanka show a later peak incidence among women aged 60-64 years.[13]

Considering current demographic trends, breast cancer is poised to become an increasingly important public health challenge in Pakistan. This concern is further amplified by the scarcity of robust, population-based data on breast cancer patterns within the country.[14] These projections emphasize the urgent need for strengthened resource allocation toward timely diagnosis, subtype-based risk stratification, and appropriate treatment planning. Against this background, the present study aimed to estimate the frequency of breast cancer

incidence and to evaluate age-related trends in molecular subtypes within the local population.

METHODS

This retrospective, observational cross-sectional study was conducted at the Surgical Department of Akbar Niazi Teaching Hospital, Islamabad, Pakistan, between August 2022 and August 2024. A total of 100 patients were enrolled from the hospital's breast cancer registry using non-probability convenience sampling. The study was designed and reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.[15]

The sample size was calculated using the World Health Organization sample size calculator, assuming a 6% incidence of breast cancer among females,[16] a 95% confidence interval, and a 5% margin of error. Eligible participants were women aged ≥20 years with biopsy-proven breast cancer at any stage. Male patients, cases of biopsy-proven lobular carcinoma, phyllodes tumors, sarcoma or lymphoma, and records with missing age data were excluded. Ethical approval was obtained from the institutional ethics committee (Approval No. 84/IMDC/IREB-2022, dated 01 August 2022).

The hospital database provided comprehensive information on patient demographics (age), social characteristics (family history and parity status), clinical variables (body mass index, breastfeeding history, and menopausal status), pathological features (histological characteristics and expression of estrogen receptors [ER], progesterone receptors [PR], and human epidermal growth factor receptor-2 [HER2]), and treatment modalities (neoadjuvant therapy, adjuvant therapy, and surgical management).

Unlike most previous studies that primarily focus on older women, the present study specifically examined breast cancer occurrence in younger women aged 20-50 years. For this analysis, breast cancer incidence was defined as newly diagnosed cases within the local hospital population during the study period. Therefore, the incidence estimates reported here reflect institutional data and should not be interpreted as national incidence figures for Pakistan derived from population-based cancer registries.

Molecular subtypes were determined using immunohistochemical (IHC) surrogates for estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor-2 (HER2). ER and PR status were classified as positive or negative based on IHC staining. HER2 status was assessed using IHC and, where indicated, fluorescence in situ hybridization (FISH). Tumors with IHC scores of 0 or 1+ were considered HER2-negative, those with a score of 3+ were considered HER2-positive, and equivocal cases (2+) were further evaluated by FISH. Equivocal cases with positive FISH were classified as HER2-positive, those with negative FISH as HER2-negative, and cases without available FISH results were labeled as HER2-unknown.

Based on receptor expression, tumors were categorized into four molecular subtypes: luminal A (ER and/or PR positive, HER2 negative), luminal B (ER and/or PR positive, HER2 positive), triple-negative breast cancer (ER negative, PR negative, HER2 negative), and HER2-enriched (ER negative, PR negative, HER2 positive).

Statistical analyses were performed using SPSS version 25. Linear regression analysis was used to estimate age-related frequency and incidence trends of breast cancer subtypes. Associations between categorical clinicopathological variables and age groups were assessed using the chi-square test, with Bonferroni correction applied for post-hoc comparisons. A p-value ≤ 0.05 was considered statistically significant.

Table I: Demographics and clinical features of patients

Variables		Frequency (n=100)	Percentage
Age (years)	20-35	11	11.0
	36-50	36	36.0
	>50	53	53.0
Body Mass Index (kg/m^2)	<18.5	15	15.0
	18.5-22.9	53	53.0
	23-24.9	26	26.0
	25-29.9	6	6.0
Family history	No	90	90.0
	Yes	10	10.0
Parity status	None	12	12.0
	1-2 children	29	29.0
	3-4 children	44	44.0
	5 and above	15	15.0
Site	Right	42	42.0
	Left	53	53.0
	Bilateral	5	5.0
Age at menopause (years)	<45	37	37.0
	45-55	60	60.0
	>55	3	3.0
Breastfeeding history	No	19	19.0
	Yes	81	81.0

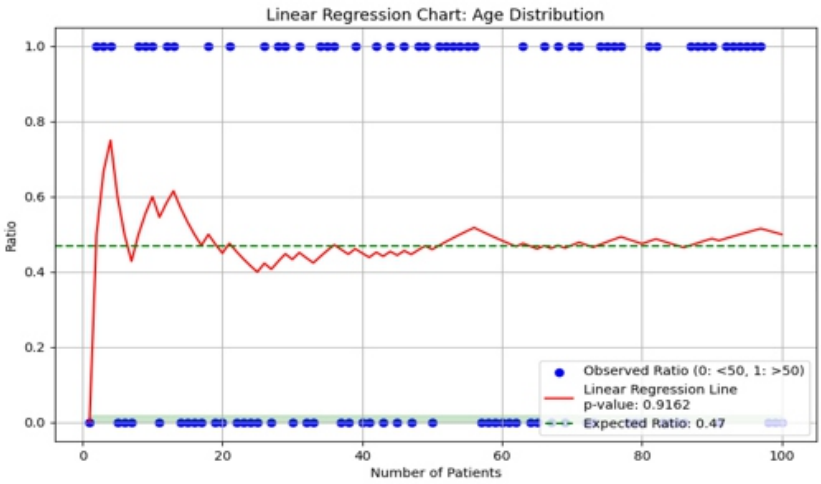

Figure 1: Regression test of possible factor of age predicting breast cancer, n=100

Table II: Pathological and histological features

Variables		Frequency (n=100)	Percentage
Estrogen receptors	Positive	70	70.0
	Negative	30	30.0
Progesterone receptors	Positive	56	56.0
	Negative	44	44.0
HER2	Positive	20	20.0
	Negative	80	80.0
Subtypes	HR+/HER2- (Luminal A)	55	55.0
	HR+/HER2+ (Luminal B)	15	15.0
	HR-/HER2- (TNBC)	25	25.0
	HR-/HER2+ (HER2)	5	5.0
pT*	T0, T1	21	21.0
	T2, T3, T4	79	79.0
pN*	N0, N1	82	82.0
	N2, N3	18	18.0
Neoadjuvant therapy	No	53	53.0
	Yes	47	47.0

HER2: Human epidermal growth factor receptor-2; TNBC: Triple-Negative Breast Cancer; *Pathological stages of tumor and lymph nodes

RESULTS

A total of 100 women with breast cancer were included in the study. The mean age was 50.51±12.01 years (range: 20-75 years). Among 100 breast cancer cases, 47 (47%) occurred in women aged ≤50 years, while 53 (53%) were aged >50 years. The mean body mass index was 21.26±2.35 kg/m². Sociodemographic characteristics (age, family history, parity) and clinical variables (BMI, breastfeeding history, and menopausal status) were evaluated and are summarized in Table I.

The frequency and incidence of cancer subtypes have been studied by pathological and histological variations (Table II).

Early-onset breast cancer (20-50 years) accounted for 47% of cases (Table I). Neoadjuvant therapy was administered to 47% of patients, while all underwent adjuvant therapy and breast-conserving surgery (Table II). Stratified analysis showed no significant association between age and hormonal receptor status (ER, PR, HER2) ($p \geq 0.05$). In contrast, breast cancer subtypes differed significantly across age groups ($p=0.043$; Table III). Post-hoc analysis revealed that this association was primarily driven by the luminal A subtype after adjustment for multiple comparisons. Both univariate and multivariate regression tests were employed to identify potential independent predictors of breast cancer (Table IV).

The linear regression test suggests a non-significant relationship between patient ages and breast cancer odds ratio [OR]: 1.13, 95% confidence interval [CI: 0.41-2.50, p=0.549). The breast cancer frequency in women aged <50 years is 47%, while in those aged >50 years, it is 53%, indicating a non-significant difference. Table IV explores other potential predictive factors, revealing their insignificance when analyzed in relation to age.

The observed and expected ratios are depicted, revealing a lack of significant predictive value between the ages (> 50 & < 50 years) of the patients, with an observed p-value of > 0.05 (Figure 1).

DISCUSSION

This single-center study highlights a substantial burden of early-onset breast cancer in our population. Nearly half of the patients (47%) were diagnosed at or before 50 years of age, with 37% being premenopausal. Although ER, PR, and HER2 positivity did not differ significantly across age groups, breast cancer subtypes showed a significant age-related variation, driven mainly by the predominance of the luminal A subtype (55%). Most patients presented with advanced primary tumors (T2-T4, 79%), while nodal disease was limited in the majority (N0-N1, 82%). These findings suggest a shifting age pattern of breast cancer locally, with early-onset luminal A disease contributing significantly to the

Table III: Stratification of hormonal receptors and cancer subtypes with ages of patients, n=100

Variables		Ages in categories			Total	Chi value	p-value
		20-35 years	36-50 years	>50 years			
ER	Negative	9	13	15	30	1.445	.486
	Positive	2	23	38	70		
PR	Negative	4	15	25	44	.556	.757
	Positive	7	21	28	56		
HER2	Negative	7	28	45	80	2.749	.253
	Positive	4	8	8	20		
Subtypes	Luminal A	6	15	34	55	12.41	.043
	Luminal B	3	8	4	15		
	TNBC	1	13	11	25		
	HER2	1	0	4	5		

ER: Estrogen receptors, PR: Progesterone receptors, HER2: Human epidermal growth factor receptor-2; TNBC: Triple-Negative Breast Cancer

Table IV: Statistical analysis of possible factors independently predicting breast cancer (n=100)

Variables		Univariate analysis			Multivariate analysis		
		OR	95% CI	p value	OR	95% CI	p value
Ages (years)	≤50	1.13	0.41-2.50	.549	0.87	0.32-1.18	.432
	>50						
ER	Negative	1.19	0.50-2.80	.694	-	-	-
	Positive						
PR	Negative	0.76	0.34-1.68	.498	-	-	-
	Positive						
HER2	Negative	0.52	0.19-1.41	.193	0.63	0.21-1.32	.188
	Positive						
pT*	T0, T1	1.03	0.39-2.71	.949	-	-	-
	T2, T3, T4						
pN*	N0, N1	0.86	0.31-2.40	.778	-	-	-
	N2, N3						

ER: Estrogen receptors, PR: Progesterone receptors, HER2: Human epidermal growth factor receptor-2; pathological stages of tumor and lymph nodes; Note: Linear regression test; OR: odds ratio; 95% confidence interval

overall burden.

A Korean study reported a mean patient age of 50 years (range: 40-108 years), with early-onset breast cancer occurring at a mean age of 50 years (range: 40–69 years).[16] Similarly, a Chinese study documented a mean age at diagnosis of 49.9±10.5 years.[17] In Pakistan, a Karachi-based study projecting age-specific breast cancer incidence from 2004 to 2025 demonstrated a marked increase in annual incidence, particularly among women aged 40-54 years.[18] These age distributions closely mirror the findings of our study, supporting the consistency of early-onset breast cancer patterns across regional populations.

In developed regions, women aged ≥70 years account for 32.1% of breast cancer cases among those aged ≥40 years.[2] In contrast to the steady age-related increase in incidence observed in Western populations,[19] breast cancer incidence in Korea peaks at 45-49 years and declines thereafter.[20] Although the prevalence of early-onset breast cancer in Pakistan remains lower than in Western countries, our findings indicate a discernible shift toward Western age-distribution patterns, suggesting that younger age is emerging as an important risk factor. This rising trend may reflect age-related biological changes, including increased estrogen receptor sensitivity, alterations in mammary epithelial biology, changes in the tumor microenvironment, and immune senescence, all of which may enhance susceptibility to breast cancer.[2]

In this study, ER-positive breast cancer accounted for 70% of cases, which may be partly explained by the substantial proportion of premenopausal patients (37%). Notably, a rising trend in ER-positive tumors has been observed in the region over the past year, consistent with previous reports.[20,21] Although the underlying causes remain uncertain, this pattern may be related to increasing obesity rates and declining fertility. Similar observations by Wang Q, et al., demonstrated a progressive rise in mean body mass index and obesity prevalence among women, which may contribute to higher ER-positive rates.[17] Further studies are warranted to explore these potential risk factors in greater depth. In this study, the HER2-positive rate was 20%, consistent with reports from China and other Asian countries,[20,22,23] but higher than rates documented in studies from the United States.[21] Such inter-country variations in receptor expression may reflect differences in genetic predisposition and the distribution of underlying risk factors.[24]

This study has several limitations. First, the true burden of breast cancer may be underestimated, as patients treated at other regional centers were not included. Second, incomplete clinical records, particularly regarding hormone receptor and HER2 status, limited data completeness. Finally, the absence of follow-up and survival

outcome data precluded assessment of prognosis and long-term outcomes.

CONCLUSION

This study demonstrates a rising proportion of early-onset breast cancer across age groups in the region; however, a substantial number of patients still present with late-onset and locally advanced or metastatic disease. These findings highlight the urgent need for strengthened early detection strategies, including public awareness initiatives, self-examination practices, and promotion of healthy lifestyles, to facilitate timely diagnosis and improve breast cancer outcomes.

REFERENCES

1. Ferlay J, Colombet M, Soerjomataram I, Mathers C, Parkin DM, Pineros M, et al. Estimating the global cancer incidence and mortality in 2018: GLOBOCAN sources and methods. Int J Cancer 2019;144(8):1941-53. https://doi.org/10.1002/ijc.31937
2. Lodi M, Scheer L, Reix N, Heitz D, Carin AJ, Thiebaut N, et al. Breast cancer in elderly women and altered clinico-pathological characteristics: a systematic review. Breast Cancer Res Treat 2017;166(12):657-68. https://doi.org/10.1007/s10549-017-4448-5
3. Azamjah N, Soltan-Zadeh Y, Zayeri F. Global trend of breast cancer mortality rate: a 25-year study. Asian Pac J Cancer Prev 2019;20(7):2015-20.https://doi.org/10.31557/APJCP.2019.20.7.2015
4. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2018;68(6):394-424. https://doi.org/10.3322/caac.21492
5. Youn HJ, Han W. A review of the epidemiology of breast cancer in Asia: focus on risk factors. Asian Pac J Cancer Prev 2020;21(4):867-80.https://doi.org/10.31557/APJCP.2020.21.4.867
6. Shoukat Z, Shah AJ. Breast cancer awareness and associated factors among women in Pakistan: a cross-sectional descriptive study. Asian Pac J Cancer Prev 2023;24(5):1561-70.https://doi.org/10.31557/APJCP.2023.24.5.1561
7. Sultan N, Memon SA, Mooghal M, Wali S, Khan W, Tahseen H, et al. Ethnic predisposition, risk factors and breast cancer presentation; a 10-year data. Single centered prospective cohort study from Karachi. Ann Med Surg (Lond) 2022;82(10):104612. https://doi.org/10.1016/j.amsu.2022.104612
8. Begum N. Breast cancer in Pakistan: a looming epidemic. J Coll Physicians Surg Pak 2018;28(2):87-8.https://doi.org/10.29271/jcpsp.2018.02.87
9. Carroll PS, Utshudiema JS, Rodrigues J. The British breast cancer epidemic: trends, patterns, risk factors, and forecasting. J Am Physicians Surg 2017;22(1):8-16.
10. Toyoda Y, Tabuchi T, Nakayama T, Hojo S, Yoshioka S, Maeura Y. Past trends and future estimation of annual breast cancer incidence in Osaka, Japan. Asian Pac J Cancer Prev 2016;17(6):2847-52.
11. Mathew A, George P, Arjunan A, Augustine P, Kalavathy MC, Padmakumari G, et al. Temporal trends and future prediction of breast cancer incidence across age groups in Trivandrum, South India. Asian Pac J Cancer Prev 2016;17(6):2895-9.
12. Park EH, Min SY, Kim Z, Yoon CS, Jung KW, Nam SJ, et al. Basic facts of breast cancer in Korea in 2014: the 10-year overall survival progress. J Breast Cancer 2017;20(1):1-11. https://doi.org/10.4048/jbc.2011.14.1.1
13. Fernando A, Jayarajah U, Prabashani S, Fernando EA, Seneviratne SA. Incidence trends and patterns of breast cancer in Sri Lanka: an analysis of the national cancer database. BMC Cancer 2018;18(1):1-6. https://doi.org/10.1186/s12885-018-4408-4
14. Qureshi MA, Mirza T, Khan S, Sikandar B. Cancer registration in Pakistan: a dilemma that needs to be resolved. Int J Cancer 2015;136(6):E773.https://doi.org/10.1002/ijc.29253
15. Von Elm E, Altman DG, Egger M, Pocock SJ, Gotzsche PC, Vandenbroucke JP, et al. The strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. Int J Surg 2014;12(12):1495-9. https://doi.org/10.1016/j.ijsu.2014.07.013
16. Paik HJ, Kim SJ, Kim KS, Kim Y, Lee SK, Kang SH, et al. Characteristics and chronologically changing patterns of late-onset breast cancer in Korean women of age≥ 70 years: a hospital based-registry study. BMC Cancer 2022;22(1):1261.https://doi.org/10.1186/s12885-022-10295-y
17. Wang Q, Wu H, Lan Y, Zhang J, Wu J, Zhang Y, et al. Changing patterns in clinicopathological characteristics of breast cancer and prevalence of BRCA mutations: analysis in a rural area of southern China. Int J Gen Med 2021;14:7371-80.https://doi.org/10.2147/IJGM.S333858
18. Zaheer S, Shah N, Maqbool SA, Soomro NM. Estimates of past and future time trends in age-specific breast cancer incidence among women in Karachi, Pakistan: 2004-2025. BMC Public Health. 2019;19(1):1-9. https://doi.org/10.1186/s12889-019-7330-z
19. Lee SK, Kim SW, Yu JH, Lee JE, Kim JY, Woo J, et al. Is the high proportion of young age at breast cancer onset a unique feature of Asian breast cancer? Breast Cancer Res Treat 2019;173(1):189-99. https://doi.org/10.1007/978-3-030-16391-4_7
20. Kang SY, Kim YS, Kim Z, Kim HY, Lee SK, Jung KW, et al. Basic findings regarding breast cancer in Korea in 2015: data from a breast cancer registry. J Breast Cancer 2018;21(1):1-10. https://doi.org/10.4048/jbc.2018.21.1.1

21. DeSantis CE, Ma J, Gaudet MM, Newman LA, Miller KD, Sauer AG, et al. Breast cancer statistics, 2019. CA Cancer J Clin 2019;69(6):438-51.https://doi.org/10.3322/caac.21583

22. Linghu RX, Si W, Li Y, Yang J. Epidemiological and clinicopathological characteristics of patients with breast cancer: a retrospective analysis of 3846 case. Acad J PLA Postgrad Med Sch 2015;36(10):1017-21. https://doi.org/10.3969/j.issn.2095-5227.2015.10.015

23. Nakamura K, Okada E, Ukawa S, Hirata M, Nagai A, Yamagata Z, et al. Characteristics and prognosis of Japanese female breast cancer patients: the BioBank Japan project. J Epidemiol 2017;27(3S):S58-S64. https://doi.org/10.1016/j.je.2016.12.009

24. Argolo DF, Hudis CA, Iyengar NM. The impact of obesity on breast cancer. Curr Oncol Rep 2018;20(6):1-8. https://doi.org/10.1007/s11912-018-0688-8

AUTHORS' CONTRIBUTION

The Following authors have made substantial contributions to the manuscript as under:

MA: Conception and study design, acquisition, analysis and interpretation of data, drafting the manuscript, approval of the final version to be published

RA & SH: Acquisition, analysis and interpretation of data, critical review, approval of the final version to be published

AR, MM & TA: Acquisition, analysis and interpretation of data, drafting the manuscript, approval of the final version to be published

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

CONFLICT OF INTEREST

Authors declared no conflict of interest, whether financial or otherwise, that could influence the integrity, objectivity, or validity of their research work.

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DATA SHARING STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request

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