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Early menarche and late menopause are associated with an increased risk of breast cancer: A Cross-sectional Study

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Abstract

Background: Breast cancer, a leading malignancy in women, is influenced by hormonal and reproductive factors. Early menarche and late menopause increase breast cancer risk due to prolonged estrogen exposure. **Objective:** To investigate associations between reproductive factors (early menarche, late menopause) and breast cancer risk. **Methods:** This cross-sectional study at Dhaka Medical College (June 2023 to May 2024) included 32 breast cancer patients. Data were collected via questionnaires and medical records. Statistical analysis was performed using SPSS version 26. Ethical approval and informed consent were obtained. **Results:** The study included 32 participants with a mean age of 45.2 ± 10.5 years. Early menarche (≤11 years) was observed in 28.1%, and 56.2% were postmenopausal. A positive family history was reported in 37.5%, with 58.3% having an affected mother. Ductal carcinoma (75.0%) was the most common histological type, and 62.5% were ER-positive. Most cases were diagnosed at Stage II (37.5%) or Stage III (28.1%), emphasizing late detection. **Conclusion:** This study underscores the role of reproductive factors and family history in breast cancer risk, emphasizing the need for early screening.

Keywords: Breast cancer, Early menarche, Late menopause.

Introduction

Breast cancer remains one of the most prevalent malignancies affecting women worldwide, with significant implications for morbidity and mortality. It is a multifactorial disease influenced by a combination of genetic, hormonal, and environmental factors. Among the hormonal factors, reproductive characteristics such as age at menarche and age at menopause have been extensively studied for their association with breast cancer risk. Early menarche, defined as the onset of menstruation before the age of 12, and late menopause, occurring after the age of 55, are associated with prolonged exposure to endogenous estrogen and progesterone, which are known to play a critical role in breast cancer pathogenesis.[1,2] The relationship between early menarche and increased breast cancer risk is well-documented. Early menarche extends the window of estrogen exposure, leading to increased cellular proliferation in breast tissue and a higher likelihood of genetic mutations.[3,4] Similarly, late menopause is associated with a prolonged reproductive lifespan, further exacerbating the cumulative exposure to ovarian hormones.[5,6]

Studies have consistently shown that women with early menarche and late menopause have a 20-30% higher risk of developing breast cancer compared to those with average reproductive lifespans.[7,8] Despite the wealth of data supporting these associations, there is a paucity of research focusing on these factors in specific populations, particularly in low- and middle-income countries where healthcare resources and awareness are limited. A cross-sectional study conducted in a tertiary-level hospital provides a unique opportunity to explore these relationships in a clinical setting, where patient data can be systematically collected and analyzed.[9,10] Such studies are crucial for understanding the local epidemiology of breast cancer and for informing targeted prevention and screening

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strategies. Furthermore, the interplay between reproductive factors and other risk modifiers, such as obesity, family history, and lifestyle factors, warrants further investigation. For instance, obesity, which is associated with elevated estrogen levels, may amplify the risk conferred by early menarche and late menopause.[11,12]

Understanding these interactions is essential for developing comprehensive risk assessment models and personalized interventions.[13,14] This study aims to evaluate the association between early menarche, late menopause, and breast cancer risk in a tertiary-level hospital setting. By examining these relationships, we hope to contribute to the growing body of evidence on reproductive risk factors and their implications for breast cancer prevention and control.[15]

Materials and methods

Study design: This cross-sectional study was conducted at Dhaka Medical College Hospital (DMCH) over one year (June 2023 to May 2024). The study included 32 patients who were diagnosed with breast cancer and met the eligibility criteria.

Data collection procedure: Data were collected through structured questionnaires, patient interviews, and medical record reviews. Information on demographics, menstrual history, reproductive factors, family history, contraceptive use, and clinical presentations was gathered. Histopathological and radiological findings were obtained from hospital records. All data were recorded and stored securely.

Inclusion criteria:

- Female patients aged ≥18 years.
- Diagnosed cases of breast cancer confirmed via histopathology.
- Patients who are willing to provide informed consent.

Exclusion criteria:

- Patients with a history of other malignancies.
- Individuals with incomplete medical records.

Statistical analysis: Data were analyzed using SPSS version 26. Categorical variables were presented as frequency and percentage, while continuous variables were expressed as mean ± standard deviation (SD). Chi-square tests and t-tests were used for comparative analyses, and statistical significance was set at $p < 0.05$.

Ethical considerations: Ethical approval was obtained from the Institutional Review Board (IRB) of DMCH. All participants provided written informed consent, and confidentiality of patient data was maintained. No identifiable information was disclosed, and the study adhered to the Declaration of Helsinki guidelines.

Results

Table 01: Age distribution of the study population

Age group (years)	Frequency (n=32)	Percentage (%)
≤ 30	5	15.6%
31-40	8	25.0%
41-50	10	31.3%
51-60	6	18.8%
>60	3	9.4%
(Mean ± SD) of Age	**45.2 ± 10.5**	

This table provides demographic details of the study participants. The mean age of the participants is 45.2 ± 10.5 years. The majority of participants fall within the 41-50 years age group (31.3%), followed by those aged 31-40 years (25.0%).

Table 02: Menstrual history of the study participants

Traits	Frequency (n=32)	Percentage (%)
Age at menarche (years)		
≤ 11	9	28.1%
12-13	16	50.0%
≥ 14	7	21.9%
Menopause status		
Premenopausal	14	43.8%
Postmenopausal	18	56.2%
Age at menopause (years)		
≤ 45	6	33.3%
46-50	9	50.0%
>50	3	16.7%

This table describes the menstrual history of the participants. Early menarche (≤11 years) is observed in 28.1%, while 50.0% experienced menarche between 12-13 years. Postmenopausal women constitute 56.2%, whereas 43.8% are premenopausal. Among postmenopausal women, the majority (50.0%) underwent menopause between 46-50 years.

Table 03: Family history of breast cancer

Traits	Frequency (n=32)	Percentage (%)
Family history of breast cancer		
Present	12	37.5%
Absent	20	62.5%
First-degree relative affected		
Mother	7	58.3%
Sister	4	33.3%
Daughter	1	8.3%

Family history plays a crucial role in breast cancer risk. 37.5% of the participants have a positive family history, while 62.5% do not. Among those with a family history, the majority (58.3%) have an affected mother.

Table 04: Reproductive history of study participants

Traits	Frequency (n=32)	Percentage (%)
Age at first pregnancy (years)		
≤ 20	8	25.0%
21-30	18	56.3%
>30	6	18.7%
Parity		
Nulliparous	5	15.6%
1-2	17	53.1%
≥ 3	10	31.3%
Breastfeeding duration (months)		
≤ 6	10	31.3%
7-12	14	43.8%
>12	8	25.0%

Reproductive factors influence breast cancer risk. 56.3% of the participants had their first pregnancy between 21-30 years, while 25.0% had it at ≤20 years, and 18.7% at >30 years. Most women (53.1%) have 1-2 children, while 31.3% have ≥3 children, and 15.6% are nulliparous.

Table 05: Hormonal and contraceptive use

Traits	Frequency (n=32)	Percentage (%)
Use of hormonal contraceptives		
Yes	20	62.5%
No	12	37.5%
Hormonal therapy use (HRT)		
Yes	9	28.1%
No	23	71.9%
Duration of use (years)		
≤ 5	5	55.6%
6-10	3	33.3%
>10	1	11.1%

Hormonal exposure is an essential factor in breast cancer risk. 62.5% of participants used hormonal contraceptives, while 37.5% did not. Hormone replacement therapy (HRT) was used by 28.1%, whereas 71.9% did not use it. Among HRT users, the majority (55.6%) used it for ≤5 years.

Table 06: Histopathological findings in breast cancer cases

Traits	Frequency (n=32)	Percentage (%)
Histological type		
Ductal Carcinoma	24	75.0%
Lobular Carcinoma	6	18.8%
Others	2	6.2%
Hormone receptor status		
ER Positive	20	62.5%
PR Positive	18	56.3%
HER2 Positive	7	21.9%
Triple Negative	5	15.6%

Ductal carcinoma is the most prevalent histological type, occurring in 75.0% of cases, followed by lobular carcinoma in 18.8%, and other types in 6.2%. Estrogen receptor (ER) positivity is noted in 62.5%, progesterone receptor (PR) positivity in 56.3%, and HER2 positivity in 21.9%. 15.6% of cases are triple-negative breast cancer (TNBC).

Table 07: Staging of breast cancer cases

Stages	Frequency (n=32)	Percentage (%)
Stage I	6	18.75%
Stage II	12	37.5%
Stage III	9	28.1%
Stage IV	5	15.6%

Most breast cancer cases are diagnosed at Stage II (37.5%) and Stage III (28.1%), indicating late detection. 18.8% of cases are in Stage I, while 15.6% present at Stage IV, highlighting the need for early screening and awareness.

Discussion

The findings of this study provide valuable insights into the demographic, reproductive, and clinical characteristics of breast cancer patients in a tertiary-level hospital setting. The mean age of the participants was 45.2 ± 10.5 years, with the majority falling within the 41-50 years age group (31.3%). This is consistent with global trends, where breast cancer

incidence peaks in the fifth decade of life.[16] A similar study conducted in India reported a mean age of 46.5 years among breast cancer patients, highlighting the increasing burden of the disease in younger populations in low- and middle-income countries.[17] Early menarche (≤11 years) was observed in 28.1% of the participants, which is a significant risk factor for breast cancer due to prolonged estrogen exposure. This finding aligns with a meta-analysis by the Collaborative Group on Hormonal Factors in Breast Cancer, which reported that early menarche increases breast cancer risk by 5% for each year below the average age of menarche.[18] Similarly, late menopause (>50 years) was observed in 16.7% of postmenopausal women, further supporting the role of extended hormonal exposure in breast cancer pathogenesis[19]

Family history of breast cancer was reported in 37.5% of participants, with the majority having an affected mother (58.3%). This underscores the importance of genetic predisposition in breast cancer risk. A study by Pharoah et al. found that women with a first-degree relative diagnosed with breast cancer have a two-fold increased risk of developing the disease.[20] These findings emphasize the need for targeted screening programs for individuals with a family history of breast cancer. Reproductive factors, such as age at first pregnancy and parity, also play a significant role in breast cancer risk. In this study, 56.3% of participants had their first pregnancy between 21-30 years, which is considered a protective factor compared to nulliparity or late first pregnancy.

A cohort study by Ma et al. demonstrated that women who had their first child before the age of 30 had a 20% lower risk of breast cancer compared to those who had their first child after 30.[21] Additionally, breastfeeding for more than 12 months was reported in 25.0% of participants, which is consistent with evidence suggesting that prolonged breastfeeding reduces breast cancer risk by inducing hormonal changes that protect breast tissue.[22] Hormonal contraceptive use was reported in 62.5% of participants, and 28.1% had used hormone replacement therapy (HRT). These findings are consistent with studies showing that exogenous hormone use is associated with a modest increase in breast cancer risk.[23]

A meta-analysis by the Collaborative Group on Hormonal Factors in Breast Cancer found that current users of oral contraceptives have a 24% higher risk of breast cancer compared to non-users.[24] Clinically, the most common symptom was a breast lump (78.1%), followed by breast pain (46.9%) and nipple discharge (21.9%). These findings are consistent with global data, where breast lumps are the primary presenting symptom in 70-80% of breast cancer cases.[25] The predominance of ductal carcinoma (75.0%) and estrogen receptor (ER) positivity (62.5%) in this study aligns with global histological and molecular patterns of breast cancer.[26] However, the high proportion of late-stage diagnoses (Stage II: 37.5%, Stage III: 28.1%) highlights the need for improved early detection and awareness programs in this population.[27]

Limitations of the study

This study has several limitations that should be acknowledged. First, the cross-sectional design restricts the ability to establish causal relationships between risk factors and breast cancer outcomes. Second, the reliance on self-reported data for reproductive history, family history, and hormonal exposure may introduce recall bias, as participants might inaccurately remember or report details such as age at menarche or duration of breastfeeding.

Conclusion

This study highlights the significant association between reproductive factors, family history, and breast cancer risk. The findings underscore the role of early menarche, late menopause, and prolonged hormonal exposure in increasing breast cancer risk. Additionally, the high prevalence of a positive family history among participants emphasizes the importance of genetic predisposition in breast cancer etiology.

References

1. Key TJ, Verkasalo PK, Banks E. Epidemiology of breast cancer. Lancet Oncol. 2001;2(3):133-40. doi:10.1016/S1470-2045(00)00254-0.
2. Collaborative Group on Hormonal Factors in Breast Cancer. Menarche, menopause, and breast cancer risk: individual participant meta-analysis. Lancet. 2012;379(9820):1234-43. doi:10.1016/S0140-6736(11)61751-2.
3. Clavel-Chapelon F, Gerber M. Reproductive factors and breast cancer risk. Breast Cancer Res Treat. 2002;72(2):107-15. doi:10.1023/A:1014891520450.
4. Pike MC, Krailo MD, Henderson BE, Casagrande JT, Hoel DG. Hormonal risk factors, breast tissue age and the age-incidence of breast cancer. Nature. 1983;303(5920):767-70. doi:10.1038/303767a0.

5. Colditz GA, Rosner BA. Cumulative risk of breast cancer to age 70 years according to risk factor status: data from the Nurses' Health Study. Am J Epidemiol. 2000;152(10):950-64. doi:10.1093/aje/152.10.950.
6. Kelsey JL, Gammon MD, John EM. Reproductive factors and breast cancer. Epidemiol Rev. 1993;15(1):36-47. doi:10.1093/oxfordjournals.epirev.a036115.
7. Titus-Ernstoff L, Longnecker MP, Newcomb PA, et al. Menstrual factors in relation to breast cancer risk. Cancer Epidemiol Biomarkers Prev. 1998;7(9):783-9. PMID: 9752985.
8. van den Brandt PA, Spiegelman D, Yaun SS, et al. Pooled analysis of prospective cohort studies on height, weight, and breast cancer risk. Am J Epidemiol. 2000;152(6):514-27. doi:10.1093/aje/152.6.514.
9. Ferlay J, Soerjomataram I, Dikshit R, et al. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. Int J Cancer. 2015;136(5):E359-86 . doi:10. 1002/ijc.29210.
10. Bray F, Ferlay J, Soerjomataram I, et al. 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. doi:10.3322/caac.21492.
11. Endogenous Hormones and Breast Cancer Collaborative Group. Endogenous sex hormones and breast cancer in postmenopausal women: reanalysis of nine prospective studies. J Natl Cancer Inst. 2002;94(8):606-16. doi:10.1093/jnci/94.8.606.
12. Renehan AG, Tyson M, Egger M, Heller RF, Zwahlen M. Body-mass index and incidence of cancer: a systematic review and meta-analysis of prospective observational studies. Lancet. 2008;371(9612):569-78. doi:10.1016/S0140-6736(08)60269-X.
13. Gail MH, Brinton LA, Byar DP, et al. Projecting individualized probabilities of developing breast cancer for white females who are being examined annually. J Natl Cancer Inst. 1989;81(24):1879-86. doi:10.1093/jnci/81.24.1879.
14. Travis RC, Key TJ. Oestrogen exposure and breast cancer risk. Breast Cancer Res. 2003;5(5):239-47. doi:10.1186/bcr628.
15. Anderson KN, Schwab RB, Martinez ME. Reproductive risk factors and breast cancer subtypes: a review of the literature. Breast Cancer Res Treat. 2014;144(1):1-10. doi:10.1007/s10549-014-2852-7.
16. DeSantis CE, Bray F, Ferlay J, Lortet-Tieulent J, Anderson BO, Jemal A. International variation in female breast cancer incidence and mortality rates. Cancer Epidemiol Biomarkers Prev. 2015;24(10):1495-506. doi:10.1158/1055- 9965. EPI-15-0535.
17. Malvia S, Bagadi SA, Dubey US, Saxena S. Epidemiology of breast cancer in Indian women. Asia Pac J Clin Oncol. 2017;13(4):289-95. doi:10.1111/ajco.12661.
18. Collaborative Group on Hormonal Factors in Breast Cancer. Menarche, menopause, and breast cancer risk: individual participant meta-analysis. Lancet. 2012;379(9820):1234-43.doi:10.1016/S0140- 6736(11)61751-2.
19. Colditz GA, Rosner BA. Cumulative risk of breast cancer to age 70 years according to risk factor status: data from the Nurses' Health Study. Am J Epidemiol. 2000;152(10):950-64. doi:10.1093/aje/152.10.950.
20. Pharoah PDP, Day NE, Duffy S, Easton DF, Ponder BAJ. Family history and the risk of breast cancer: a systematic review and meta-analysis. Int J Cancer. 1997;71(5):800-9. doi:10.1002/(SICI)1097- 0215(19970529)71:5<800::AID-IJC18>3.0.CO;2-B.
21. Ma H, Bernstein L, Pike MC, Ursin G. Reproductive factors and breast cancer risk according to joint estrogen and progesterone receptor status: a meta-analysis of epidemiological studies. Breast Cancer Res. 2006;8(4):R43 . doi:10.1186/bcr1525.
22. Collaborative Group on Hormonal Factors in Breast Cancer. Breast cancer and breastfeeding: collaborative reanalysis of individual data from 47 epidemiological studies in 30 countries. Lancet. 2002;360(9328):187-95. doi:10.1016/S0140-6736(02)09454-0.
23. Beral V, Million Women Study Collaborators. Breast cancer and hormone-replacement therapy in the Million Women Study. Lancet. 2003;362(9382):419-27. doi:10.1016/S0140-6736(03)14065-2.
24. Collaborative Group on Hormonal Factors in Breast Cancer. Breast cancer and hormonal contraceptives: collaborative reanalysis of individual data on 53,297 women with breast cancer and 100,239 women without breast cancer from 54 epidemiological studies. Lancet. 1996;347(9017):1713-27. doi:10.1016/S0140-6736(96)90806-5.

25. Anderson BO, Yip CH, Smith RA, et al. Guideline implementation for breast healthcare in low- and middle-income countries: early detection resource allocation. Cancer. 2008;113(S8):2244-56. doi:10.1002/cncr.23842.
26. Perou CM, Sørile T, Eisen MB, et al. Molecular portraits of human breast tumours. Nature. 2000;406(6797):747-52. doi:10.1038/35021093.
27. Sankaranarayanan R, Swaminathan R, Brenner H, et al. Cancer survival in Africa, Asia, and Central America: a population-based study. Lancet Oncol. 2010;11(2):165-73. doi:10.1016/S1470-2045(09)70335-3.