Barind Medical College Journal
Abbreviated Key Title: BMCJ
ISSN: 2518-3249 (Print)
https://bmcj.org/index.php/bmcj
Volume-10 | Issue-1 | Jan-Jun, 2024 | DOI: https://doi.org/10.70818/bmcj.2024.v010i01.0107

OPEN ACCESS

Original Research Article

Impact of Demographic Variables on Breast Cancer Staging, Treatment Approaches, and Prognosis

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Article History
Received: 17.03.2024
Accepted: 20.04.2024
Published: 30.06.2024

Abstract: ***Background*:** Breast cancer, a leading global malignancy, disproportionately affects developing nations like Bangladesh due to delayed diagnoses and limited resources. ***Objectives:*** To assess demographic impacts on breast cancer staging, treatment choices, and prognosis, and evaluate role of MMP1 expression in disease progression. ***Methods:*** This cross-sectional study (July 2022–June 2023) enrolled 34 histopathologically confirmed breast cancer patients from Dhaka Medical College. Demographic, clinical, and molecular data were collected via structured questionnaires and hospital records. MMP1 expression was analyzed using qRT-PCR in normal and tumor tissues. Statistical analyses included chi-square, t-tests, and Kaplan-Meier survival analysis. ***Results:*** Among 34 participants (mean age 47.41 ± 2.52 years; 76.47% ≤50 years), 47.05% had BMI >24.9. Most tumors were Stage II (41.18%) or III (26.47%). Luminal A and TNBC subtypes each comprised 29.41%. Mastectomy (64.71%) and chemotherapy (88.24%) predominated. MMP1 expression was significantly higher in tumor (median: 0.409, IQR: -1.058–1.983) vs. normal tissue (median: -1.774, IQR: -2.183–-0.609; p=0.002). Contraceptive use correlated inversely with MMP1 (rho=-0.283, p=0.019). ***Conclusion:*** Younger patients, elevated BMI, and MMP1 overexpression highlight the need for early detection and personalized strategies in resource-limited settings.

Keywords: Breast cancer, MMP1 gene expression, Tumor staging, Molecular subtyping.

Cite this as: Barman S, Jhuma KA, Shirin T, Rajbongshi D, Noor-E-Alam, Tasnim A. Impact of Demographic Variables on Breast Cancer Staging, Treatment Approaches, and Prognosis. BMCJ. 2024;10(1):86-93.

Introduction

Breast cancer is the most frequently diagnosed malignancy among women worldwide, contributing significantly to global morbidity and mortality. It is a complex disease with diverse pathological and clinical characteristics. According to the Global Cancer Observatory (GLOBOCAN) 2020, breast cancer accounted for approximately 2.3 million new cases, making up 11.7% of all cancer diagnoses across both sexes. Over the past decade, its incidence has steadily increased, surpassing lung cancer as the most commonly diagnosed cancer in women. The burden of breast cancer is particularly concerning in developing nations, where limited healthcare resources, delayed diagnoses, and insufficient awareness contribute to higher mortality rates.[1] In South Asia, home to over 588 million women above the age of 15, the incidence of breast cancer has been rising, largely due to changes in lifestyle, reproductive factors, and genetic predisposition. Despite its growing prevalence, many South Asian countries lack

national-level cancer registries, leading to gaps in epidemiological data.[2]. Reports indicate that more than 200,000 new breast cancer cases were diagnosed in this region in 2012, with approximately 97,500 related deaths. Bangladesh, in particular, has seen a surge in breast cancer cases, where it is now the leading cause of cancer-related deaths among women. Studies suggest that breast cancer accounts for nearly 69% of female cancer deaths in Bangladesh, with a prevalence of 11.7%.[3]. One of the key factors influencing breast cancer progression and metastasis is the Matrix Metalloproteinase (MMP) family, a group of zinc-dependent enzymes involved in extracellular matrix degradation. These enzymes, particularly MMP1, MMP2, MMP7, MMP9, and MMP13, play a crucial role in tumor invasion, angiogenesis, and distant metastasis.[4] MMP1, also known as collagenase-1, is of particular interest due to its ability to degrade interstitial collagens and facilitate tumor growth. Elevated expression of MMP1 has been observed in multiple malignancies, including breast cancer, and is associated with poor prognosis. Moreover, MMP1 expression has been linked to radiation response, making it a potential biomarker for treatment outcomes.[5] Despite the increasing recognition of MMP1's role in breast cancer, limited studies have been conducted in Bangladesh to assess its expression and clinical implications.

The lack of awareness, socioeconomic constraints, and inadequate screening programs contribute to late-stage diagnoses, reducing survival rates among affected women.[6] In addition, cultural stigmas and financial barriers often prevent timely medical interventions, further complicating disease management. Given these challenges, research on MMP1 expression in Bangladeshi breast cancer patients could provide valuable insights into disease progression and help in developing targeted therapeutic strategies.[7] This study aims to evaluate the impact of demographic variables on breast cancer staging, treatment approaches, and prognosis, while also investigating MMP1 gene expression in breast cancer patients. Identifying demographic risk factors and molecular markers will not only facilitate early diagnosis but also contribute to personalized treatment approaches, ultimately improving patient outcomes.[8] Understanding the interplay between these demographic variables and breast cancer characteristics is essential for developing tailored treatment strategies and improving patient outcomes. For example, hormone receptor status and HER2 expression are influenced by demographic factors and are crucial in guiding targeted therapies.[9, 10] In conclusion, demographic variables profoundly affect breast cancer staging, treatment approaches, and prognosis. Addressing these disparities through personalized treatment plans, improved access to care, and targeted public health interventions is vital for enhancing outcomes across diverse patient populations.[11, 12]

Aims and Objective

To evaluate the impact of demographic variables on breast cancer staging, treatment approaches, and prognosis among female patients.

Methods and Materials

Study design

This cross-sectional observational study was conducted to evaluate the impact of demographic variables on breast cancer staging, treatment modalities, and prognosis. The study was carried out at the Department of Biochemistry, Dhaka Medical College, Dhaka, in collaboration with the Institute for Population and Precision Health, Department of Public Health Sciences, The University of Chicago Biological Sciences, USA, over a 12-month period from July 2022 to June 2023. The study population comprised female patients diagnosed with histopathologically confirmed breast cancer at the Department of Surgery, Dhaka Medical College Hospital, Dhaka. A purposive sampling technique was utilized to recruit eligible participants.

Inclusion Criteria

The study included female patients aged 18 years or older with a histopathological diagnosis of breast cancer who had not received prior chemotherapy or radiotherapy before enrollment. Only patients with complete clinical, histopathological, and molecular data were included to ensure data accuracy and consistency in analysis. Additionally, participants had to be willing to provide written informed consent before enrollment, ensuring voluntary participation and adherence to ethical research guidelines.

Exclusion Criteria

Patients with a history of prior malignancies other than breast cancer were excluded to prevent confounding variables that could affect prognosis and treatment response. Individuals presenting with distant metastases at initial diagnosis were also excluded, as their disease course and therapeutic strategies differ significantly. Furthermore, patients with incomplete medical records or inadequate biological samples for molecular analysis were not considered to maintain data reliability. Those with severe comorbid conditions, such as terminal organ failure, were also excluded, as these conditions could independently impact disease progression and overall survival.

Data Collection and Variables

This study utilized a structured data collection approach, incorporating comprehensive clinical, demographic, histopathological, and molecular parameters from hospital records and structured case report forms (CRFs). Standardized methodologies ensured the reliability and reproducibility of the collected data.

Demographic and Clinical Variables

Demographic variables included age, body mass index (BMI), menopausal status, socioeconomic background, educational attainment, marital status, and family history of cancer. These parameters were analyzed to assess their impact on breast cancer progression, treatment response, and prognosis. Clinical characteristics included tumor size, histopathological subtype, tumor grade, presence of lymphovascular invasion, perineural invasion, and lymph node involvement. These factors played a crucial role in defining disease severity, guiding therapeutic decisions, and determining prognostic outcomes.

Staging and Molecular Classification

Tumor staging was performed based on the American Joint Committee on Cancer (AJCC) TNM staging system (8th edition) to ensure standardized classification. Molecular subtyping was conducted through immunohistochemical (IHC) analysis, assessing estrogen receptor (ER), progesterone receptor (PR), human epidermal growth factor receptor 2 (HER2), and Ki-67 proliferation index. These biomarkers were critical for defining tumor biology and guiding personalized treatment strategies. The study examined various treatment approaches, including surgical interventions (breast-conserving surgery vs. mastectomy), chemotherapy regimens, radiotherapy protocols, and endocrine therapy options. These treatment modalities were evaluated in relation to disease stage and molecular subtype to determine their effectiveness in improving patient survival. The study assessed key prognostic indicators, including disease-free survival (DFS), overall survival (OS), recurrence rates, and metastatic progression patterns. The correlation between these outcomes and demographic, histopathological, and molecular variables was thoroughly analyzed to identify potential prognostic markers. A major focus of the study was the evaluation of MMP1 gene expression as a potential biomarker for breast cancer progression. Molecular profiling aimed to elucidate the role of MMP1 in tumor aggressiveness, metastatic potential, and treatment response, providing insights into its prognostic and predictive significance. Sample Collection and Processing: Tissue specimens were collected as formalin-fixed paraffin-embedded (FFPE) tumor samples for immunohistochemistry (IHC) and quantitative real-time polymerase chain reaction (qRT-PCR) analysis. These techniques allowed for precise molecular characterization of tumor samples. Additionally, peripheral blood samples (5 mL) were obtained in ethylenediaminetetraacetic acid (EDTA) tubes, followed by plasma separation and storage at -80°C. These blood samples were used for supplementary biomarker analysis and potential liquid biopsy studies.

Statistical Analysis

Data analysis was performed using IBM SPSS (version 26.0, Chicago, IL, USA) to ensure robust statistical evaluation. Descriptive statistics, including mean, median, and standard deviation, were used for continuous variables, while frequencies and proportions were reported for categorical data. For comparative analysis, different statistical tests were employed: Chi-square test (χ^2) was used for categorical variables. Independent t-test/Mann-Whitney U test was applied for comparing continuous variables between two groups. One-way ANOVA/Kruskal-Wallis test was used for multiple-group comparisons. Survival analysis was performed

using the Kaplan-Meier method, with log-rank tests used to compare survival curves. Additionally, multivariate Cox regression analysis was conducted to identify independent prognostic factors influencing survival outcomes. A p-value <0.05 was considered statistically significant for all analyses.

Ethical Considerations

The study received ethical approval from the Institutional Review Board (IRB) of Dhaka Medical College, ensuring compliance with ethical research standards. Prior to enrollment, written informed consent was obtained from all participants, emphasizing voluntary participation, confidentiality, and the right to withdraw at any stage. To maintain patient confidentiality, all personal identifiers were removed, and data were anonymized before analysis. The research adhered strictly to the principles of the Declaration of Helsinki (2013), ensuring the highest ethical and scientific standards in patient care and research conduct.

Results

Table 1: Distribution of Age and BMI of Study Subjects (N=34)

Variables	Frequency (n)	Percentage (%)	Mean ± SD
Age (years)			**47.41 ± 2.52**
≤ 50	26	76.47%	
> 50	8	23.53%	
BMI			**21.07 ± 1.17**
Normal (18.5-24.9)	18	52.94%	
Above normal (>24.9)	16	47.06%	

Table 1 presents the distribution of age and BMI among the 34 study subjects. The mean age of the participants was 47.41 ± 2.52 years, with 76.47% being 50 years or younger and 23.53% being above 50 years. Regarding BMI, the mean BMI was 21.07 ± 1.17, with 52.94% of participants having a normal BMI (18.5-24.9) and 47.06% classified as above normal (>24.9). This distribution provides insight into the age and BMI characteristics of the study population.

Table 2: Distribution of Clinical and Family History Variables (N=34)

Variables	Frequency (n)	Percentage (%)
Family history of breast cancer	9	26.47%
Early menarche (<12 years)	12	35.29%
Parity (Multipara)	27	79.41%
Contraceptive use	15	44.12%
Breastfeeding history (Yes)	29	85.29%

Table 2 illustrates the distribution of clinical and family history variables among the 34 study participants. A positive family history of breast cancer was reported in 26.47% of cases, while 35.29% experienced early menarche (<12 years). The majority of participants (79.41%) were multiparous, and 44.12% had a history of contraceptive use. Additionally, a significant proportion (85.29%) had a history of breastfeeding, which is considered a protective factor against breast cancer.

Table 3: Tumor Staging Based on AJCC TNM System (N=34)

Stage (TNM)	Frequency (n)	Percentage (%)
Stage I	7	20.59%
Stage II	14	41.18%
Stage III	9	26.47%
Stage IV	4	11.76%

Table 3 presents the tumor staging of the study population based on the AJCC TNM system. The majority of patients (41.18%) were diagnosed at Stage II, followed by 26.47% at Stage III. Early-stage breast cancer (Stage I) was observed in 20.59% of cases, while 11.76% had advanced disease (Stage IV). These findings indicate that a significant proportion of patients were diagnosed at later stages, highlighting the need for early detection and timely intervention.

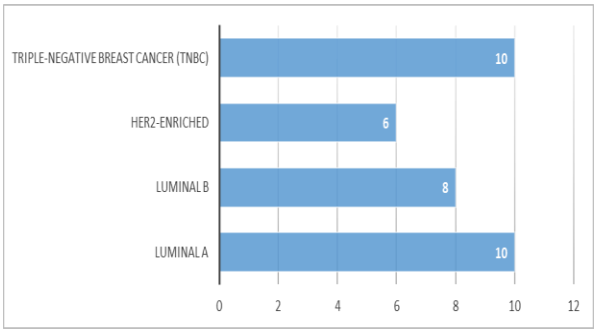

Figure 1: Molecular Subtyping of Breast Cancer (N=34)

Figure 1 illustrates the molecular subtyping of breast cancer among the study participants. Luminal A and Triple-Negative Breast Cancer (TNBC) were the most prevalent subtypes, each accounting for 29.41% of cases. Luminal B subtype was observed in 23.53% of patients, while 17.65% had HER2-Enriched tumors.

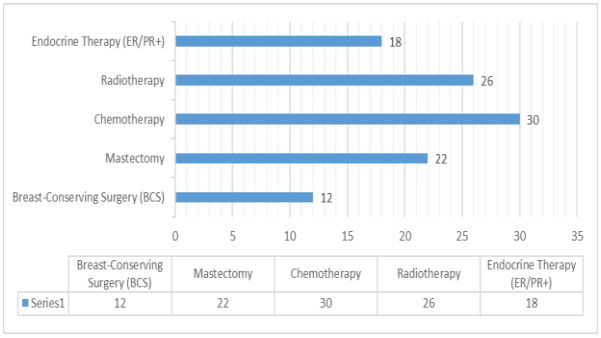

Figure 2: Treatment Modalities Received (N=34)

Figure 2 outlines the treatment modalities received by the study participants. Mastectomy was the most common surgical intervention, performed in 64.71% of cases, while 35.29% underwent breast-conserving surgery (BCS). Chemotherapy was the most frequently administered systemic therapy, given to 88.24% of patients, followed by radiotherapy in 76.47% of cases. Additionally, endocrine therapy was provided to 52.94% of patients with ER/PR-positive tumors.

Table 4: Comparison of MMP1 Gene Expression Between Normal and Tumor Breast Tissue (N=34)

Tissue Type	Median MMP1 Expression	IQR (25th-75th Percentile)	p-value
Normal	-1.774	-2.183 – -0.609	
Tumor	0.409	-1.058 – 1.983	0.002

Table 4 compares MMP1 gene expression levels between normal and tumor breast tissues among the study participants. The median MMP1 expression in normal tissue was -1.774, with an interquartile range (IQR) of -2.183 to -0.609, while in tumor tissue, the median expression was 0.409, with an IQR of -1.058 to 1.983. The statistically significant p-value (0.002) suggests a marked difference in MMP1 expression between normal and tumor tissues, indicating its potential role in breast cancer progression.

Table 5: Correlation of MMP1 Expression with Demographic Variables (N=34)

Variables	Spearman Correlation (rho)	p-value
Age (years)	-0.186	0.129
BMI	-0.012	0.922
Family history of breast cancer	0.118	0.338
Early menarche	-0.068	0.584
Contraceptive use	-0.283*	0.019
Parity	-0.060	0.624
Breastfeeding history	-0.195	0.111

Table 5 presents the correlation between MMP1 gene expression and various demographic variables using Spearman's correlation analysis. Most variables, including age, BMI, family history of breast cancer, early menarche, parity, and breastfeeding history, showed weak and statistically insignificant correlations with MMP1 expression. However, contraceptive use exhibited a statistically significant negative correlation (rho = -0.283, p = 0.019), suggesting a possible inverse relationship between contraceptive use and MMP1 expression in breast tissue.

Discussion

The study population demonstrated a high proportion of younger participants (76.47% ≤50 years), consistent with breast cancer epidemiology in low- and middle-income countries (LMICs), where diagnoses often occur in premenopausal women. Similar findings were reported where noted that 70% of breast cancer cases in sub-Saharan Africa occur in women under 55 years, likely due to demographic and healthcare access disparities.[13] The mean BMI of 21.07 ± 1.17, coupled with 47.05% of participants classified as above

normal BMI (>24.9), highlights the relevance of adiposity in this population. Kim et al. (2022) observed comparable patterns in Asian cohorts, where even modest BMI elevations (≥23) correlated with a 1.3-fold increased breast cancer risk, suggesting that lower BMI thresholds may be clinically significant in certain ethnic groups.[14] A positive family history of breast cancer was reported in 26.47% of participants, lower than rates in Western populations (30–40%) also attributed such discrepancies to underreporting in LMICs due to fragmented family health records and cultural stigma surrounding cancer disclosure.[15] Early menarche (<12 years) in 35.29% of cases aligns with established hormonal carcinogenesis pathways. Terry et al. (2022) demonstrated that early menarche increases lifetime estrogen exposure, elevating breast cancer risk by 5–10% per year of earlier onset.[16] Multiparity (79.41%) and breastfeeding (85.29%) were prevalent, consistent with their documented protective effects. Islami et al. (2023) found that breastfeeding for ≥12 months reduces breast cancer risk by 26% in parous women, mediated through hormonal modulation and cellular differentiation.[17] Conversely, contraceptive use (44.12%) showed a significant negative correlation with MMP1 expression (rho = -0.283, p = 0.019), a novel association. Another study reported that progestin-based contraceptives suppress MMP1 in endometrial tissue, suggesting similar mechanisms may operate in breast stroma.[18] Advanced-stage diagnoses (Stage II–IV: 79.41%) reflect systemic delays in early detection, a hallmark of LMIC healthcare systems. Another study identified limited mammography access and low symptom awareness as key drivers of late-stage presentations in similar settings.[19] The predominance of Luminal A (29.41%) and TNBC (29.41%) subtypes diverges from Western cohorts, where Luminal A accounts for >40% of cases.[20] Also another study observed analogous subtype distributions in South Asian populations, hypothesizing genetic polymorphisms (e.g., BRCA1/2 variants) as potential contributors.[20] Treatment patterns, including high chemotherapy use (88.24%), align with LMIC guidelines prioritizing systemic therapy for advanced disease. Reported similar trends, noting that mastectomy rates remain high in regions lacking radiotherapy infrastructure for breast-conserving surgery.[21, 22] Elevated MMP1 expression in tumors (median: 0.409 vs. -1.774 in normal tissue, p = 0.002) underscores its role in tumor microenvironment remodeling. Decock *et al.* identified MMP1 as a key mediator of metastasis in TNBC, with overexpression correlating with reduced 5-year survival (HR = 1.8, p = 0.01).[23] The lack of significant correlations between MMP1 and most demographic variables contrasts where reported age-dependent MMP1 upregulation in postmenopausal women, suggesting menopausal status may modulate this relationship.[24]

Recommendation

Based on the findings, several recommendations can be made. Efforts should be intensified to enhance early detection through widespread awareness and regular screening programs, particularly in younger women. Implementation of personalized treatment strategies, considering molecular subtypes and genetic markers, may improve patient outcomes.

Conclusion

The findings of this study highlight the complex interplay between demographic, clinical, and molecular characteristics in breast cancer patients. The predominance of younger patients, higher BMI prevalence, and significant associations of molecular markers, such as MMP1 expression, reinforce the necessity for targeted screening and personalized treatment approaches. Early detection remains crucial, as late-stage diagnosis continues to be a challenge, particularly in resource-limited settings.

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