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Global Breast Cancer Risk Factors and Their Relevance to the Pakistani Population

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ABSTRACT

Breast cancer is the most frequently diagnosed malignancy among women and remains the second leading cause of cancer-related deaths worldwide. In Pakistan, the increasing incidence of breast cancer is particularly concerning, yet the absence of a centralized cancer registry limits comprehensive risk assessment and effective disease monitoring. The present study was designed to explore potential risk factors for breast cancer in a Pakistani cohort by analyzing hospital-based epidemiological data in conjunction with previously published findings from the same population. Data were collected from patients at hospitals in Rawalpindi and Islamabad through a structured questionnaire covering demographic, reproductive and lifestyle variables such as age at diagnosis, age at menarche, marital status, parity, age at first childbirth, breastfeeding history, menopausal status, family history, occupation, socioeconomic background and substance use. Clinical features including stage, histological type, metastasis, obesity, receptor status, and tumor grade were also evaluated. Comparative analysis with earlier reports revealed that none of the conventionally recognized breast cancer risk factors exhibited a significant association with disease prevalence in this population, suggesting a divergence from global patterns. These findings emphasize the possibility that genetic, molecular, or population-specific determinants may contribute more substantially to breast cancer susceptibility in Pakistani women. Therefore, large-scale genetic and molecular investigations are urgently needed to clarify the underlying causes of this rising trend and to inform more effective strategies for prevention, early detection, and management.

INTRODUCTION

Breast cancer is the most frequently diagnosed malignancy among women worldwide and continues to pose a serious public health challenge due to its increasing incidence, complex risk profile, and high mortality burden. In 2020, more than 2.2 million new cases were identified globally, corresponding to a lifetime risk of approximately one in twelve women, while the disease claimed around 685,000 lives [2]. These figures place breast cancer as not only the most prevalent cancer among women but also the second leading cause of cancer-related deaths. Although breast cancer is a universal disease, considerable disparities exist across regions in terms of incidence, survival, and mortality, reflecting variations in genetic susceptibility, environmental exposure, lifestyle behaviors, healthcare infrastructure, and access to early detection and treatment. Epidemiological trends show that nearly 42% of all breast cancer cases are reported from developing nations, where outcomes are often poor due to delayed diagnosis and limited treatment options. In contrast, higher incidence rates are observed in industrialized regions such as Australia, North America, and Europe, yet survival rates there are considerably better owing to established screening programs and advanced therapeutic approaches [2]. Prognosis and clinical outcomes are influenced by several clinicopathological factors, including tumor grade, lymph node involvement, histological subtype, tumor size, and the molecular status of biomarkers such as Her-2/Neu and hormone receptors [3]. These indicators not only guide therapeutic strategies but also serve as predictors of recurrence and survival. Globally, breast cancer accounts for almost 30% of all cancers in women, underscoring its dominance as the most common female malignancy [4]. In Pakistan, the burden is particularly alarming. The disease ranks among the top 20 causes of mortality in the country [4] and exhibits the highest incidence rate across Asia, with one in every nine women estimated to be affected during her lifetime [5].

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This prevalence surpasses that of most Western nations and highlights Pakistan as a high-risk population where breast cancer has become a pressing public health concern. The disproportionately high rates, combined with limited awareness, cultural barriers, and insufficient healthcare infrastructure, contribute to poor outcomes for many Pakistani women. Breast cancer affects women of all races, ethnicities, and geographic locations, confirming its multifactorial nature [6]. Both modifiable and non-modifiable factors contribute to disease onset, including age, reproductive history, hormonal status, family history, lifestyle choices, obesity, and physical inactivity [7]. Environmental exposures and evolving sociodemographic trends further shape disease dynamics. Despite well-established risk factors at the global level, significant differences in survival, mortality, and prognosis are evident across populations. In resource-rich countries, improved awareness, early detection, and targeted therapies have significantly enhanced survival, whereas women in low- and middle-income countries, including Pakistan, often present with advanced disease stages that severely limit treatment options [8, 4]. One of the critical challenges in Pakistan is the lack of a national cancer registry, which restricts comprehensive epidemiological surveillance and limits the ability to evaluate the impact of established risk factors on disease burden. Current knowledge is based on fragmented hospital-based reports or regional studies that are often inconsistent in their findings. For example, reproductive variables such as age at first childbirth, parity, and breastfeeding which are protective in many populations have shown conflicting associations in Pakistani cohorts. Similarly, lifestyle-related factors such as obesity, socioeconomic status, and occupation have been variably linked with disease occurrence, leaving uncertainty regarding their relevance to this population. These discrepancies raise an important question: are globally recognized risk factors equally applicable in Pakistan, or do unique genetic, molecular and environmental determinants drive the high incidence observed? This study was designed to address this question by systematically evaluating demographic, reproductive, lifestyle, and clinical risk factors among breast cancer patients from Rawalpindi and Islamabad, while also comparing findings with previously published national data. By integrating hospital-based information with earlier reports, this study aimed to clarify whether conventional risk factors demonstrate consistent associations with disease risk in the Pakistani context. Interestingly, the analysis demonstrated that none of the widely recognized breast cancer risk factors were significantly associated with increased disease prevalence in the studied cohort. This divergence from international data suggests that classical models of breast cancer risk may not adequately explain the disease in Pakistani women. Instead, the findings point toward the likelihood of alternative determinants particularly genetic predispositions, molecular alterations, and population-specific environmental exposures playing a central role in disease onset and progression. There is an urgent need to expand breast cancer research in Pakistan beyond conventional epidemiology. Large-scale, multicenter studies that integrate genomic profiling, molecular characterization, and population-based epidemiology are essential to uncover novel risk determinants and develop context-specific strategies for prevention, early detection, and management. Such efforts would not only improve clinical outcomes for Pakistani women but also contribute valuable insights to the global understanding of breast cancer biology.

METHODOLOGY

This study employed a cross-sectional design to evaluate the association of demographic, reproductive, lifestyle, and clinical parameters with breast cancer in the Pakistani population. A total of 500 confirmed breast cancer patients were recruited between January 2022 and December 2024 from tertiary care hospitals in Rawalpindi and Islamabad. Specifically, data were collected from the Holy Family Hospital and Combined Military Hospital (CMH) in Rawalpindi, as well as the Nuclear Medicine, Oncology, and Radiotherapy Institute (NORI) and the Pakistan Institute of Medical Sciences (PIMS) in Islamabad. These hospitals serve as referral centers that are accessible to patients from diverse geographic regions across Pakistan, ensuring a heterogeneous study population. Data collection was conducted using a structured questionnaire administered to patients following written informed consent. Ethical approval was obtained from the respective institutional review boards prior to study initiation. The questionnaire captured information on a broad range of variables, including age at onset of cancer, age at menarche, marital status, parity, age at first childbirth, lactation history, menopausal status, stage of cancer, type of cancer, presence of metastasis, family history of breast or other cancers, occupation, obesity status (BMI-based), receptor status (ER, PR, and Her-2/Neu), economic status, tumor grade, and any history of addiction (e.g., smoking, betel nut, or other substances). These variables were selected based on previously reported risk factors for breast cancer and their relevance to the local population. To strengthen the contextual analysis, data from previously published studies on Pakistani breast cancer patients were also reviewed and compared with findings from the present cohort. This comparative approach facilitated evaluation of consistency, variation, and potential new trends in the studied population. All data were coded and entered into SPSS for statistical analysis. Descriptive statistics were calculated for demographic and clinical parameters, while chi-square tests and logistic regression models were applied to assess associations between risk factors and breast cancer characteristics. Statistical significance was considered at $p < 0.05$.

Ethical Considerations

The study was conducted in accordance with the Declaration of Helsinki. The study protocol was approved by the ethical review committee of PMAS Arid Agriculture University, Rawalpindi, and the hospitals of Rawalpindi and Islamabad, Pakistan (PMAS-AAUR/D. FoS/269). Participation was voluntary, and all patients provided written informed consent before data collection. Patient confidentiality was maintained by coding personal identifiers and restricting access to data solely for research purposes.

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RESULTS

Demographic Characteristics

This study included 500 breast cancer patients, with a mean age at diagnosis of 48.46 years. The largest proportion of cases occurred in the 41–50-year age group (33.19%), followed by women aged 51–60 years (27.86%). A smaller fraction of cases was identified in younger women aged 20–30 years (4.91%), while only 2.45% of patients were older than 70 years. Overall, more than 60% of cases were diagnosed before the age of 50, indicating a relatively younger age of onset compared to global averages.

Reproductive and Hormonal Factors

The mean age at menarche was 13.16 years, with the majority of patients (67.95%) experiencing onset between 12 and 14 years of age. The mean age at first childbirth was 22 ± 6 years, with most women (22.38%) delivering their first child at 25 years. In terms of parity, 59.11% of women had four or fewer children, while 33.49% had more than four children. A smaller fraction was nulliparous (5.41%), infertile (0.98%), or reported no conception (0.49%). Notably, 96% of patients had breastfed, reflecting the persistence of lactation practices in this population.

Family and Marital History

A family history of breast cancer was present in 17% of patients, while the remaining 83% reported no such background. Marital status analysis showed that 83.95% were married, 9.87% widowed, 4.52% single, and 1.64% divorced.

Socioeconomic and Lifestyle Characteristics

The majority of patients were homemakers (88.93%), while 6.14% were engaged in professional work. Socioeconomic classification indicated that 60.10% belonged to lower-income households, 36.86% were from middle-income groups, and only 2.11% were from higher-income families. Lifestyle evaluation revealed that 8.33% of patients reported substance use, including smoking, hookah, or pan, whereas 91.66% denied any addictive habits. In terms of nutritional status, 33.47% were obese, 59.83% were of normal weight, and 6.69% were underweight.

Clinical Presentation

Most patients were diagnosed at advanced stages of disease. Only 2.5% presented at stage I, while 20% were diagnosed at stage II, 25% at stage III, and 52.5% at stage IV, highlighting delayed diagnosis in the majority of cases. Tumor grading revealed that 60% of cases were grade II, 30% grade III, 6.66% grade I, and 3.33% grade IV. Histopathological evaluation showed that ductal carcinoma was the predominant type (81%), whereas lobular carcinoma accounted for 19%.

Metastasis and Hormonal Receptor Status

A high proportion of patients (77%) presented with metastatic disease, while only 23% were non-metastatic at diagnosis. Hormone receptor profiling showed that 55.55% were estrogen receptor (ER)-positive, 44.44% were progesterone receptor (PR)-positive, and 40% expressed HER2neu, while the remainder were receptor-negative. The overall findings highlight that Pakistani women with breast cancer are frequently diagnosed at a younger age and at more advanced disease stages, with a considerable proportion presenting with metastasis. Despite protective reproductive patterns, such as early childbirth and widespread breastfeeding, late-stage diagnosis, socioeconomic challenges, and limited screening opportunities appear to be the major contributors to the disease burden in this population.

Table 1

Distribution of Demographic and Clinical Parameters Among Women Diagnosed with Breast Cancer

Variables	Mean	Similarities of the current study with the literature
Age of patients (at the time of occurrence)	48.46 years	48 [10], 48 [15],48 [18], 48[20],48 [21], 48 [22], 48[40], 47.6 ± 12[27], 46±1.5[28], 49.5 (±13) [11], 47.5+11.02 [14],48.6 ±12.2[30]
Age at menarche	13.16 years	13.4±1.4 [45],13.2 ±1.2 [46], 13.2 ±1.2 [47]
Age at 1st childbirth	22 ±6years	23.1±5.3 [85], 23.7 ±4.9 [47]
	Percent	
Family History	Present 17 Absent 83	Present 16.50 Absent 83.50 [36] Present 6.66 Absent 93.33[37]
Marital status	Married 83.95 Single 4.52 Widow 9.87 Divorced 1.64	Married 88 Single 12 [52]
Parity	Yes (≤4) 59.11 Yes (> 4) 33.49 Infertile 0.98 Nulliparous 5.41 No conception 0.49 Pregnant 0.49	No 19.20 Yes (1) 15.50 Yes (2) 38.20 Yes (3) 18.40 Yes (4 or more) 8.70 [53]
Lactation History	Positive 96 Negative 4	Positive 92.60 Negative 7.40 [48]
Menopausal Status	Premenopausal 51 Postmenopausal 49	Premenopausal 56 Postmenopausal 44 [39] Premenopausal 57.30 Postmenopausal 42.70[36], [48] Premenopausal 65.42 Postmenopausal 34.58[59]
Occupation	Housewife 88.93 Working women 6.14	Housewife 83.90 Working women 16.1[33]
Economic Status	Poor economic category 60.10 Middle category 36.86 Upper economic category 2.11	Poor economic category 67.20 [37] Poor economic category 41.80 Middle category 51.80 Upper economic category 6.30[79]
Addiction	Smokers 8.33 Non- smokers 91.66	Smokers 31.31 Non- smokers 68.70 [52]
Obesity	Obese 33.47 Normal body weight 59.83 Underweight 6.69	Obese 30 [8]
Stage of Cancer	I 2.5 II 20 III 25 IV 52.50	I & II 18.60 III, IV 81.35 [32]
Grade of the cancer	I 6.66 II 60 III 30 IV 3.33	I 22 II 55 III 23 [81]

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Type of Cancer/ Histology	Ductal carcinoma 81 Lobular carcinoma 19	Ductal carcinoma 95.50 Lobular carcinoma 4.5 [8] Ductal carcinoma 88 Lobular carcinoma 12 [37] Invasive Ductal carcinoma 91 Invasive Lobular carcinoma 2 [65].
Metastasis	With metastasis 23 Without metastasis 77	lymph node metastasis 56 distant metastasis 8.30
ER	Positive 55.55 Negative 44.44	Positive 62 Negative 38[37]
PR	Positive 44.44 Negative 55.55	Positive 47 Negative 53 [37]
HER2	Positive 40 Negative 60	Positive 49 Negative 51 [37]

DISCUSSION

This study provides a comprehensive overview of breast cancer risk factors and clinicopathological features among Pakistani women, revealing patterns that are distinct from those reported in Western populations. The mean age at diagnosis in our cohort was 48.46 years, nearly a decade younger than the median age reported in high-income countries, where breast cancer is typically diagnosed after the age of 60 [39,41]. Such early onset has also been documented in other South Asian populations, underscoring potential genetic, environmental, and lifestyle contributions unique to the region [9–40]. The younger age at diagnosis is clinically significant, as it is frequently associated with more aggressive tumor biology, poorer prognosis, and greater socioeconomic and psychological burdens for women in their most productive years of life. These observations not only reinforce the urgency of region-specific screening and awareness programs but also highlight the need to investigate genetic and molecular determinants that may underlie the earlier onset of disease in Pakistan. Reproductive characteristics play an important role in modulating breast cancer risk. The current study reported a mean menarcheal age of 13.16 years, which is consistent with earlier findings ranging from 13.2 to 13.4 years [45,46]. Although early menarche has been suggested as a risk factor [8,43,49,50], the overall frequency in this cohort was not markedly elevated compared to regional data [36,39,48]. Similarly, marital status did not emerge as a significant factor, as the majority of patients were married, in agreement with prior local reports [39,52]. Parity and age at first childbirth are established determinants of breast cancer susceptibility. Our results showed that 59.11% of women had ≤4 children, while only a small proportion were nulliparous. These observations align with other studies from Pakistan, where lower parity is uncommon [47,48,52]. Although global evidence suggests that nulliparity and delayed childbirth increase breast cancer risk [54,57,58], the relatively early maternal age at first birth observed in this population (23–25 years) suggests that this factor may not be a major contributor in Pakistan [47,55,56]. Moreover, the overwhelming prevalence of breastfeeding (96%) further reinforces the protective effect of lactation, which has consistently been documented in both local and international studies [8,48,59]. With respect to menopausal status, nearly equal proportions of premenopausal and postmenopausal patients were identified, similar to previous Pakistani cohorts [39,60]. Unlike Western populations, where postmenopausal cases predominate [61], this distribution suggests that menopausal status may not be a decisive determinant in the Pakistani context. In terms of clinical staging, a majority of patients presented with advanced-stage disease, with over half diagnosed at stage IV. Comparable patterns of late-stage presentation have been widely reported in Pakistan and neighboring countries [32,37,39,63]. This contrasts sharply with Western populations, where screening programs allow early detection and timely intervention [37]. The predominance of invasive ductal carcinoma (81%) observed in this study also mirrors both local and international literature [8,37,64–66], confirming its global relevance as the leading histological type.

Metastatic involvement was observed in 23% of patients, highlighting its role as a determinant of poor prognosis [67]. Prior studies have shown higher nodal and distant metastasis rates in Pakistani patients than in Western cohorts, likely reflecting delays in diagnosis and lack of awareness about screening [68,69]. Family history was positive in 17% of cases, consistent with previous findings from Pakistan [33,35–37,39,52]. While family history is an established risk factor [8], the majority of patients had no such history, suggesting that sporadic rather than hereditary factors predominate in the Pakistani population. Sociodemographic patterns further illustrate the local context. Most patients were housewives (88.93%), consistent with earlier reports [33,36], and unlike Western studies that highlight occupational risks such as long-term night-shift work [70,71]. Obesity was identified in approximately one-third of patients, similar to national estimates [8,35,72,73]. However, unlike in Western settings where obesity strongly correlates with breast cancer risk and prognosis, its role in Pakistan appears less pronounced, possibly due to differences in lifestyle, diet, and reproductive behavior [35]. Tumor receptor profiling revealed that just over half of patients were ER- or PR-positive, while HER2 positivity was observed in 40% of cases. These results are broadly consistent with prior Pakistani studies [37,47,73,74,76]. Notably, HER2 positivity is higher in Pakistan compared to Western populations, while ER/PR positivity remains comparatively lower [37]. This receptor distribution has significant therapeutic implications, as HER2-positive disease is often more aggressive but also responsive to targeted therapies [75]. Socioeconomic disparities were also evident, with the majority of patients belonging to lower-income groups. These findings align with prior research demonstrating the association between limited financial resources and increased breast cancer burden in Pakistan [39,77–80]. Financial constraints likely contribute to delayed diagnosis and treatment, reinforcing the need for equitable access to cancer care. Lifestyle-related exposures were limited, with only 8.33% of patients reporting addictions such as smoking or pan use. While smoking has been linked to breast cancer risk, particularly with early initiation and long-term exposure [83,84], its prevalence was relatively low in this cohort, indicating that other non-lifestyle factors may play a more dominant role. This study confirms that the Pakistani

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breast cancer population is characterized by younger age at onset, high rates of advanced-stage diagnosis, predominance of ductal carcinoma, relatively low influence of parity and reproductive factors, a high prevalence of HER2-positive tumors, and socioeconomic vulnerability. These findings emphasize the urgent need for public health interventions focused on early detection, awareness, and affordable treatment access.

CONCLUSION

This study highlights the distinctive epidemiological and clinical characteristics of breast cancer in Pakistani women. The findings demonstrate a younger mean age at diagnosis, advanced stage presentation, and a predominance of invasive ductal carcinoma, accompanied by a relatively high frequency of HER2-positive and triple-negative tumors. Despite widespread protective reproductive practices such as early childbirth and prolonged breastfeeding, the disease burden continues to rise, indicating that genetic predisposition, molecular alterations, and socioeconomic barriers may play a more decisive role than classical risk factors in this population. The late-stage diagnosis and the limited impact of lifestyle-related exposures further emphasize systemic challenges, including lack of awareness, absence of national screening programs, and restricted access to timely diagnostic and therapeutic services. Collectively, these results underscore the urgent need for population-specific interventions, such as cost-effective screening strategies, widespread awareness campaigns, and expansion of molecular diagnostics to enable personalized therapy. Establishing a national breast cancer registry and integrating genetic testing into clinical practice would provide deeper insights into the unique disease biology of Pakistani women. Strengthening healthcare infrastructure and reducing socioeconomic disparities are essential to improving early detection, treatment outcomes, and overall survival. Ultimately, a multifaceted approach that combines epidemiological research, public health initiatives, and personalized medicine is critical to mitigating the growing burden of breast cancer in Pakistan.

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