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## **Review Article**

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## Risk Factors of Breast Cancer Among Western Algerian Women Under 40 years' old

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#### **Abstract**

**Background:** The frequency of patients developing Breast Cancer (BC) among all other types of cancers exceeds 35% in Western Algeria. The main objective here was to determine which risk factors were associated with this high frequency of BC occurrence in young adult women (<40 years old) in Western Algeria.

Methods: A BC case-control study matching with the woman age was conducted. The total number of participants was 484 women from Western Algeria. Inclusion criteria were BC and age <40 and women older than 40 or without documented BC were excluded.

**Results:** Univariable analysis showed that i) there was an increased risk of BC; OR = 1.77 [1.06 to 2.93] in married women using oral contraception drugs; ii) in contrast there was a lesser risk; OR = 0.43 [0.28 to 0.65] of BC in multiparous compared to nulliparous women; iii) similarly there was a lesser risk; OR = 0.45 [0.26 to 0.76] of BC in married, divorced and widowed women compared to single women. Multivariable analysis showed a higher risk; OR = 2.34 [1.05 to 5.22] of BC in non-breastfeeding than lactating women.

**Conclusion:** The use of oral contraception drugs, nulliparity, lack of breastfeeding and the single unmarried status are risk factors associated with increased BC in young adult women (<40) from Western Algeria.

**Keywords:** Breast Cancer, Risk Factor, Young Women, North Africa, Algeria

#### **Abbreviations**

ATCD: Familial Antecedent BC: Breast Cancer

BRCA1: BReast CAncer Gene 1

OR: Odds Ratio

SD: Standard of Deviation

#### Introduction

Cancer remains the highest threat to human health, since in 2018 over 18 million individuals developed cancer worldwide [1]. Breast cancer (BC) is one of the most frequent cancers in women all over the world, associated with a high mortality. Although it is well established that BC mainly affects women with the age over

40, there is an increasing occurrence of BC in younger women in many places in the world [2-9]. Over 2 million women worldwide were estimated to be diagnosed with BC in 2018 [1]. The incidence of BC is in a continuous increase worldwide in all ages individuals including in Algeria [1]. With 36.1% frequency among cancers in women living in western Algeria, according to the cancer file records, BC remains the most frequent malignancy in this women population during the last three years (2016-2018), affecting 30 out of 100 000 women yearly. The highest age-dependent frequency of BC in Algeria has been found to be 48.1 years [1]. While a low BC incidence of 6.7% was recorded in women younger than 35 year old, a dramatic increase to 22% is observed in women older than 35 and up to over 40 [1, 2]. The high incidence of BC in women of North Africa and Algeria highlights the need of a close investigation of the risk factors associated with the occurrence of this malignancy and that can be used for early disease detection [3].

Several risk factors associated with BC were reported in the literature, among which, early menstruation, late menopause, hormonal treatment of ovarian activity, no or late pregnancy, no or short breast feeding, obesity, alcohol consumption, genetic predisposition and familial antecedent were found to be the most important [4-6].

In young women, BC has particular epidemiology, diagnostic and prognostic characteristics. BC is diagnosed at early age as it has high morbidity and mortality, compared to in older women [10]. In Algerian, BC affects women at 48-51 years whereas in Europe and North America, women are affected mainly at 61-63 years. The occurrence of BC in Algeria is mainly related to genetic predisposition, such as the BRCA1 gene mutation [3]. The aim of the present study is the determination of risk factors that affect the occurrence of BC in your women (<40 years> in west of Algeria.

#### **Experimental design and statistics**

We carried out an age-dependent case-control BC study.

#### **Study Population**

Forty years old or younger women (n=242) newly diagnosed for BC during 2016-2018 were selected for this study. All BC in these women were diagnosed by histopathology of breast biopsies, at the Regional Military Hospital of Oran. Controls (n=242) were volunteer women that were normal visitors to the hospital not affected with Breast cancer.

#### **Definition of Sample Collection**

The variables used in the study for sample collection were; marital status, parity, age at first delivery, age at first menstruation, familial antecedent of BC (ATCD), breast feeding, oral contraception, smoking and abortion. The dependent variable was the occurrence of Breast cancer. Women older than 40 years were excluded from this study.

## Samples/Organisms Allocation

The patient group was composed of women affected by breast cancer and treated in the hospital. The control group was composed with healthy women not affected with breast cancer and were just visitors to the hospital.

### Sample Assessment by Human Investigator

Case data were collected from the medical records of the hospital and patients were contacted by phone calls and the specific questions from a questionnaire were asked to fill out the missing data. Control data were collected by interviewing the volunteer women at the hospital.

### **Data Analysis and Statistical Methods**

All the collected data were quantitative variables, and descriptive analysis of the sociodemographic and clinic characteristics of the participants were conducted. Chi-square test was used for bivariable analysis of possible association between BC and explicative variables. Multivariable analysis with conditional logistic regression was used to select risk factors associated with BC occurrence. All statistical tests were conducted using Epi Info (V 3.5.3) and SPSS (V 17.0) software. The Odds ratio (OR) of each risk factor was then calculated. Data are presented as average  $\pm$  standard deviation (SD). All tests were considered significant at P<0.05.

### **Results**

## **Description of The Studied Population**

The characteristics of the studied population are summarized at the (Table I). By the end of the study, a total of 484 women were included. The general average of age was 34.7±3.5 years and the age class of 35-39 was the most dominant (60.7%). The average of parity was 1.7±1.4 baby. Three out four (75.6%) women included in the study were married. Only three women out of the 484 were smokers. The great majority to f women gave birth to their first baby before age of 30 (88.7%). The great majority of the participants (85.3%) stated that they had their first menstruation between 12-15 years of age. The highest proportion (89%) performed breast feeding. Oral contraception was used in 63.8% but abortion in only 17.4% of participant women. Finally, only 14.5% had ATCD of BC.

### **Bivariable Analysis**

A significant association was found when the parity the occurrence of BC (OR=0.43, 95%CI=0.28-0.65) was analysed (Table II). Women that had at least one baby have lower risk at developing BC compared to nulliparous. There was also an association between the marital status and the occurrence of BC (OR=0.45, 95%CI=0.26-.076). Married, divorced and widowed women have lower risk at developing breast cancer than single women. Furthermore, women taking oral contraception piles had higher risk at developing BC (OR=1.77, 95%CI=1.06-2.93). Association of all the other variables with the risks of development of BC were not significant in this studied population.

**Table 1: Characteristics of the study population** 

Characteristics		Total (484) N (%)	Case (242) N (%)	Control (242) N (%)
Age	20-24 25-29 30-34 35-39 Average ± SD	2 (0.4) 48 (9.9) 140 (29) 294 (60.7) 34.7 ± 3.5ans	1 (0.4) 24 (9.9) 70 (29) 147 (60.7)	1 (0.4) 24 (9.9) 70 (29) 147 (60.7)
Marital status	Married Divorced Widow	76 (15.7) 366 (75.6) 39 (8.1) 3 (0.6)	50 (20.7) 163 (67.4) 26(10.7) 3 (1.2)	26 (10.7) 203 (83.9) 13 (5.4)
Smoking	Yes	3 (0.6)	2 (0.8)	1 (0.4)
	No	481 (99.4)	240 (99.2)	241 (99.6)
Parity (babies)	0 1-3 >3 Average ± SD	140 (28.9) 294 (60.8) 50 (10.3) 1.7±1.4	90 (37.2) 124 (51.2) 28 (11.6)	50 (20.7) 170 (70.2) 22 (9.1)
Age at the first delivery (years)	< 30	297 (88.7)	126 (88.1)	171 (89.1)
	≥ 30	38 (11.3)	17 (11.9)	21 (10.9)
Age at first menstruation (years)	< 12	43 (8.9)	15 (6.2)	28 (11.6)
	12- 15	412 (85.3)	204 (84.7)	208 (85.9)
	> 15	28 (5.8)	22 (9.1)	6 (2.5)
Breast feeding	Yes	284 (89)	118 (92.9)	166 (86.5)
	No	35 (11)	9 (7.1)	26 (13.5)
Breast feeding duration (months)	< 6	76 (30.2)	19 (22.1)	57 (34.3)
	≥ 6	176 (69.8)	67 (77.9)	109 (65.7)
Abortion	Yes	83 (17.4)	44 (18.8)	39 (16.1)
	No	393 (82.6)	190 (81.2)	203 (83.9)
ATCD BC	Yes	70 (14.5)	37 (15.3)	33 (13.6)
	No	414 (85.5)	205 (84.7)	209 (86.4)
Oral contraception	Yes	309 (63.8)	155 (64)	154 (63.6)
	N0	175 (36.2)	87 (36)	88 (36.4)

Table II: Association of the studied variables and BC occurrence

	<b>Total (484)</b>	Case (242)	Control (242)	OR	95%CI	P
Smoking	3 (0.6)	2 (0.8)	1 (0.4)	2.03	0.1-22.9	0.56
Abortion	83 (17.4)	44 (18.8)	39 (16.1)	1.21	0.7-1.9	0.42
Breast feeding	284 (89)	118 (92.9)	166 (86.5)	1.91	0.8-4.2	0.11
Breast feeding duration	176 (69.8)	67 (77.9)	109 (65.7)	1.75	0.9-3.2	0.05
Parity	344 (71.1)	152 (62.8)	192 (79.3)	0.43	0.2-0.6	< 0001
Marital status	408 (84.3)	192 (79.3)	216 (89.3)	0.45	0.2-0.7	< 0.003
Age at first menstruation	412 (85.3)	204 (84.7)	204 (84.7)	208 (85.9)	1.10	0.6-1.8
Age at first delivery	38 (11.3)	17 (11.9)	21 (10.9)	1.16	0.5-2.3	0.74
ATCD	70 (14.5)	37 (15.3)	33 (13.6)	1.14	0.6-1.9	0.60
Oral contraception	366 (75. 6)	163 (67. 4)	203 (83.9)	1.77	1.06-2.93	0.01

#### **Multivariable Analysis**

The retained model summarized in (table III) clearly shows that the risk at developing BC in women who never breast feed their babies was over two-fold higher compared to women who performed breast feeding (adjusted OR=2.34, 95%CI=1.05-5.22, P=0.04). Likewise, the risk at developing BC in married women who regularly take oral contraception was over two-fold higher at early age compared to those who do not undergo oral contraception (adjusted OR=2.55, 95%CI=1.45-4.5, P=0.001). Surprisingly, the highest risk at developing BC was found to be associated with parity, since nulliparous women had over seven times the risk at developing BC compared to women who gave birth of at least one baby (adjusted OR=7.14, 95%CI=2.56-20.0, P=0.0002). In contrast, marital status was found to be associated with a protective role, since married had less risk at developing BC, compared to single, divorced or widow women (adjusted OR=0.50, 95%CI=0.26-0.93, P=0.03). However, no interaction between the retained variables was reported in the final model.

Table III. Final model of the conditional logistic regression of risk factors associated with BC occurrence in young women.

	Adjusted OR	95%CI	P
Breast feeding (yes/no)	2,34	[1,05-5,22]	0,04
Oral contraception (yes/no)	2,55	[1,45-4,5]	0,001
Parity (yes/no)	7,14	[2,56-20,0]	0,0002
Marital status (yes/no)	0,50	[0,26-0,93]	0,03
Constant	*	*	0,002

#### **Discussion**

BC is a multifactorial disease, and many risk factors are associated with the occurrence of this malignancy. In the present first casecontrol study our main aim was to investigate the risk factors associated with increased BC occurrence in young western Algerian women. Data presented in this study, highlight the association of four risk factors with the increase of BC occurrence in young North-Western Algerian women between 2016 and 2018. While the marriage was found to be associated with protective effect compared to single, the association of marriage with use of oral contraception was found to increase the risk at developing BC. This type of observation has been reported in previous studies [11-16]. Likewise, our data are in accordance with those in the literature reporting that nulliparous women have an increased risk of BC [13, 15, 16]. In contrast, like previously reported, married women and those practicing the breast feeding were found to be more protected against BC [17-20]. While a larger study extended to a population of higher number of women would provide data with higher statistical significance, data reported in the present study represent the only available source about the risk factors of BC in young women in Algeria.

#### **Conclusion**

The present study confirmed four risk factors associated with BC in

young women in the western part of Algeria, mainly parity, breast feeding, marital status and oral contraception. This pilot study is the first and the only case-control study in Algeria. A larger study extended to a large number of women from all part of Algeria and the age classes, young and old women will certainly provide more insights in these BC risk factors.

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