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RESEARCH ARTICLE

Association between age at first oral contraceptive use and breast cancer in women-Nouakchott, Mauritania, May - October 2021

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ABSTRACT

Introduction: In Mauritania, breast cancer affects 44.9 women per 100,000 inhabitants in 2020 and is the most common cancer. In a context where two-thirds of women use oral contraceptives and nearly one-third of marriages are early, this study examines the association between the age of first use of oral contraceptives and breast cancer among women in Mauritania.

Methods: A case-control study (192 cases for 192 controls) was conducted at the Nouakchott Oncology Center from 01 May 2021 to 31 October 2021. A case was defined and so was a witness. A logistic regression was performed with SAS® 9.4 software to estimate the odds ratio of breast cancer associated with age of first oral contraceptive use independent of other characteristics.

Results: Half of the patients were from Nouakchott (50.5%), 41.7%, 57.8% and 85.4% were married, uneducated and housewives, respectively. The median age was similar in cases and controls. About 11% of cases and 18.7% of controls used oral contraceptives for the first time before the age of 24, and more than 64% had never used oral contraceptives. After adjusting for possible confounders, age at first oral contraceptive use (<24 years) was significantly associated with breast cancer (adjusted OR = 3.07, 95% CI 1.09-8.82; p = 0.0372) independently of other characteristics.

Conclusions: The study shows that the age of first use of oral contraceptives, less than 24 years, is a risk factor for breast cancer in women followed at the Nouakchott Oncology Center. Sensitization of women on alternative contraceptive methods and early marriage is recommended.

Keywords: Oral contraceptives, Breast cancer, Logistic regression, Nouakchott, Mauritania.

Introduction

Breast cancer is the most common form of cancer and the leading cause of cancer death among women worldwide, with an estimated 2.26 million cases and 685,000 deaths in 2020[1]. Breast cancer incidence accounts for 24.5% of all cancer cases and 15% of all cancer deaths in women[2] these incidences are increasing year by year, apparently due to both changes in women's lifestyle and early detection programs[3].

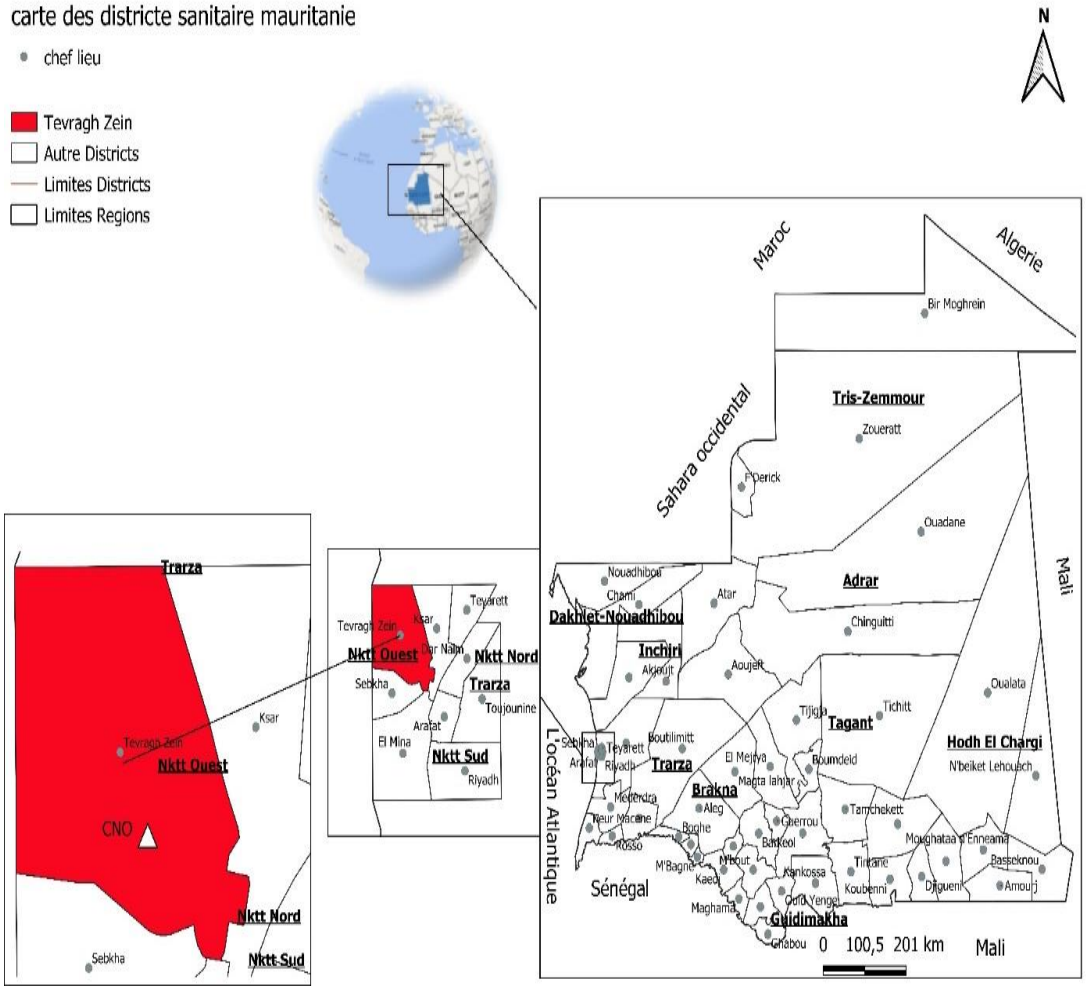
According to GLOBOCAN 2020, in Mauritania, breast cancer is the leading cancer and accounts for 270 deaths. Its prevalence is 44.9 per 100,000 inhabitants over a period of 5 (five) years with 521 new cases in 2020[4]. Also, it is the first type of cancer in women with 27.9% of all cancers diagnosed in 2020 in this population, in Mauritania[4]. Risk factors include inactivity, obesity, hormone therapy used to alleviate menopause (hormone replacement therapy), alcohol consumption and oral contraceptive (OC) use[5]. However, most of these factors are modifiable, meaning that the risk of breast cancer can be reduced by taking preventive measures[6]. The use of oral contraceptives (OCs) is associated with an increased risk of breast cancer[7,8]. Several epidemiological studies and meta-analyses have shown an association between breast cancer incidence and OC use[9–13]. Studies have shown that the risk of cancer is increased in the age groups between 25-34 years for a duration of OC use of at least one year (compared to less than one year) against a non-existent risk or even protection in women 35-44 years[14,15]. The risk of breast cancer is increased by about 25% in women who routinely use oral contraceptives. However, this increase in risk drops as soon as consumption is stopped, so that, 10 years after stopping use, no significant increase in risk is evident[16]. A nationwide prospective cohort study involving all women in Denmark showed an increased risk of breast cancer in women aged 25-34 and over 45 and younger in those aged 35-44. This risk would also increase with the duration of OC use[14]. In Mauritania, the relationship between age at OC intake and breast cancer risk has not yet been verified. Our objective is to verify whether there is an age effect that modifies the link between OC intake and breast cancer risk in the female population in Mauritania. This is explained by the fact that in Mauritania, women marry very early (15.6% of women marry before the age of 15, 35.2% before the age of 18 and 27.8% of married women are aged 15 to 19)[17]a proportion of pill use among women in Mauritania of 67.3% (PMA2020)[18].

Methods

FRAMEWORK OF THE STUDY

Mauritania is a country in West Africa. Its area is 1,036,000 km2. Mauritania is divided into sixty-three health districts. Our study took place at the Nouakchott Oncology Center (NOC) which was inaugurated on December 26, 2008, and is in the district of Tevragh Zein, Nouakchott West Region, with the mission of cancer management in general in Mauritania Figure 1. The Nouakchott (Nktt) Region, Mauritania's political capital, occupies a central position. It is divided into three sub-regions (Nouakchott North, South and West). It is located over a length of more than 700 km on the coast of the Atlantic Ocean. Its population is 2,364,861 inhabitants or (52% of the national population). Given that its area is about 1,000 km², the density is the highest in all of Mauritania at 948 inhabitants/km² [19].

Figure 1: Map of health districts in Mauritania



TYPE AND PERIOD OF STUDY

An unmatched case-control study was conducted from 01 May 2021 to 31 October 2021 over three years, from 1 January 2018 to 31 December 2020.

STUDY POPULATION AND CASE DEFINITIONS

The study population consists of all confirmed cancer cases, reported in the Nouakchott Oncology Center from 1 January 2018 to 31 December 2020. The following case definition was used:

One case was all live patients, registered in the oncology hospital of Nouakchott and followed for breast cancer in the period from 2018 to 2020.

A control was any live patient, registered in the oncology hospital of Nouakchott in the period from 2018 to 2021 and followed for a cancer other than breast cancer for which a link with CO intake is not established in the scientific literature (anal cancer, cavum, motile tongue, elbow, conjunctiva, hypopharynx, maxilla, kidney, esophagus, bladder, orbit, lymphomas).

SAMPLE SIZE

Our sample size was calculated using SAS 9.4. We considered an odds ratio of 2.25 of breast cancer associated with OC intake based on the study by Bardaweel et al[20] Considering a statistical power of 80%, a ratio of one case to one control, a proportion of pill use among

women in Mauritania of 67.3% (PMA2020) and a non-response rate of 10% [18]the total sample size is 384 patients to be included, i.e. 192 cases and 192 controls. Cases and controls were recruited from the same health facility based on definitions.

DATA ANALYSIS

Excel® 2019 was used for data entry and SAS® 9.4 for data analysis. Frequencies, proportions, and rates were calculated for descriptive analysis. For the univariate analysis, we looked for possible associations between breast cancer and the selected variables by calculating ORs with 95% confidence intervals and p-value. For multivariate analysis, we included in the logistic regression model all variables with a p-value less than or equal to (≤) 0.20. We calculated adjusted ROs with their 95% confidence intervals (95% CI) and the p-value and independent risk factors were retained with a significance level of 5%.

Results

SOCIODEMOGRAPHIC CHARACTERISTICS OF THE STUDY POPULATION

We interviewed a total of 384 women with and without breast cancer, including 192 cases and 192 controls, of which, the majority were from Nouakchott (50.5%). 41.7%, 57.8%, and 85.4% were married, out of school, and domesticated, respectively. The median age was 52 years (I IQ (45 years-58 years)) in cases and 53 years (IIQ (43 years-64 years)) in controls. About 11% of cases and 18.7% of controls used OCs for the first time before the age of 24 years and 23.96% of cases and 9.90% of controls used OCs for the first time after the age of 24 years and more than 64% never used OCs. 82.81% of cases had a history of mastectomy Table 1.

Table 1: Characteristics of the study population (N = 384), Mauritania 2018-2020

Characteristics	Case (n=192) n (%)	Controls(n=192) n (%)	p-value
Place of residence			0,9691
Nouakchott	97 (50,52)	102 (53,13)	
Other cities	95 (49,48)	90 (46,87)	
History of mastectomy			< 0,0001
No	33 (17,19)	192 (100)	
Yes	159 (82,81)	0 (0,00)	
Marital status			0,9039
Bachelor	13 (6,77)	14 (7,29)	
Divorcee	63 (32,81)	62 (32,29)	
Bride	80 (41,67)	81 (42,19)	
Widow	36 (18,75)	35 (18,23)	
History of OC use			0,1556
No	124 (64,58)	137 (71,35)	
Yes	68 (35,42)	55 (28,65)	

Characteristics	Case (n=192) n (%)	Controls(n=192) n (%)	p-value
Age at menarche			0,1837
<12	43 (22,40)	53 (27,60)	
12-13	111 (57,81)	108 (56,25)	
>13	38 (19,79)	31 (16,15)	
Age at first use of OC			0,0079
Never use	124 (64,58)	137 (71,35)	
< 24 years	22 (11,46)	36 (18,75)	
>or= 24 years	46 (23,96)	19 (9,90)	
Abbreviations: OC: oral contraceptives			

Factors associated with breast cancer

In univariate analysis, the factors associated with breast cancer were: OC-utilization levels, yes OR = 1.37; 95% CI (0.89-2.10), age at first use of CO, <24 years OR = 2.48; 95% CI (1.87 - 3.82), age at first childbearing, 19-28 years OR = 2.27; 95% CI (1.30 – 3.95), number of children, >4 OR children = 2.07; 95% CI (1.13 – 3.84), duration of OC use, 2-4 years OR = 5.83; 95% CI (2.14-15.90) and duration of OC use, >4 years OR = 8.75; 95% CI (2.55-30.05) Table 2.

Table 2: Odds ratios of raw breast cancer associated with women's characteristics, Mauritania 2018-2020

Characteristics	OR (IC 95%)	p-value
Values of use of OC		0,1557
No	1	
Yes	1,37 (0,89 – 2,10)	
Age at first use of OC		0,0007
Never used	1	
< 24 years	2,48 (1,87 - 3.82)	
≥24 years	0,37 (0,20 – 0,67)	
Age at menarche		0,4093
< 12 years old	1	
12 – 13 years	0,79 (0.49 - 1.27)	
> 13 years old	0,66 (0.35 - 1.23)	
Age range		0,0012
41-91	1	
17-40	0,20 (0,06 – 0,71)	
Age at first motherhood		< 0,0001
≤ 18 years	1	
19-28 years	2,27 (1,30 – 3,95)	

Characteristics	OR (IC 95%)	p-value
≥ 29 years old	0,25 (0,08 – 0,81)	
Age at last maternity		**0,0035**
< 37 years	1	
≥ 37 years	0,50 (0,31 – 0,80)	
Duration of use		**0,0007**
≤ 1 year	1	
2-4 years	5,83 (2,14-15,90)	
>4 years	8,75 (2,55-30.05)	
Number of children		**0,0192**
No children	1	
1-4 children	1,22 (0,68 – 2,20)	
>4 children	2,07 (1,13 – 3,84)	
Abbreviations: OC: oral contraceptives, OR: Odds ratios, CI: confidence interval		

In multivariate analysis, age at first OC use, <24 years versus ≥ 24 years, showed a significant association with breast cancer occurrence (adjusted OR = 3.07, 95% CI (1.09-8.82); p = 0.0372) Table 3.

Table 3: Multivariate analysis, effect of age at first oral contraceptive use on breast cancer risk in women, Mauritania 2018 – 2020

Characteristics	Adjusted OR (95% CI)	p-value
Age at first use of OC, <24 vs. ≥ 24	**3,07** (1,09 - 8,82)	**0,0372**
Number of children, < 4 vs ≥ 4	1,06 (0,26- 4,33)	0,9385
Age range, (17-40) vs (41-91)	1,15 (0,07 - 17.87)	0,7701
Age at first motherhood, < 28 years vs ≥ 28 years	16,85 (1,70 – 166,51)	0,0539
Age at last maternity, ≥ 37 < 37	0,56 (0,15 – 2,15)	0,3986
Duration of use, ≥ 4 years vs <4 years	2,76 (0,53 – 14,22)	0,1330
Abbreviations: OC: oral contraceptives, OR: Odds ratios, CI: confidence interval, VS: versus		

Discussion

To our knowledge, this is the first case-control study to assess the link between the effect of age at first use of OCs and breast cancer risk in women in Mauritania. Our study has some limitations. The retrospective type of our study that may have created memory bias in some of the variables; for example, age of menarche, age at first and last childbearing, duration of OC use. In addition, not all women in the study were able to report the type of OC they used and, therefore, analysis based on the different combined doses was not possible. These factors, together with the lack of information in the database and the monocentric nature of the study, make the results of this study non-generalizable to all Mauritanian women. Despite these limitations, our study identified that the risk of breast cancer is multiplied by 3 when the age at first

use is less than 24 years compared to women who use OC and are over 24 years old.

The link between age at first use of OCs and breast cancer risk in Mauritanian women has been established and significantly. This result is like those reported in the literature in longitudinal studies such as that performed by Tryggvadottir L et al in a case-control study nested in an Icelandic cohort, and by Ji LW et al in a meta-analysis of longitudinal studies. In the first study, the authors show a significant effect between the use of OC and breast cancer in women born between 1951 and 1967, but the risk disappears when we include those born well before between 1945 and 1950 [21]. In the same vein, the longitudinal study of Karlsson T et al conducted among British women, shows a limited effect of the use of CO in the risk of breast cancer [22] However, Ji LW et al. show in a meta-analysis a dose-response effect between age at first use of OC and a significant risk of 1.24 (1.10 – 1.41) with a p-value of nonlinearity of 0.518 [23].

We have 69% of cases were married before the age of 30 and 57.81% of cases and controls were out of school and housewives were (more than 59%) among cases and controls, so early marriage and low income and multiparity, median = 4 children (2 - 5), can also explain our results. This finding is like the conclusions of Abdou Azaque Zouré et al [24] who reported the same result.

Conclusion

The study shows that the age of first use of oral contraceptives, less than 24 years, is a risk factor for breast cancer in women followed at the oncology center of Nouakchott. Raising awareness about the use of other contraceptive methods and early marriages could help prevent breast cancer among women in Nouakchott, Mauritania.

Competing interests

The authors declare that they have no Competing interests.

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Nil.

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Ethical statements

Our study protocol has obtained the approval of the coordination of the BFELTP program and ethics committee in Mauritania (letter number 001/2019/ECA/UNA). The data collected is confidential and has been stored in a password-protected computer. Anonymity numbers are assigned before data processing.

Authors' contributions

The protocol and the review of the literature were conducted by Mohamedou Hmeied Maham, Deoula Meimouna, Mohamedou Mohamed Salem and corrected by Jean Kaboré and supervised by Yanogo Pauline and Nicolas Meda, Djibrile Barry, Yoda Herman. Data collection and analysis were conducted by Mohamedou Hmeied Maham, Selma Mohamed Brahim and supervised by

Ekhtel benina Zein and Ahmedou Tolba. The article was conducted by Mohamedou Hmeied Maham and corrected by Jean Kaboré and supervised by Yanogo Pauline and Nicolas Meda, all authors have read and approved the final article.

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