**Association of reproductive factors with triple-negative breast cancer and hormone receptor–positive breast cancer among Bangladeshi women**

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**ABSTRACT**

**Objective**

Despite Bangladesh's high breast cancer prevalence (19.3 cases per 100,000 individuals), data are scarce regarding the reproductive epidemiology of breast cancer in Bangladesh. We investigated whether reproductive factors are associated with hormone receptor–positive breast cancer (Hr+BC) and triple-negative breast cancer (TNBC) in Bangladeshi women.

**Methods and Analysis**

In a tertiary hospital-based setting, we surveyed 1000 adult Bangladeshi females aged 18 or older. Of which 250 had TNBC, 250 had Hr+BC, and the remaining 500 were non-cancer individuals. Propensity score matching (PSM) was carried out to match the age and age of menarche of the potential 500 healthy individual with 250 TNBC and 250 Hr+BC individuals in separate estimates. The presence of TNBC or Hr+BC was the outcome variable, and the participants’ previous histopathology report confirmed it. We collected participants; detailed reproductive characteristics and demographics through a structured questionnaire. Those significant variables in the bivariate model were finally included in the adjusted multivariate multinomial logistic regression.

**Results**

The mean ages of participants in the Hr+BC, TNBC, and healthy groups were 44.96, 42.74 and 39.31 years, respectively. Adjusted binary multivariate logistic regression suggested that women living in rural areas with increased number of abortions, experiencing irregular menstruation, and consumption of hormonal contraceptives increased the risk for Hr+BC and TNBC compared to the healthy individuals. However, the magnitude of the risk varies across the types of breast cancer. One year increase in the age of menarche significantly increased the risk for Hr+BC by 1.71 times; however, it decreased the risk for TNBC by 30%.

**Conclusion**

Our findings imply that women's reproductive factors play a pivotal role in developing Hr+BC and TNBC; however, the degree of risk differs between the different types of breast cancer.

**Keywords:** Breast cancer, Bangladesh, Reproductive factors, Hospital-based study.

**INTRODUCTION**

Breast cancer is the leading cause of cancer-related death in women worldwide and in Bangladesh (1). The rate of breast cancer occurrence in Bangladesh is 22.5 cases per 100,000 females of all ages per year and among females aged 15 to 44 years, breast cancer has a higher incident rate of 19.5 cases per 100,000 women, than any other type of cancer (2). Among the most aggressive types of breast cancer is triple-negative breast cancer (TNBC), which is immunohistochemically negative for estrogen receptors, progesterone receptors, and HER2 receptors and has a high metastatic potential, relapse tendency, and poor prognosis (3). There is a racial and geographic disparity in the incidence of TNBC, which accounts for 10% to 25% of all cases of invasive breast cancer (4). A luminal A-like subtype (ER-positive, PR-positive, and HER2-negative, low Ki67) accounts for 62%-67% of all invasive cases of breast cancer (5); whereas a luminal B–like (ER-positive and/or PR-positive, HER2-negative, high Ki67) subtype only accounts for 11.2% (6). Younger and premenopausal women are more likely than older and postmenopausal women to develop TNBC. TNBC occurs more often in Asian and African American women than in women of other races (7–9). Patients with TNBC have a 5-year survival rate at least 10% lower than that of women with the luminal A–like type. Furthermore, treatment options for TNBC are limited to chemotherapy, PARP inhibitor therapy, and immunotherapy (10).

Breast cancer incidence is increasing in Asia, and there is evidence that urbanization is one of the key factors contributing to the increase (11,12). Bangladesh is one of South Asia's most rapidly urbanizing countries, with the proportion of the country classified as urban increasing by 1.69% per year. In previous studies in the United States and China, modified lifestyles and altered reproductive behaviors due to urbanization were shown to be directly related to a higher incidence of breast cancer (13,14). Modified lifestyles and familial histories have also been shown to impact survival and other breast cancer outcomes in developing countries (15).

A literature review showed that alterations in reproductive factors like age at menarche, age at menopause, parity, breastfeeding, age at first marriage, age at first birth, use of hormonal contraceptives, and use of hormone replacement therapy are some of the primary reasons associated with the breast cancer incidence (16). A number of relationships between reproductive risk factors and the risk of breast cancer have been established. However, the reproductive patterns and breast cancer risk are different for TNBC and HR-positive breast cancer (Hr+BC). For example, nulliparity is associated with decreased risk of TNBC but increased Hr+BC (17). Additionally, earlier age at first full-term pregnancy and earlier age at menopause is associated with an increased risk of TNBC (18). A history of breastfeeding for more than 36 months is associated with a lower risk of TNBC (18). Women who use oral contraceptives have a greater risk of TNBC than those who do not (19). But some other studies have shown that oral contraceptives are associated with reduced risk of TNBC since reproductive factors vary with the types of breast cancer (19–21). Reproductive risk factors for TNBC were unclear in earlier studies, partly because most published studies had lower sample sizes (9).

Breast cancer mortality remained a significant hidden burden in Bangladesh despite recent gains in screening programs and treatment facilities, accounting for 69% of deaths among women in the nation (1). Although the relationships between female reproductive factors and female breast cancer have been well documented in earlier studies, data are scarce in Bangladesh. Therefore, we investigated whether TNBC and Hr+BC are associated with female reproductive factors among Bangladeshi women.

**MATERIALS AND METHODS**

**Carers involvement**

This study's concept and execution included input from caregivers (medication officers serving both outpatients and inpatients). They were first invited to attend the initial brainstorming session on the study topic, and among those who attended that session were asked if they would voluntarily participate in the study design. The hospital medical officers took part in a discussion on formulating the research question, anticipating possible outcomes, and recruiting of study participants. The published copy of the study will be shared with all outpatients and inpatients medical officers working in the study site hospital.

***Study design and population***

We conducted a hospital-based cross-sectional comparative survey among 1000 Bangladeshi women aged 18 years or older. In the study, we recruited 250 women with TNBC, 250 women with Hr+BC, and 500 women who were generally healthy with no known cancer or existing disease. Participants were recruited between 2019 and 2020 from the outpatient department of medical oncology of the National Institute of Cancer Research & Hospital (NICRH), a tertiary care center in Dhaka, Bangladesh. NICRH is a government-funded 500-bed tertiary dedicated to multidisciplinary cancer patient care and research; it treats patients across all disease stages. The outpatient medical oncology department is estimated to see 400 patients per day.

***Data collection tools and techniques***

Data were collected by six trained interviewers (outpatient medical officers) through a structured questionnaire. All interviewers were registered physicians with experience in oncology and were trained for data collection by the principal investigator (RI). At first, interviewers evaluated the previous histopathology reports for incoming patients aged 18 years or older to confirm whether they had TNBC or Hr+BC. Patients with these breast cancer types were asked if they were willing to participate in our study. Patients who gave verbal consent were then given the written informed consent form and asked to read it carefully. If they agreed to participate, they were requested to sign the form to indicate their consent. For patients who could not read, interviewers read the consent form aloud. Regardless of the ability to read and sign, a patient attendant was present during the informed consent process. Each patient was interviewed separately and individually in the outpatient clinical room by a female outpatient medical officer since the questionnaire had sensitive questions regarding female reproductive health.

For the healthy-individuals group, the medical officers enrolled female attendants of hospital patients from any hospital department. Similar informed consent and interview procedures were followed for this group, except that interviews were conducted in the inpatient medical oncology department.

***Variables assessed***

The outcome variable of the study was the presence of TNBC or Hr+BC. We relied on the previous histopathology report signed by a registered medical histopathologist; however, we did not differentiate between recent and earlier diagnoses. TNBC was defined as the absence of ER, PR, and Her-2 in the immunohistochemistry (IHC) report. In contrast, Hr+BC was defined as the presence of ER, PR, or Her-2 in the IHC report. Our study medical officer did not participate in diagnosing the patients’ breast cancer.

Regarding the reproductive factors of the study participants, we collected their age at first marriage, age at first birth, parity, number of abortions, the time between menarche and first birth (in full years), and time between menarche and first birth (in full years). In addition, we collected demographic variables, including age, height, weight, residence (urban or rural), and years of education (0-5; 6-12; or >12 years). We used the standard method to calculate body mass index (BMI) (weight in kg divided by the square of the height in meters) (22), and we used the World Health Organization cut-offs to categorize BMI (underweight, <18.5 kg/m2; normal, 18.5-24.9 kg/m2; pre-obese, 25-29.9 kg/m2; and obese, ≥ 30 kg/m2) (23). Additionally, the study collected several reproductive categorical variables, including current menstrual status (premenopausal or post-menopausal), menstrual regularity among premenopausal women (regular or irregular), history of continuous breastfeeding for at least 6 months (yes or no), type of contraceptive use (hormonal or non-hormonal), and mode of delivery (vaginal or caesarian), and continuous variables, including

***Statistical analysis***

We used STATA version 14 to run two separate propensity score matching models to match the 250 participants with TNBC and the 250 participants with Hr+BC to the sampling frame of 500 healthy individuals. Two sets of propensity score matching (PSM) was carried by age and age at menarche, one PSM between 250 Hr+BC patients and 500 healthy individuals, and another PSM set was between 250 TNBC and 500 healthy individuals. It revealed that 714 (n=243 Hr+BC and n=471 healthy) matched participants out of the total of 750 participants in the Hr+BC PSM set and 715 (n=244 TNBC and n=471 healthy). Descriptive and inferential statistics were run on the matched participants. The continuous measures are presented as means with standard errors, and the group differences [(Hr+BC vs healthy) and (TNBC vs. healthy)] were determined using independent Student’s t-test. Normality was considered based on Skewness value between − 3 and + 3 (Griffin & Steinbrecher, 2013). Categorical variables are presented as numbers and percentages by groups. We used the chi-square test to measure the association among categorical variables. Finally, we ran multivariate binary logistic regression to calculate the likelihood of suffering from TNBC or Hr+BC compared to healthy individuals (as a reference category) after adjustment for the potential reproductive factors. Collinearity statistics were run to determine possible multicollinearity among the continuous variables before they were included in the final model. The age at first birth and the gap between menarche and first birth had high variance inflation factors (7.11 and 7.94, respectively); therefore, there were removed from the final model. Additionally, we excluded age at first marriage from the final model because participants’ mean age by groups was not meaningfully early years of age. Data analyses were carried out using SPSS software, version 28.0.1.1. Both bivariate and multivariate analyses were done in jamovi, version 2.0 (jamovi project, 2021). The significance cut-off was set at p <0.05.

**RESULTS**

Table 1 presents the demographic and reproductive characteristics of the study participants in the Hr+BC, TNBC, and healthy groups. The mean ±SEM age was 44.96±0.65 years in the Hr+BC group, 42.74±0.65 years in the TNBC group, and 39.31±0.55 years in the healthy group. Compared to the healthy patients, patients with Hr+BC and TNBC were older, were older at first marriage, were older at first birth, and had had more abortions. In addition, both demographic and reproductive categorical factors were found to be associated with Hr+BC and TNBC. Compared to the healthy patients, patients with Hr+BC and TNBC were more likely to be postmenopausal, have irregular menstruation, have had vaginal delivery, and have breastfed for more than 6 months, and to have used hormonal contraceptives.

Table 2 presents the association of various reproductive factors with the risk of having Hr+BC or TNBC. The adjusted model showed that delayed menarche was associated with an increased risk of Hr+BC (odds ratio [OR] 1.71) but decreased risk of TNBC (OR 0.70). A longer time between first marriage and first birth (OR, 1.4), irregular menstruation (OR 2.83), and use of hormonal contraceptives (OR 5.68) were associated with increased risk of Hr+BC; pre-obesity was associated with decreased risk of Hr+BC (OR 0.36). Irregular menstruation (OR 4.30) and use of hormonal contraceptives (OR 8.54) were also associated with a higher risk of TNBC. Higher number of abortions was associated with increased risk of TNBC (OR 2.27) but not Hr+BC. For both Hr+BC and TNBC, living in a rural area of Bangladesh was associated with increased risk of disease (Hr+BC: OR 4.81; TNBC: OR 16.77).

**DISCUSSION**

In the study reported here, we investigated the relationships between female reproductive factors and the risk of Hr+BC and TNBC among adult Bangladeshi women. We found that delayed menarche was associated with increased risk of Hr+BC; however, we noted reduced risk of TNBC. We also found that rural residence, experiencing irregular menstruation, and using hormonal contraceptives were risk factors for both Hr+BC and TNBC. In addition, longer time between first marriage and first birth was associated with higher risk of Hr+BC, and abortion was associated with higher risk of TNBC.

Our finding that late menarche was associated with a reduced risk of TNBC is consistent with findings from an epidemiological study of African American women, which showed that the risk of ER-negative breast cancer was reduced with later age at menarche (21). One of the potential reason could be the breast tissue maturation that begins at menarche and continues at a constant rate until the first birth (24). According to experimental rodent research, ductal cells are vulnerable to carcinogens and DNA damage prior to terminal differentiation in the breast ducts, which is considered to occur during a full-term pregnancy (25). There is some evidence that ER-positive and ER-negative tumors may both originate from a standard luminal progenitor cell population, which then differentiates into ER-positive and ER-negative cells with the pattern of differentiation possibly influenced by the hormonal environment during critical windows of vulnerability (26,27). This could be a reasonable explanation for why the impact of the timing of menarche appears to be different for different types of breast cancer. Contrary, several prospective studies showed an inverse relationship between age at menarche and risk of Hr+BC (28–30). Our finding of significantly higher risk of Hr+BC among women with a longer time between first marriage and first birth is in line with earlier findings. A woman whose first birth happens at an early age is protected from developing breast cancer, and a woman whose hormonal status produces a delay in becoming pregnant has an increased risk of breast cancer (31–34).

Our finding indicated that those who used hormonal contraceptive are at higher risk for Hr+BC or TNBC. These findings are in line with earlier evidence that use of hormonal contraceptive methods, either pills or another form of hormonal intervention, increases the risk of developing breast cancer because of prolonged exposure to estrogen (35–38). Other studies supported this pathway because they showed that pregnancy lowers the long-term risk of developing breast cancer (39). Increased breast cancer risk has previously been shown to be associated with late marriage, a late first birth, and a longer interval between pregnancies (40). Greater risk of hormonally sensitive breast cancer is linked to a longer time between menarche and the first pregnancy in white women. In a case-control study from the United States, women who had at least 21 years between menarche and their first child had a 1.45-times higher risk of breast cancer than those who had only 10 years or less between these two milestones. (41). Late pregnancy was a substantial and independent risk factor for developing breast cancer in a meta-analysis of eight population-based studies of breast cancer and reproductive factors in the Nordic nations, which included a total of 5568 cases (42). An unanticipated finding of our study was that use of hormonal contraceptives was associated with a much greater increase in the risk of TNBC (OR 8.54) than in the risk of Hr+BC (5.68). These results may be due to TNBC participants’ having used oral combined hormonal contraceptives. Previous research found that using oral combined hormonal contraceptives increased the risk of breast cancer by 0-60% (43).

We did not find a relationship between parity and risk of Hr+BC or TNBC; however, prior evidence suggested a lower risk of breast cancer for parous women than for nulliparous women (44). The relationship between breast cancer and parity is not straightforward. After the first pregnancy, the chance of having breast cancer increases, although it drops after 10 to 15 years (45). Furthermore, prior research suggested that only women over 40 years of age may benefit from parity's preventive effects (44). We speculate that other reproductive factors may have also played a role in our cohorts. We found that women who experienced irregular menstrual cycles had a higher chance of developing Hr+BC or TNBC, and the odds were greater for TNBC. An earlier study showed that women with irregular cycles had a higher risk of developing postmenopausal breast cancer (46). In contrast, one study found that a longer menstrual cycle was protective against breast cancer (47).

We found that abortion was associated with increased risk of TNBC. Two ecological epidemiological studies, the 1989 Remennick study and the 2007 Carroll study found an association between induced abortion and breast cancer (48,49). However, a recent systemic review and meta-analysis comprises of 14 articles covering cohort and case-control studies concluded that no association between abortion (induced or spontaneous) and breast cancer among the nulliparous women (Tong et al., 2020). However, these studies on abortion and breast cancer are retrospective in nature and threat to recall bias because women with breast cancer were, on average, more likely to disclose past abortions than other women.

In our study, we found that TNBC patients was younger (by their mean age) than the Hr+BC patients, and women living in rural areas. Most rural women, particularly those without formal education, are reluctant to seek health care (51). Proper education of patients is a key factor in prevention and early detection of breast cancer (52–54). There are significant barriers to breast cancer research and management due to a lack of formal education and awareness (55). As TNBC is the most aggressive subtype of breast cancer and associated with a poor prognosis regardless of stage, only early detection and prevention can bring a change in overall survival of patients with TNBC. Special attention to women's education on breast cancer risk factors, self-examination practices, national health programs, and availability of treatment options may facilitate early detection and aid in combating ignorance and misinformation about TNBC in Bangladesh.

Our results showed that rural residents are at risk for developing both Hr+BC and TNBC, which is in line with another study that additionally reported that rural residents had a higher risk of being diagnosed with later-stage breast cancer (56). However, the exact reason for the relationship between rural residence and breast cancer risk is not clear. As would be consistent with the results of the above-mentioned study, one possible explanation could be that rural Bangladeshi women were diagnosed with late-stage breast cancer; hence, sought treatment at the tertiary hospital. Since the study is based on tertiary hospital setting, it is likely that we captured more rural residents with Hr+BC and TNBC in our sample. This pattern would result in a relatively high proportion of rural residents among patients with breast cancer seen at our hospital. However, we did not have any evidence to support such explanation. While several studies indicated that changes in a woman's reproductive lifestyle due to rapid urbanization may be one of the major causes of breast cancer (57–59).

Like other studies, this study is not immune to limitations. We could not establish a causal relationship between reproductive factors and the development of Hr+BC and TNBC because of the cross-sectional data. We recommend exercising caution when interpreting the findings. Another limitation is recall bias, as we asked older women, including postmenopausal women, to recall their age at menarche, menopausal date, age at first marriage, age at first birth, number of abortions, number of years between menarche and first birth, and number of years between first marriage and first birth. We assumed that women with and without breast cancer would experience recall bias equally. This assumption is based on another Bangladeshi study (60). Additionally, the risk of nondifferential misclassification among the participants with Hr+BC and TNBC likely occurred as random since they were unaware of the potential risk factors for breast cancer. In addition, because the age at menarche is concentrated at 13 years, more densely in the Hr+BC groups than in the TNBC groups, it may introduce a nonprobability sampling bias and affect the results.

This study has several implications. First, it adds to our understanding of breast cancer epidemiology in Bangladesh. We did not find other studies that covered the association between reproductive factors and Hr+BC and TNBC. Second, the study findings will help public health professionals to design appropriate reproductive health education programs focusing on breast cancer screening and family planning, particularly among the rural residents. Third, the study sheds light on the important associations between the reproductive life of Bangladeshi women and their risk of breast cancer which may motivate future researchers to design prospective studies to establish causal inferences.

**CONCLUSION**

In Bangladeshi women, several reproductive health factors were significant predictors of Hr+BC and TNBC. All of these factors except for age at menarche and the regularity of menstrual cycles are modifiable. They can be improved through proper reproductive education, mainly focusing on family planning education.

**Declarations**

**Ethics approval and consent to participate:**

All experiments were performed in accordance with relevant guidelines and regulations following the Declaration of Helsinki.

Informed consent was obtained from all subjects and their legal guardian(s).

The study received ethical approval from the National Institute of Cancer Research and Hospital Ethics committee (Ref: NICHR/Ethics/2021/89).

**Consent for publication:** Not applicable

**Availability of data and material:** The datasets used and/or analysed during the current study available from the corresponding author on reasonable request.

**Competing interests:** Authors have no conflict of interest to disclose.

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**Authors' contributions:**

Muhammad Rafiqul Islam: Conceptualization, Data curation, Investigation, Methodology, Project administration, Validation, Visualization, Writing - original draft, Writing - review & editing

Hongxu Zhu: Data curation, Resources, Software, Formal analysis

Syeda Masuma Siddiqua: Investigation, Project administration, Resources, Supervision,

Syed Mohammad Ariful Islam: Data curation, Writing - review & editing

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Naoto T. Ueno: Investigation, Methodology, Resources, Supervision, Validation, Visualization, Writing - review & editing.

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Table 1: Participant characteristics.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Characteristic** | **Hormone receptor–positive breast cancer (n=243)** | **Healthy (n=471)** | **p\*** | **Triple-negative breast cancer (n=244)** | **Healthy (n=471)** | **p\*** |
|  | |  | |
| **Continuous variables, reported as mean (SEM)** | | | | | | |
| Age, years | 44.96 (0.65) | 39.31 (0.55) | <0.001 | 42.74 (0.65) | 39.31 (0.55) | <0.001 |
| Age at menarche, years | 13.03 (0.02) | 12.66 (0.50) | <0.001 | 12.06 (0.07) | 12.66 (0.50) | 0.759 |
| Age at first marriage, years | 18.59 (0.22) | 17.14 (0.23) | <0.001 | 17.49 (0.19) | 17.14 (0.23) | <0.001 |
| Age at first birth, years | 20.07 (0.35) | 17.63 (0.32) | <0.001 | 19.25 (0.26) | 17.63 (0.32) | <0.001 |
| Parity | 2.67 (0.08) | 2.18 (0.06) | 0.593 | 2.50 (0.07) | 2.18 (0.06) | 0.014 |
| Number of abortions | 0.35 (0.04) | 0.25 (0.02) | <0.001 | 0.45 (0.03) | 0.25 (0.02) | <0.001 |
| Time between menarche and first birth, years | 7.58 (0.24) | 6.28 (0.18) | 0.123 | 7.41 (0.21) | 6.28 (0.18) | <0.001 |
| Time between first marriage and first birth, years | 2.27 (0.11) | 1.84 (0.07) | 0.157 | 2.08 (0.09) | 1.84 (0.07) | 0.356 |
| **Categorical variables, reported as n (%)** | | | | | | |
| Residence |  |  |  |  |  |  |
| Rural | 149 (20.9) | 101 (14.1) | <0.001 | 185 (25.9) | 101 (14.1) | <0.001 |
| Urban | 94 (13.2) | 370 (51.8) | 58 (8.3) | 370 (51.7) |
| Years of education |  |  |  |  |  |  |
| 0-5 | 192 (26.9) | 87 (12.2) | <0.001 | 194 (27.1) | 87 (12.2) | <0.001 |
| 6-12 | 38 (5.3) | 247 (34.6) | 39 (5.5) | 247 (34.5) |
| >12 | 13 (1.8) | 137 (19.2) | 11 (1.5) | 137 (19.2) |
| Body mass index, kg/m2 |  |  |  |  |  |  |
| Underweight (<18.5) | 16 (2.2) | 15 (2.1) | <0.001 | 12 (1.7) | 15 (2.1) | <0.001 |
| Normal (18.5-24.9) | 93 (13.0) | 142 (19.9) | 103 (14.4) | 142 (19.9) |
| Pre-obese (25-29.9) | 91 (12.7) | 258 (36.1) | 93 (13.0) | 258 (36.1) |
| Obese (≥30) | 43 (6.0) | 56 (7.8) | 36 (5.0) | 56 (7.8) |
| Menstrual status |  |  |  |  |  |  |
| Premenopausal | 101 (14.1) | 311 (43.6) | <0.001 | 131 (18.3) | 311 (43.5) | 0.001 |
| Postmenopausal | 142 (19.9) | 160 (22.4) | 113 (15.8) | 160 (22.4) |
| Menstrual regularity |  |  |  |  |  |  |
| Regular | 162 (22.7) | 389 (54.6) | <0.001 | 170 (23.8) | 389 (54.5) | <0.001 |
| Irregular | 80 (11.2) | 82 (11.5) | 73 (10.2) | 82 (11.5) |
| Mode of delivery |  |  |  |  |  |  |
| Vaginal | 157 (28.0) | 240 (42.8) | <0.001 | 183 (30.8) | 240 (40.4) | <0.001 |
| Caesarian | 24 (4.3) | 140 (25.0) | 31 (5.2) | 140 (23.6) |
| History of breastfeeding for >6 months |  |  |  |  |  |  |
| No | 12 (1.8) | 36 (5.4) | <0.001 | 5 (0.7) | 36 (5.4) | <0.001 |
| Yes | 231 (34.5) | 390 (58.3) | 239 (35.7) | 390 (58.2) |
| Contraceptive use |  |  |  |  |  |  |
| Nonhormonal contraceptives | 8 (2.0) | 66 (16.7) | <0.001 | 3 (0.8) | 66 (16.8) | <0.001 |
| Hormonal contraceptives | 117 (29.5) | 205 (51.8) | 118 (30.1) | 205 (52.3) |

\*P values calculated with one-way ANOVA for continuous variables and χ2 test for categorical variables.

Table 2: Association of reproductive factors with types of breast cancer.

|  |  |  |
| --- | --- | --- |
| **Variables** | **Hormone receptor positive breast cancer** | **Triple negative breast cancer** |
| **OR (CI 95%)** | **OR (CI 95%)** |
| Age | 1.06 (1.02-1.10)\*\* | 1.02 (0.98-1.06) |
| Age of menarche (years) | 1.71 (1.19-2.44)\* | 0.70 (0.52-0.95)\* |
| Abortion | 1.30 (0.76-2.23) | 2.27 (01.30-3.98)\* |
| Parity | 0.96 (0.67-1.37) | 0.91 (0.60-1.37) |
| Time between first marriage and first birth (in full years) | 1.40 (1.10-1.78)\* | 1.15 (0.88-1.49) |
| **Residence** |  |  |
| Urban | Ref | Ref |
| Rural | 4.81 (2.55-9.03)\*\* | 16.77 (8.3-33.87)\*\* |
| **Body mass index (BMI)** |  |  |
| Normal (18.5- 24.9) | Ref | Ref |
| Underweight (<18.5) | 2.19 (0.43-11.18) | 1.06 (0.16-6.64) |
| Pre-Obesity (25-29.9) | 0.36 (0.18-0.72)\* | 0.65 (0.41-1.34) |
| Obese (≥30) | 0.78 (0.26-2.28) | 1.22 (0.36-4.07) |
| **Menstrual regularity** |  |  |
| Regular | Ref | Ref |
| Irregular | 2.83 (1.31-6.10)\* | 4.30 (1.87-9.42)\*\* |
| **Pattern of contraceptive use** |  |  |
| Non-hormonal contraceptives | Ref | Ref |
| Hormonal contraceptives | 5.68 (1.52-21.25)\* | 8.54 (1.81-40.14)\* |

\*p <0.05; \*\*p <0.001

Multivariate binary logistic regression with reference to healthy population.