

The Relationship between Reproductive Factors and Risk of Breast Cancer among Pre –Menopausal Women

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Abstract

Background: Breast cancer is the most common type of cancer in women and the first cause of death among the women. Women who develop breast cancer in the pre- menopausal years are more likely to have a higher tumor grade. **Aim:** to assess the relationship between reproductive factor and risk of breast cancer among premenopausal women. **Design:** A descriptive study design was utilized. **Setting:** was conducted at outpatient clinics and inpatient department in oncology institute. **Subjects:** Purposive sample of 100 women diagnosed with breast cancer. **Tools:** Two tools were used. **Tool I :** A structured interviewing questionnaire including two parts to assess (demographic data, women health history) . **Tool II :**Assessment of reproductive risk factors: such as age of menarche, age at first pregnancy ,abortion , degree of consanguinity , using post-menopausal hormonal therapy. **Result:** More than half of them were previously diagnosed with breast cancer breast . Regarding reproductive risk factors ,it was found that, two third of them were using contraceptive pills , majority of them had their menarche age from (12-24) years and half of them had their first pregnancy at age from (20-30) years , less than three quarter of them were overweight, more than two third of them are first degree consanguinity, more than three quarter of them used post-menopausal hormone therapy. **Conclusion:** There was evidence of differing relationship between age, marital status, gravidity, abortion, age of menarche, age of first pregnancy, abortion, age at first birth, mode of breast feeding, body weight, menopause, and risk of premenopausal breast cancer . **Recommendation:** Implementing education programs to enhance awareness of premenopausal women regarding reproductive risk factors associated with breast cancer .

Keywords: *Reproductive Factors, Risk of Breast Cancer, Pre–Menopausal women.*

Introduction :

Breast cancer (BC) is the most prevalent cancer in women and the leading cause of women's cancer-related deaths and morbidity worldwide. Breast cancer occurs when abnormal cells in the breast grow in an uncontrolled way, forming a tumor. Breast cancer can start in the ducts or lobules of the breast. The site where the cancer starts is called the primary cancer. Breast cancer can be non-invasive (sometimes called pre-cancer) is where cancer cells stay in the ducts and lobules of the breast. invasive is where the cancer cells spread into the surrounding tissue, or to other parts of the body such as the bones or liver to become metastatic (or secondary or advanced) cancer (*Kumar et al., 2022*). The risk factors for developing breast cancer can be categorized into non-modifiable and modifiable factors. Non-modifiable risk factors, which cannot be changed, include: **Family History:** Having a family history of breast or ovarian cancer, as these cancers may be linked. **Inherited Genetic Factors:** The presence of a faulty or mutated gene, such as BRCA1 or BRCA2. **Medical History:** Previous exposure to radiation therapy, for instance, for conditions like Hodgkin Lymphoma, and a history of other types of cancer. **Breast Density:** Having dense breasts, which may increase the risk. **Age:** Advancing age is a significant non-modifiable risk factor for breast cancer. **Reproductive History:** Factors related to reproductive history, such as starting menstruation at a young age, reaching menopause late, or not having given birth. These non-modifiable risk factors contribute to an individual's overall risk of developing breast cancer and understanding them can aid in early detection and preventive measures. It is



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important for individuals with such risk factors to discuss their situation with healthcare professionals for personalized risk assessment and appropriate monitoring (*Feruz., 2021*).

Perimenopause is a natural transitional phase that precedes menopause and can extend for several years, ranging from a few months to up to 10 years. During this period, estrogen levels in the body undergo fluctuations, leading to symptoms such as irregular menstrual cycles, hot flashes, night sweats, weight gain, mood swings, breast tenderness, changes in blood cholesterol levels, and decreased bone density. Perimenopause is associated with an increased risk of depression. The manifestations of perimenopause can vary among women, and the onset and duration of this phase also differ. On a related note, breast cancer is a form of cancer that originates in breast tissue. It poses a significant health concern for women across various age groups. Regular screening and awareness are crucial for early detection and effective management of breast cancer. Women experiencing perimenopausal symptoms should maintain regular medical check-ups to address any health concerns, including the risk of breast (*Abedalrahman et al., 2020*).

Also, Breast cancer incidence is increasing with an unacceptably high mortality rate in premenopausal women; it is not clear what specifically might cause breast cancer to develop in women who have not reached menopause. However, there are several known risk factors for early-onset breast cancer, including obesity. Known factors associated with premenopausal breast cancer include age at menarche, age at first birth, and parity. Later age at menarche and earlier age at first birth are consistently associated with lower risk of breast cancer, though there are known differences between estrogen and progesterone hormone statuses (*Ntiringanya et al., 2021*). Certain types of breast cancer are more common in younger women than in women who have gone through menopause. HER2-positive breast cancer occurs when a protein found on the surface of breast cells called human epidermal growth factor receptor 2 (HER2) grows uncontrollably. Triple-negative breast cancer does not have receptors for the hormone's estrogen or progesterone or the HER2 protein (*Sopik., 2021*). Nurses play a crucial role in educating women about breast cancer risk factors, screening, and prevention strategies, provide information on the importance of regular breast self-examination, clinical breast examination, and mammography screening. Nurses can also provide counseling to women regarding the potential risks and benefits of hormonal contraceptives and hormone replacement therapy. Additionally, nurses can help women understand the importance of maintaining a healthy lifestyle, including regular exercise, healthy eating habits, and avoiding smoking and alcohol consumption (*Mahadevaiah et al., 2021*).

Significant of study:

Breast cancer stands out as the most frequently diagnosed cancer globally, surpassing an estimated 2 million new cases in 2020. Tragically, it holds the top position as the leading cause of cancer-related deaths in women, claiming the lives of more than 680,000 individuals. Despite variations in breast cancer incidence rates between developed and developing countries, the disease continues to be the most prevalent type of female cancer in Egypt, characterized by an age-specific incidence rate of 48.8 per 100,000 individuals. Projections for 2050 anticipate around 46,000 new cases (*Azim et al., 2023*). Premenopausal women contribute significantly to the global burden of breast cancer, accounting for 30.9% of all diagnosed cases (*Heer et al., 2020*). In 2020, the World Health Organization reported a staggering 684,996 deaths worldwide due to breast cancer. (*WHO., 2020*). The American Cancer Society's 2021 report estimated that 281,550 new cases of invasive breast cancer would be diagnosed in women in the United States, along with 49,290 cases of ductal carcinoma in situ (DCIS). The mortality rate was projected at 43,600 women succumbing to the disease. Notably, incidence rates have shown a recent increase of 0.5% per year (*ACS, 2021*). In Egypt, breast cancer is identified as the most common malignancy in women, constituting 38.8% of cancer cases. The estimated number of breast cancer cases in 2020 was nearly 22,700, with a forecasted increase to approximately 64,000 by 2050. The breast cancer mortality rate is estimated at around 11%, making it the second leading cause of cancer-related mortality after liver cancer (*Ibrahim et al., 2018*). The challenge posed by breast cancer is not only significant on a global scale but also holds substantial implications for specific regions and populations, necessitating ongoing efforts in research, awareness, and medical intervention.

Aim of the study:

The aim of this study is to assess the relationship between reproductive factors and risk of breast cancer among pre-menopausal women.

**Research question:**

what is the relationship between reproductive factors and risk of breast cancer among premenopausal women?

Subject and method :**Research Design:**

A descriptive design was utilized for conducting this study.

Setting:

This study was conducted at outpatient clinics and inpatient department oncology institute in Sohag. The institute consists of two buildings, a surgical building, and an oncology building.

Subject:**Type of sample:**

Purposive sample was used in this study.

Sample Size:

The sample size included 100 women diagnosed with breast cancer within period of three months from beginning March 2023 to end May 2023.

Tools for data collection:

Two tools were used after reviewing the related literature putting into considerations the aim of the study and the data needed to be collected from the studied subject.

Tool (I): A structured interviewing questionnaire:

This tool was designed by the researcher . It was written in a simple Arabic language including the following two parts:

Part (I): Demographic data of the studied women:

This part composed of (4) questions aimed to collect data related to age, marital status, level of educations, and occupational status.

Part (II) Assessment of women Health History: This part composed of (41) questions aimed to collect data related to the following.

- **Medical history:** This part composed of (6) question aimed to collect data related to medical history such as(heart disease, chronic hypertension, diabetes, renal infection, anemia ,other medical condition).
- **Family History:** This part composed of (7) question aimed to collect data related to family history such as(Breast cancer, hypertension ,heart disease , renal disease , congenital anomaly, diabetes other medical condition) .
- **Menstrual history:** This part composed of (6) question aimed to collect data related to menstrual history such as (Age of menarche ,duration, menstrual cycles ,regularity , amount ,menstrual disorder).
- **Obstetric history:** This part composed of (8) question aimed to collect data related to obstetric history such as(Gravidity, parity ,nulliparous, multipara ,abortion ,stillbirth, newborn death ,any complication related to previous deliveries) .
- **Family planning history:** This part composed of (4) question aimed to collect data related to obstetric history such as(Type of previous contraceptive method, duration of use, cause of termination ,complication while using) .
- **History of breast cancer:** This part composed of (10) question aimed to collect data related to history of breast cancer such as (Diagnosis , time of initiation breast cancer, signs and symptoms of breast cancer, type , stage, diagnosis are you do , medication ,type of surgery , side of surgery ,type of treatment of post-operative) .

Tool II: Assessment of Reproductive risk factors:



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This tool was adapted from **Rosato et al. (2019)**, the questionnaire comprises 11 questions designed to evaluate various reproductive factors. These questions delve into critical aspects such as the age of menarche, age at first pregnancy, term pregnancy, history of abortion, living pregnancies, age at first birth, mode of breastfeeding, weight, menopausal status, degree of consanguinity, and the use of post-menopausal hormone therapy. The comprehensive nature of the questionnaire allows for a thorough assessment of diverse reproductive factors influencing the participants' health and well-being.

Validity:

Revision of the tools for clarity, relevance, comprehensiveness, understanding, and applicability was done by panel of three expertise in maternal and newborn health nursing department at Helwan University and to measure the content validity of the tools and the necessary modifications were done accordingly .

Reliability:

Cronbach's Alpha test was used to assess the reliability of both women's reproductive factors assessment tool and quality of life assessment tool. The reliability of reproductive factors assessment scale was 0.86, while it was 0.98 for quality-of-life assessment scale.

Reliability analysis :

| Items | Cronbach alpha | P -value |
|---|----------------|----------|
| Tool (I): Assessment of women health history | 0.711 | 0.001* |
| Tool (II): Reproductive risk factors | 0.941 | 0.001* |

Ethical considerations:

An official permission to conduct the proposed study was obtained from the Scientific Research Ethics Committee from faculty of nursing Helwan University . The researcher clarified the aim of the study to the women included in the study to gain their confidence and trust. The researcher obtained written information from women. The researcher assured maintaining anonymity and confidentiality of subject's data. The women were informed that they are allowed to choose to participate or not in the study and that they have the right to withdraw from the study at any time.

II- Operational design:

Preparatory phase:

Included reviewing of past, current, national, and international related literature, and theoretical knowledge of various aspect of the study using books, articles, internet, and magazines to develop tools for data collection. The researcher constructed and prepared the different data collection tools.

Pilot study:

The pilot study was carried on 10% (10) of women under study based on sample criteria, it has been conducted to test the applicability, clarity of questions and understand ability of the tool. Then the tool was modified according to the result of the pilot study, so all of subjects who were shared on the pilot study were excluded from the studied sample.

Fieldwork:

- Actual fieldwork was conducted in outpatient clinics and inpatient oncology department during the period from beginning March up to end May 2023, the researcher attending the previous setting 2 days weekly from 9 am to 2 pm.
- At the beginning, the women were interviewed in the waiting area of the outpatient clinic. Then the researcher introduced herself and explain the purpose of study to the women to gain their confidence, cooperation, and their acceptance to participate in the study, then the written consent was obtained from them.
- After that, the researcher started the assessment of women individually data collection was through personal and single face to face .the data was collected two days on Sunday and Thursday, time taking for each woman was 20:30minuts.



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- Then the researcher used tool (I) to assess women's demographic data, family history, medical history, obstetric history, menstrual factor, family planning history, history of breast cancer.
- Then the researcher used tool (II) to assess women's reproductive factors such as (Age of menarche, age at first pregnancy, term pregnancy, abortion, living pregnancy, age at first birth, mode of breast feeding, weight, menopause, degree of consanguinity, are using post-menopausal hormone therapy).
- Finally, this interview took about 20-30 min for each woman; the woman was asked in Arabic language, documented her answer in the tools utilized, and give women chance to ask any question as needed.

III-Administrative design:

An official letter from the Dean of the Faculty of Nursing, Helwan University was directed to the administrators of Sohag oncology institute to obtain an official approval to carry out the study after explanation of the aim of the study. This permission was obtained before the initiation of the data collection.

IV-Statistical design:

Numerical data were presented as mean and standard deviation (SD) values. Qualitative data were presented as frequencies (n) and percentages (%). Reliability of the questionnaire was assessed using Cronbach's alpha reliability coefficient. Cronbach's alpha reliability coefficient normally ranges between 0 and 1. Higher values of Cronbach's alpha (More than 0.7) denote acceptable reliability. Chisquare was used to compare between studied variables. Spearman's correlation coefficient was used to determine correlations between different variables. The significance level was set at $P \leq 0.05$. Statistical analysis was performed with IBMSPSS Statistics Version 26 for Windows.

Result:

Table (1) indicates that, mean age and standard deviation of the studied women 47.64 ± 1.90 with range from 45-50 years old. Concerning marital status, 62% of them were married, while 4% were single. 70% of the studied women were illiterate and 88% were housewife, while 12% were employed and 6% were university educated.

Table (2) shows that, 8% of the studied women had a history of heart disease, 26% of them complaining chronic hypertension, and 4% of them had a renal disease, while majority 84% complained from anemia and 54% had diabetes mellitus.

Table (3) clarifies that, majority 84% of the studied women had menarche at age from (12-14), while only 8% had menarche at age < 12 and > 14 . 70% of them had a regular menstrual cycle with moderate amount of bleeding. Regarding menstrual disorder, 44% of the studied women had amenorrhea, while 14% had menorrhagia.

Figure (1) : reveals that, 44% of the studied women had amenorrhea, while 14% had menorrhagia.

Table (4) shows that, the studied women, half of them (50%) had 1-3 previous pregnancies, while 8% had > 5 pregnancies. Concerning parity, 62% of them had (1-3) deliveries, while 38% had from (4-5). 2% of them were nulliparous and 68% were multipara. Regarding complication related to previous deliveries, 38% of them had vaginal bleeding.

Table (5) demonstrates that, 56% of the studied women suffered from right breast cancer and 44% of them had left cancer. 90% of them diagnosed from (1-12) months, while only 10% of them diagnosed from (13-24) months. Concerning type of breast cancer, 56% of the studied women had Invasive ductal carcinoma, while 4% of them diagnosed with inflammatory breast cancer and ductal carcinoma insitu. Regarding diagnostic test, All of them had mammogram, complete blood count, and breast biopsy.

Table (6) reveals that, 84% of the studied women had their menarche from (12-24) years old and 50% of them had their first pregnancy at age from (20-30) years old, while 20% underage of 20 years old. Regarding weight, 72% of them are overweight, while 22% of them had a normal weight.

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Figure(2) : reveal that 68% have first-degree consanguinity, while 10% have second and third-degree consanguinity. Regarding post-menopausal hormone therapy, 78% utilized it, whereas 22% did not. In terms of consanguinity, 68% have first-degree consanguinity, while 10% have second and third-degree consanguinity. As for post-menopausal hormone therapy, 78% opted for it, while 22% did not.

Table (7) :The study demonstrates a highly statistically significant correlation between women's risk of breast cancer and certain factors, specifically age and marital status (with p-values of 0.03 and 0.01, respectively). However, there was no statistically significant correlation found between women's risk of breast cancer and their level of education and occupational status (with p-values of 0.648 and 0.522, respectively).

Table (8): shows that, there was a highly statistically significant correlation between women' risk of breast cancer, gravidity, and abortion with p-value= (0.04,and 0.02), while there was no statistically significant correlation between women' risk of breast cancer, parity, menstrual cycle, regularity of menses, multipara, nulliparous, duration of contraceptive methods and type of contraceptive with p-value= (0.124,0.755, 0.381, 0.522, 0.109, 0.547 and 0.175 respectively).

Table (9): shows that, A highly statistically significant correlation was observed between women's risk of breast cancer and various factors, including the age of menarche, age of first pregnancy, abortion, age at first birth, mode of breastfeeding, weight, and menopause (with p-values of 0.004, 0.001, 0.002, 0.001, 0.001, 0.01, 0.04, and 0.01, respectively). However, no statistically significant correlation was found between women's risk of breast cancer and factors such as term pregnancy, living children, degree of consanguinity, and post-menopausal hormone use (with p-values of 0.531, 0.518, 0.288, and 0.522, respectively)

Table (1): Distribution of demographic data for the studied women (no=100).

| Items | Studied women (no = 100) | |
|-----------------------------|--------------------------|----|
| | No | % |
| Age: | | |
| • 45-47 | 44 | 44 |
| • 48-50 | 56 | 56 |
| Mean ± SD. | 47.64±1.90 | |
| Range: | 45-50 | |
| Marital status : | | |
| • Single | 4 | 4 |
| • Married | 62 | 62 |
| • Divorce | 12 | 12 |
| • Widow | 22 | 22 |
| Level of education: | | |
| • Illiterate | 70 | 70 |
| • Basic education | 16 | 16 |
| • Secondary | 8 | 8 |
| • University | 6 | 6 |
| Occupational status: | | |
| • Housewife | 88 | 88 |
| • Employee | 12 | 12 |

Table (2): Distribution of medical history for the studied women (no=100).

| Items | Studied Women (no = 100) | |
|------------------------------|--------------------------|----|
| | No | % |
| Heart disease: | | |
| • No | 92 | 92 |
| • Yes | 8 | 8 |
| Chronic hypertension: | | |
| • No | 74 | 74 |
| • Yes | 26 | 26 |
| DM: | | |
| • No | 46 | 46 |
| • Yes | 54 | 54 |
| Renal infection: | | |
| • No | 96 | 96 |
| • Yes | 4 | 4 |
| Anemia: | | |
| • No | 16 | 16 |
| • Yes | 84 | 84 |

Table (3): Distribution of menstrual history for the studied women (no=100).

| Items | Studied Women (no = 100) | |
|--------------------------------|--------------------------|----|
| | No | % |
| Age at menarche(years): | | |
| • <12 | 8 | 8 |
| • (12-14) | 84 | 84 |
| • >14 | 8 | 8 |
| Duration(days): | | |
| • 1-3 day | 12 | 12 |
| • 3-7 day | 86 | 86 |
| • >7 | 2 | 2 |
| Frequency (days): | | |
| • <21 | 2 | 2 |
| • 21-35 | 88 | 88 |
| • >35 | 10 | 10 |
| Regularity: | | |
| • Regular | 70 | 70 |
| • Irregular | 30 | 30 |
| Amount: | | |
| • Scanty | 8 | 8 |
| • Moderate | 70 | 70 |
| • Heavy | 22 | 22 |
| Menstrual disorders: | | |
| • Amenorrhea | 44 | 44 |
| • Dysmenorrhea | 14 | 14 |

| | | |
|---|----|----|
| <ul style="list-style-type: none"> Menorrhagia Oligomenorrhea | 18 | 18 |
|---|----|----|

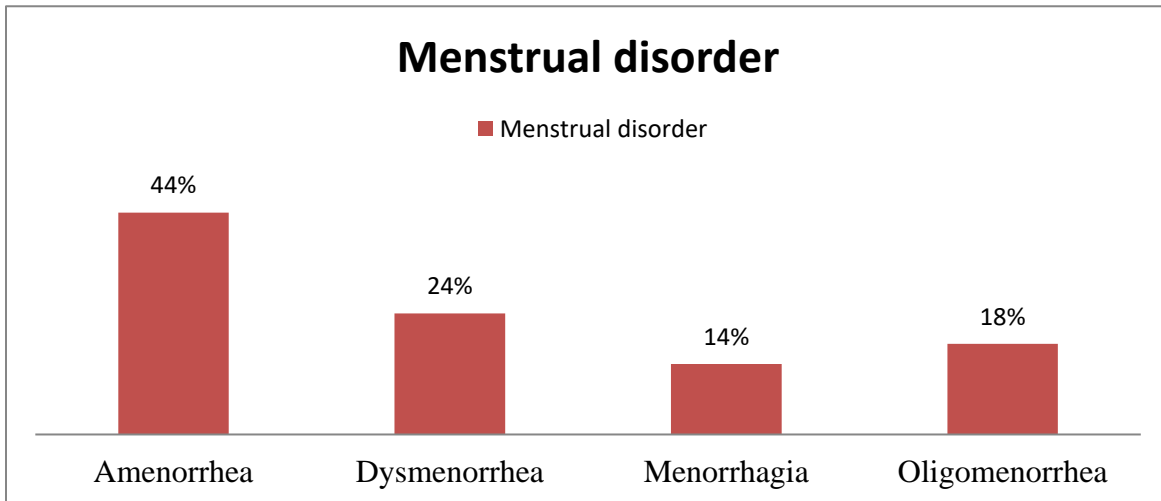


Figure (1): Bar graph representing Menstrual disorder for the studied women:

Table (4): Distribution of obstetric history for the studied women (no=100).

| Items | Studied Women (no = 100) | |
|-----------------------|--------------------------|----|
| | No | % |
| Gravidity: | | |
| • 1-3 | 50 | 50 |
| • 4-5 | 42 | 42 |
| • >5 | 8 | 8 |
| Mean ±SD | 3.44±1.506 | |
| Parity: | | |
| • 1-3 | 62 | 62 |
| • 4-5 | 38 | 38 |
| Mean ±SD | 3.16±1.261 | |
| Nulliparous: | 2 | 2 |
| Multiparty: | 68 | 68 |
| Abortion: | | |
| • 1 | 24 | 24 |
| • 2 | 2 | 2 |
| Stillbirth | 10 | 10 |
| Newborn death: | 20 | 20 |

| Complication related to previous deliveries: | | |
|--|----|----|
| Fever | 6 | 6 |
| Headache | 4 | 4 |
| Hypotension | 8 | 8 |
| Diabetes Mellitus | 4 | 4 |
| Anemia | 26 | 26 |
| Hypertension | 16 | 16 |
| Infection | 34 | 34 |
| Vaginal Bleeding | 38 | 38 |
| Pre-eclampsia | 14 | 14 |
| Postpartum depression | 16 | 16 |

Table (5): Distribution of breast cancer history for the studied women (no=100).

| Items | The studied Women | |
|--|-------------------|-----|
| | No | % |
| Diagnosis: | | |
| • Left breast cancer. | 44 | 44 |
| • Right breast cancer | 56 | 56 |
| Time of onset of breast cancer (months): | | |
| • 1-12 | 90 | 90 |
| • 13-24 | 10 | 10 |
| Mean ±SD | 9.56±5.061 | |
| Signs and symptom of breast cancer: | | |
| • A lump in the breast that feels different from surrounding tissue. | 100 | 100 |
| • Change is the shape, size, or appearance of the breast. | 82 | 82 |
| • Discharge from the nipple. . | 56 | 56 |
| • Breast rash. | 62 | 62 |
| • Changes in the skin over the breast, for example, dimpling. | 86 | 86 |
| • Breast pain. | 72 | 72 |
| • Inverted or pulling-in of the nipple. | 42 | 42 |
| • Redness and pitting of the breast skin, resembling the skin of orange. | 62 | 62 |
| Type of breast cancer: | | |
| • Invasive ductal carcinoma. | 56 | 56 |
| • Invasive lobular carcinoma. | 22 | 22 |
| • Inflammatory breast cancer. | 4 | 4 |
| • Paget disease of breast cancer. | 0 | 0 |
| • Metaplastic breast cancer. | 8 | 8 |
| • Ductal carcinoma insitu (DCIS). | 4 | 4 |
| • Lobular carcinoma insitu. | 6 | 6 |
| Stage of breast cancer: | | |
| • First stage | 60 | 60 |
| • Second stage | 40 | 40 |
| Diagnostic tests: | | |
| • Physical examination | 98 | 98 |
| • Mammogram | 100 | 100 |
| • Complete blood count (CBC) | 100 | 100 |

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| | | |
|------------------------------------|-----|-----|
| • Ultrasound | 98 | 98 |
| • Magnetic resonance imaging (MRI) | 94 | 94 |
| • Breast biopsy | 100 | 100 |

Table (6): Distribution of the studied women regarding reproductive risk factors (no=100).

| Items | Studied Women (no = 100) | |
|--|--------------------------|----|
| | No | % |
| Age of menarche (years): | | |
| • <12 | 8 | 8 |
| • (12-14) | 84 | 84 |
| • >14 | 8 | 8 |
| Age at first pregnancy (years): | | |
| • No | 6 | 6 |
| • < 20 | 20 | 20 |
| • 20-30 | 50 | 50 |
| • >30 | 24 | 24 |
| Term pregnancy: | | |
| • No | 10 | 10 |
| • Yes | 90 | 90 |
| Abortion: | | |
| • No | 74 | 74 |
| • Yes | 26 | 26 |
| Living children: | | |
| • No | 14 | 14 |
| • Yes | 86 | 86 |
| Age at first birth (years): | | |
| • No | 6 | 6 |
| • <20 | 20 | 20 |
| • 20-30 | 50 | 50 |
| • >30 | 24 | 24 |
| Mode of breast feeding: | | |
| • No | 6 | 6 |
| • Natural | 18 | 18 |
| • Artificial | 46 | 46 |
| • Mixed | 30 | 30 |
| Weight: | | |
| • Normal | 22 | 22 |
| • Underweight | 6 | 6 |
| • Overweight | 72 | 72 |
| Menopause: | | |
| • Normal | 12 | 12 |
| • Early | 20 | 20 |
| • Late | 68 | 68 |
| Degree of consanguinity: | | |
| • First | 68 | 68 |
| • Second | 10 | 10 |
| • Third | 10 | 10 |
| • Fourth | 12 | 12 |

| | | |
|--|----|----|
| Are using postmenopausal hormone therapy: | | |
| • Yes | 78 | 78 |
| • No | 22 | 22 |
| If answer yes what the type of hormone (n= 78): | | |
| • Estrogen | 14 | 14 |
| • Progestin | 6 | 6 |
| • Mixed | 58 | 58 |

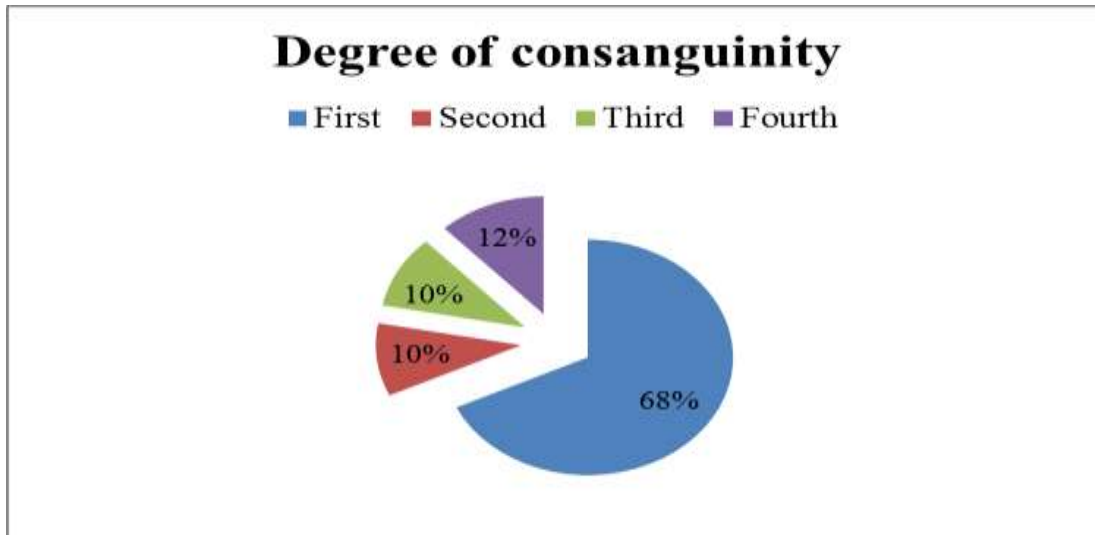


Figure (2): Pie graph representing degree of consanguinity for the studied women.

Table (7): Correlation between risk of breast cancer and demographic characteristic.

| Items | Breast Cancer | P - value |
|-----------------------------|-----------------------------|-----------|
| | Correlation coefficient (r) | |
| Age : | 0.211 | 0.03* |
| Marital status : | -0.465 | 0.01* |
| Level of education: | 0.709 | 0.648 |
| Occupational status: | -0.65 | 0.522 |

*: Significant at $P \leq 0.05$

Table (8): Correlation between risk of breast cancer, obstetric history, and type of contraceptive .

| Items | Breast Cancer | P - value |
|---------------------------------|-----------------------------|-----------|
| | Correlation coefficient (r) | |
| • Gravidity: | -0.642 | 0.04* |
| • Parity: | -0.853 | 0.124 |
| • Menstrual cycles | 0.712 | 0.775 |
| • Irregularity of menses | -0.278 | 0.381 |
| • Multi-para | -0.65 | 0.522 |
| • Nullipara | -0.161 | 0.109 |

| | | |
|--|--------|-------|
| • Abortion | -0.233 | 0.02* |
| • Duration of contraceptive methods | 0.062 | 0.547 |
| • Type of contraceptive | 0.214 | 0.175 |

*: Significant at $P \leq 0.05$

Table (9): Correlation between risk of breast cancer, and reproductive factors.

| Items | Breast Cancer | P – value |
|---|-----------------------------|-----------|
| | Correlation coefficient (r) | |
| • Age of menarche | 0.107 | 0.004* |
| • Age at first pregnancy | 0.012 | 0.001* |
| • Term pregnancy | -0.027 | 0.531 |
| • Abortion | -0.026 | 0.002* |
| • Living children | -0.009 | 0.518 |
| • Age at first birth | 0.012 | 0.001* |
| • Mode of breast feeding | -0.047 | 0.001* |
| • Weight | 0.204 | 0.04* |
| • Menopause | 0.024 | 0.01* |
| • Degree of consanguinity | 0.107 | 0.288 |
| • Postmenopausal hormone therapy | -0.179 | 0.522 |

*: Significant at $P \leq 0.05$

Discussion :

Breast cancer (BC) is the most prevalent cancer in women and the leading cause of women's cancer-related deaths and morbidity worldwide. Several reproductive factors have been shown to be associated with risk of breast cancer. Identifying these risk factors plays a significant role in primordial, primary, and secondary prevention. Breast cancer incidence varies widely among different populations globally (**Khoramdad et al., 2022**). Therefore, the aim of this study was to assess the relationship between reproductive factors and risk of breast cancer among pre-menopausal women.

Regarding demographic data of the studied women, the current study revealed that the studied women' age ranged from 45-50 years old with mean \pm SD = 47.64 \pm 1.90 years. This may be attributed to the fact that Breast cancer mainly occurs in middle-aged and older women and a small number of women diagnosed with breast cancer are younger than 45 years old. This result was supported by **Baglia et al., (2019)** who studied Reproductive and menopausal factors and risk of second primary breast cancer after in situ breast carcinoma and reported that most of the studied women were less than 50 years old. On the other hand, a study conducted by **Romieu et al., (2021)** to assess Reproductive factors and risk of breast cancer in Black South African women and reported that the median age of the studied women was 54 years.

Concerning marital status, the present study results showed that more than three fifths of the studied women were married, while minority of them were single. These results were in accordance with **El Sharif & Khatib, (2021)** who studied reproductive factors and breast cancer risk in Palestine and showed that the highest percentage of the studied women was married. In the same line, a study adopted by **Elshami et al., (2022)** entitled "Awareness of Palestinian Women about Breast Cancer Risk Factors" and found that more than three fifths of the studied women were married.

As regard educational level, the current study demonstrated that more than two thirds of the studied women were illiterate, while less than one tenth of them were university educated. Conversely, **Alsolami et al., (2019)** who



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carried out a study about determinants of breast cancer in Saudi women from Makkah region and found that the largest proportion of the studied women had primary education. Also, a study performed by **Alsareii et al., (2020)** about Awareness of breast cancer among female students and faculty from Najran University, Najran, Saudi Arabia, found that more than half of the studied women had bachelor.

Regarding occupational status, the results of the current study indicated that the majority of the women under investigation were housewives, with less than one fifth of them being employed. This aligns with the findings of a study conducted by **Tolessa et al. (2021)** titled "Risk factors associated with breast cancer among women in Addis Ababa, Ethiopia," which also reported that a significant proportion of the studied women were housewives. In contrast, a study conducted by **Abeje et al. (2019)** aimed at identifying factors associated with breast cancer screening awareness and practices among women in Addis Ababa reported a different trend. According to their findings, the majority of the women in their study were employed.

Concerning the medical history of the studied women, the present study revealed a prevalent occurrence of anemia among the majority, with over half of them also experiencing diabetes mellitus. These findings align with a study conducted by **Misganaw et al. (2023)** on mortality rates and predictors among breast cancer patients, which noted a high incidence of anemia in the studied women. Furthermore, the current research indicated that less than one in ten of the participants had a history of heart and renal diseases, while just over a quarter reported chronic hypertension. Conversely, a study conducted by **Shita et al. (2023)** in South Ethiopia, focusing on breast cancer mortality and predictors, reported a contrasting result, stating that most of their participants did not exhibit any co-morbidities.

Considering family history of the studied women, the present study results clarified that half of them had a family history of breast cancer, about two thirds of them had family history of hypertension and more than half of them had family history of diabetes mellitus, while only less than one fifth of them had family history of renal disease, heart disease and congenital anomaly. In the same line with a study carried out by **Hassen et al., (2022)** who studied Association of risk factors and breast cancer among women treated at Tikur Anbessa Specialized Hospital and reported that most of the studied sample had family history of diabetes and/or hypertension. In contrast, **Figueroa et al., (2020)** who conducted a study to assess Reproductive factors and risk of breast cancer by tumor subtypes among Ghanaian women and showed that most of the studied women had no family history of breast cancer.

Regarding occupational status, the results of the current study indicated that the majority of the studied women were housewives, with less than one fifth of them being employed. This aligns with the findings of a study conducted by **Tolessa et al. (2021)** titled "Risk factors associated with breast cancer among women in Addis Ababa, Ethiopia," which also reported that a significant proportion of the studied women were housewives. In contrast, a study conducted by **Abeje et al. (2019)** aimed at identifying factors associated with breast cancer screening awareness and practices among women in Addis Ababa reported a different trend. According to their findings, the majority of the women in their study were employed.

As well, the current study demonstrated that more than two thirds of the studied women had a regular menstrual cycle with moderate amount of bleeding. Regarding menstrual disorder, more than two fifths of them had amenorrhea, while less than one fifth of them had menorrhagia. Likewise, **Wang et al., (2020)** who studied reproductive risk factors associated with breast cancer molecular subtypes among young women in Northern China and stated that the largest proportion of the studied women had regular menstruation with moderate amount of bleeding.

Regarding the obstetric history of the studied women, the current study revealed that half of them had 1-3 previous pregnancies, with less than half experiencing more than 5 pregnancies. In terms of parity, more than three-fifths had 1-3 deliveries, while more than one-third had 4-5 deliveries. Additionally, less than one-tenth were nulliparous, and more than two-thirds had multiparity. In alignment with these findings, a study conducted by Liu et al. (2019) titled "Reproductive and lifestyle factors related to breast cancer among Japanese women" reported a similar trend, where the largest proportion of studied women had multiparity and specifically had 2 births. However,



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these results contrast with those of a study by Jia et al. (2023) investigating the causal effect of reproductive factors on breast cancer, which found that the majority of studied women had 3-4 previous pregnancies.

Regarding complications related to previous deliveries, more than one-third of the studied women experienced vaginal bleeding, while less than one-tenth reported having a fever. These findings differ from a study conducted by Minami et al. (2019), which investigated reproductive history and breast cancer survival and found that the largest proportion of studied women had not experienced previous complications related to labor.

Concerning family planning history among the studied women, the current study revealed that two-thirds were using contraceptive pills, and less than one-third were using intrauterine devices (IUDs). Regarding the duration of contraceptive use, more than two-thirds used it for 1-3 years, while less than one-tenth used it for more than five years. These results align with the findings of Ntirenganya et al. (2021), who conducted a study to evaluate premenopausal breast cancer risk factors and associations with molecular subtypes, reporting that more than half of the studied women used contraceptive pills for more than one year.

Moreover, the present study illustrated that most of the studied women had weight gain complication related to using the contraceptive, nearly half of them had pregnancy while using, and less than one third of them had vaginal bleeding, while minority of them had infection. This result was inconsistent with a study conducted by **Hamdi-Cherif et al., (2020)** to assess Socio demographic and reproductive risk factors for breast cancer. They reported that the highest percentage of participating women had not complication of using contraceptive methods.

Pertaining breast cancer history for the studied women, the current study reflected that, more than half of the studied women suffered from right breast cancer and more than two fifths of them had left cancer. Most of them were diagnosed 1 to 12 months ago, while only one tenth of them were diagnosed 13 to 24 months ago. This result was partially in agreement with **Gebretsadik et al., (2021)** whose study was about epidemiological trends of breast cancer in southern Ethiopia and clarified that the duration of diagnosis was 1 – 12 months among most of the studied women, while more than half of them had right side breast cancer.

In addition, the current study showed that more than half of the studied women had Invasive ductal carcinoma, while minority of them diagnosed with inflammatory breast cancer and ductal carcinoma insitu. Regarding diagnostic test, all of them had mammogram, complete blood count, and breast biopsy. Likewise, a study conducted by **Shiferaw et al., (2020)** to assess incidence and predictors of recurrence among breast cancer patients in Black lion specialized hospital adult oncology unit, Addis Ababa and found that the largest proportion of the studied women had invasive ductal carcinoma. Also, **Misganaw et al., (2023)** who study affirmed that most of the studied women had invasive ductal carcinoma and they diagnosed by mammogram and breast biopsy.

Regarding breast cancer treatment of the studied women, the present study portrayed that vast majority of them received chemotherapy and most of them had hormonal therapy. Concerning type of surgery, nearly half of them had total mastectomy, while minority of them had a conservative surgery. This result was supported by **Tesfaw et al., (2020)**, who studied Assessing the incidence, epidemiological description, and associated risk factors of breast cancer in western Amhara and declared that most of the studied women received chemotherapy and had total mastectomy. On the other hand, **Areri et al., (2019)** who adopted a study about survival status and predictors of mortality among Breast Cancer patients in Adult Oncology Unit at Black Lion Specialized Hospital and found that surgery associated with radiotherapy was the common mode of treatment among most of the studied women and about two third of them were reported receiving hormone therapy.

According to the studied women' reproductive factors, the current study displayed that most of the studied women had their menarche from 12 to 14 years old and half of them had their first pregnancy at age from 20 to 30 years old, while one fifth of them were underage of 20 years old. Correspondingly, a study done by **Mahmoud et al., (2023)** who reported that, the most of studied subjects had menarche at age between 12 to 14 years old. Also, **Sofi et al., (2019)** who carried out a study to investigate epidemiological characteristics of breast cancer patients attending a tertiary health-care institute in the National Capital Territory of India and affirmed that high percentage of the studied women their age at first childbirth was less than 30 years old.

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Furthermore, the present study reflected that more than two thirds of the studied women were overweight, while more than one fifth of them had a normal weight. Concerning degree of consanguinity, more than two thirds of them had first degree consanguinity, while one tenth of them had second and third degree. These results were compatible with **Duche et al., (2021)**, who carried out a study entitled "Identifying risk factors of breast cancer among women attending selected hospitals of addis ababa city" and stated that most of the studied women had first degree consanguinity. These findings were contradicted with **Bui et al., (2022)** who conducted a study entitled "Menstrual and reproductive factors in association with breast cancer risk in Vietnamese women" and reported that most of the studied women were within normal body weight.

As regard correlation between risk of breast cancer and demographic characteristic of the studied women, the current study represents that there was a highly statistically significant correlation between women' risk of breast cancer, and their age and marital status, while there was no statistically significant correlation between women' risk of breast cancer and their level of education and occupational status. This can be interpreted as the risk for breast cancer increases with age. This might duo to the fact that as we age, there is more time for damage in our cells to build up, making cancer more likely. In addition, unmarried women are more likely to have breast cancer than married women.

This result was congruent with a study carried out by **Arafat et al., (2021)** who adopted a study to assess breast cancer risk from modifiable and non-modifiable risk factors among Palestinian women and confirmed that there was association between age and the risk of breast cancer. Also, a study performed by **Hassen et al., (2022)** who stated The odd of breast cancer was higher among women aged between 40 and 49 years. Correspondingly, a study conducted by **Li et al., (2020)** entitled "Does marital status correlate with the female breast cancer risk?" and declared that marital status may correlate with the risk of developing female breast cancer. Likewise, **Yuan et al., (2021)** stated in research about the impact of marital status on stage at diagnosis and survival of female patients with breast and gynecologic cancers that married women have a higher rate of breast cancer screening than the unmarried.

In relation to correlation between risk of breast cancer, obstetric history and type of contraceptive, the present study demonstrated that, there was a highly statistically significant correlation between women' risk of breast cancer and their gravidity and abortion, while there was no statistically significant correlation with parity, menstrual cycle, regularity of menses, multipara, nulliparous, duration of contraceptive methods and type of contraceptive. This can be explained as women with multigravida and without experience of abortion seem to decrease risk of breast cancer. This may be due to the fact that prolonged endogenous and exogenous estrogen exposure increases the risk of breast cancer. In the same field, a study conducted by **Hamdi-Cherif et al., (2020)** who mentioned that there was association between risk of breast cancer and abortions, this association possibly related to variations in exposure to estrogens throughout life. Similarly, these findings were in harmony with a study performed by **Bui et al., (2022)**, declared that reduced numbers of live births being associated with an increased risk of breast cancer. On contrary, **Figueroa et al., (2020)** whose study found that there was association between risk of breast cancer and parity, hormonal contraceptives, and irregular menstruation. Also, **Manouchehri et al., (2022)** who studied menstrual and reproductive factors and risk of breast cancer in Iranian female population and stated that there was no association between the history of abortion with an increased risk of breast cancer.

Considering correlation between risk of breast cancer and the studied women' reproductive factors, the present study showed that there was a highly statistically significant correlation between women' risk of breast cancer and age of menarche, age of first pregnancy, abortion, age at first birth, mode of breast feeding, weight and menopause, while there was no statistically significant correlation with term pregnancy, living children, degree of consanguinity, and post-menopausal hormone. This can be interpreted as the high occurrence of breast cancer among women can be concurrent with numerous factors, including having older age of menarche, older age at first pregnancy and first birth, breastfeeding, overweight and menopause. This ultimately increases their exposure to estrogens and thus subsequently, upsurge the risk of developing breast cancer. These findings were compatible with **Vishwakarma et al., (2019)** who carried out a study about reproductive factors and breast cancer risk and affirmed that there was statistically significant association between breast cancer and the following reproductive factors: never breastfeed, menopausal age >50 years, menarche age 25 years and obesity. Likewise, these results were in agreement with a study adopted by **Xie et al., (2022)** stated that compared with women who first gave birth after age 30 years, earlier

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age at first birth decreased the risk of breast cancer and compared with those who had an average breastfed/birth period of more than 2 years, those with an average period less than 6 months had an elevated risk of breast cancer.

These findings partially agreed with **Baglia et al., (2019)** who stated that older age at menarche was associated with risk of breast cancer among women, while there were no associations observed for other reproductive or menopausal factors evaluated. Conversely, **Manouchehri et al., (2022)** who illustrated that menarche age and increased risk of breast cancer, nulliparity, and breastfeeding history were not associated with breast cancer risk.

Regarding correlation between risk of breast cancer and medical history of the studied women, the present study declared that there was a highly statistically significant correlation between women' risk of breast cancer, and past medical history of DM, while there was no statistically significant correlation with their past medical history of hypertension, heart disease, and renal disease. This can be explained as women with diabetes are at increased risk for cancer. This may be because abnormal insulin levels that affect cancer risk. Insulin has been shown to have mitogenic effect upon breast cancer cells in vitro through several mechanisms. It can act synergistically with estradiol and stimulate the proliferation of the cell line. These results were in accordance with those of **Arafat et al., (2021)**, who reported that, there was a statistically significant diabetes mellitus (DM) had the highest odds ratio of breast cancer. This result was supported by **Jia et al., (2023)** who reported that there was between risk of breast cancer and heart diseases, also no significant correlation was found with renal diseases. On the other hand, these results disagreed with **Seretis et al., (2019)** who studied association between blood pressure and risk of cancer development and suggested that hypertension was associated with a higher risk of breast cancer. The suggestive mechanisms to explain this association involve blocking apoptosis, adipose tissue-related hypoxia, and chronic inflammation promoting reactive oxygen species formation.

Conclusion:

In light of the present study, it can be concluded that the research investigated the relationship between various reproductive factors and the risk of premenopausal breast cancer, while considering the participants' ages. The results demonstrated specific associations with factors such as age, marital status, gravidity, abortion, age of menarche, age of first pregnancy, age at first birth, mode of breastfeeding, body weight, menopausal status, and history of diabetes mellitus. In essence, the study successfully addressed the research question concerning the relationships between reproductive factors and the risk of breast cancer among premenopausal women.

Recommendations:

Based on the findings of the study results, the following recommendations were advocated:

1. Implementing education programs to enhance awareness of premenopausal women regarding reproductive risk factors associated with breast cancer .
2. Since there are varieties of culture, food choice, feeding habit, physical activities, and other risk factors,

Further studies:

Conducting research on a larger scale and across multiple centers can provide more robust and reliable conclusions by capturing a diverse range of demographic, geographic, and healthcare contexts.

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