

Effects of Breast-feeding and Oral Contraception on the Risk of Recurrence in Breast Cancer : A Multinational Study

Teresa Lehman**, Mohammed Shaik*, Rama Modali**, Borys Hrinchenko*
 *Breslin Cancer Center, MSU Hematology/Oncology
 **ReproCELL Inc, BioServe Biotechnologies Ltd.—A ReproCELL Group Company



ABSTRACT

Introduction: Breastfeeding (BF) decreases and oral contraceptive (OCP) increases the incidence of breast cancer (BC). However, their role in the recurrence of breast cancer (rBC) has not been established. The aim of our study was to examine the association of maternal factors in the rBC.

Methods: Data were obtained from the Global Epidemiological Study (GES), an IRB approved multinational biorepository and database to assess disease risk factors. The patients were recruited from countries including Poland, Vietnam, Western Europe and the USA. Patients provided their personal history, age, BMI, age of first pregnancy, BF, number of children breastfed, radiation exposure (RE), years of OCP use, benign breast disease (BD), hysterectomy, hormone replacement therapy (HRT) and rBC. The t-test and chi-square test were used for continuous and categorical variables, respectively. The association [adjusted odds ratio (aOR)] between rBC and each risk factor was obtained using logistic regression after adjusting for all the variables including stage of cancer.

Results: A total of 2546 patients were surveyed, of which 218 patients had rBC later in life. The average age of pts with recurrence was 54 yrs and those without rBC was 56 yrs. Of the total, 73.5% had BF, 25% had used OCP, 17.3% used HRT, 5.6% had RE, 16.6% had a hysterectomy, and 16% had BD. In multivariate analysis, age, BF, OCP and RE each had significant impacts on the rBC. Pts who did not BF had a 3-fold increased risk of recurrence compared to those who breastfed at least 3 children [aOR of 2.9 (1.7-4.9)]. Pts who did not use OCPs were 53% less likely to have rBC compared to those who used OCPs [aOR of 0.47 (0.32-0.69)]. A statistically significant dose-effect for number of children breastfed and rBC, and years of OCPs usage and rBC was found. BMI, HRT, hysterectomy, BD, and age at first pregnancy did not have an effect on rBC.

Conclusion: Our study suggests that breastfeeding decreases the risk of recurrence of breast cancer, while OCP usage increases the risk of recurrence of breast cancer. Further studies are needed to validate our results.

INTRODUCTION

- Breast cancer (BC) is the most common malignancy in women in the United States.
- The American Cancer Society estimates that 235,030 Americans will be diagnosed with invasive breast cancer and 40,430 will die of the disease in the United States in 2014^[1].
- There is good evidence that breast-feeding(BF), and prior radiation exposure (RE) have been shown to be associated risk of initial breast cancer^{[3][4]}.
- Recently, a case control study found an association between the oral contraceptive (OCP) use and the incidence of breast cancer in African American population^[5].
- However, the role of these factors in the recurrence of breast cancer (rBC) has not been established.

STUDY AIM

- The **aim of our study** was to examine the association between maternal factors including age, BMI, age of first pregnancy, BF, number of children breastfed, RE, years of OCP use, benign breast disease(BD), hysterectomy, and hormone replacement therapy (HRT) with the recurrence of breast cancer.

IRB

IRB approval was obtained at Chesapeake IRB — **Approval number** - #CR00025267
Approval data - 01/06/2014 — **Phone Number** - (410) 884-2900

METHODS

- This is a secondary study done on data from the Global Epidemiological Study (GES), which is an IRB approved multinational study to assess disease risk factors.
- The subjects were recruited from countries including Poland, Vietnam, Western Europe and the USA.
- GES is linked to bio-repository.
- Patients provided their personal history, age, BMI, age of first pregnancy, BF, number of children breastfed, radiation exposure (RE), years of OCP use, benign breast disease (BD), hysterectomy, hormone replacement therapy (HRT) and rBC
- In this study we examined association is between these risk factors and recurrence of breast cancer.

Statistical Analyses:

- Univariate analysis was done using **t-test** and the **chi-square test** for continuous and categorical variables.
- The association between the recurrence of breast cancer and risk factors (age, BMI, age of first pregnancy, BF, number of children breastfed, RE, years of OCP use, BD, hysterectomy, HRT) was computed using **logistic regression analysis**.
- Forward selection** method was used to obtain the final regression model.
- The 2 sided p-value of <0.05 was considered statistically significant.
- Statistical software SAS 9.3 was used to analyze

RESULTS

- Breastfeeding (BF) decreases and oral contraceptive (OCP) increases the incidence of breast cancer (BC). A total of **2546** patients were surveyed, of which **218** patients had recurrence of breast cancer later in life.
- The average age in the group with recurrence of breast cancer compared to those without recurrence of breast cancer was, **54 years vs. 56 years**, respectively.
- Of the total, **73.5%** had BF, **25%** had used OCP, **17.3%** used HRT, **5.6%** had RE, **16.6%** had a hysterectomy, and **16%** had BD.
- Data regarding risk factors included age, BMI, age of first pregnancy, breast feeding, number of children breastfed, radiation exposure, years of OCP use, benign breast disease, hysterectomy, hormone replacement therapy (HRT) was used to compare the two groups.
- In multivariate analysis, age, BF, OCP and RE each had **significant impacts** on the recurrence of breast cancer.
- In the multivariate analysis the BMI, HRT, hysterectomy, benign breast disease, and age at first pregnancy **did not** have an influence on the recurrence of breast cancer.
- After adjusting for other co-factors Patients who **did not** breastfed had a **3-fold increased risk of recurrence** compared to those who breastfed at least 3 children [aOR of **2.9 (1.7-4.9)**].
- Patients who did not use OCPs were **53% less likely** to have rBC compared to those who used OCPs [aOR of **0.47 (0.32-0.69)**].
- A statistically significant dose-effect for number of children breastfed and rBC, and years of OCPs usage and rBC was found. (Table 1).

Predictors of Recurrence of Breast Cancer (RBC)

VARIABLES	β ESTIMATE	ADJUSTED OR (CI)	p-VALUE
Age	0.022	1.02 (1.008-1.03)	0.002
Breastfed (BF, none vs. >3 children)	1.06	2.9 (1.7-4.9)	<0.0001
Breastfed (BF, < 3 vs. > 3 children)	0.74	2.09 (1.2-3.5)	0.006
Oral Contraceptive use (OCP, no vs. yes)	-0.743	0.47 (0.32-0.69)	0.0001
Radiation exposure (RE, no vs. yes)	-1.31	0.26 (0.16- 0.13)	<0.0001
HRT (no vs. yes)	0.4	1.49 (0.96-2.3)	0.07

CONCLUSIONS

- Our study showed **breastfeeding** decreases significantly the risk of recurrence of breast cancer, while **oral contraceptive** usage and **exposure to radiation** in past increases the risk of recurrence of breast cancer.
- Further prospective trials are needed to validate our findings.

REFERENCES

- Rebecca Siegel, Jiemin Ma, et al. Cancer Statistics, 2014. CA: A Cancer Journal for Clinicians, 2014
- Collaborative Group on Hormonal Factors in Breast Cancer: Breast cancer and breastfeeding: collaborative reanalysis of individual data from 47 epidemiological studies in 30 countries, including 50302 women with breast cancer and 96973 women without the disease; Lancet. 2002 Jul 20;360(9328):187-95
- Millikan, RC., Player, J., Decotret, A., Tse, C., & Keku, T. (2005). Polymorphisms in DNA repair genes, medical exposure to ionizing radiation, and breast cancer risk. Cancer Epidemiol Biomarkers Prev, 14, 2326–2334.
- Elisabeth F. Beaber, Diana S.M. Buist et al; Recent Oral Contraceptive Use by Formulation and Breast Cancer Risk among Women 20 to 49 Years of Age; Cancer Res August 1, 2014 74:4078.
- Bethea TN, Rosenberg L, Hong CC, et al; A case-control analysis of oral contraceptive use and breast cancer subtypes in the African American Breast Cancer Epidemiology and Risk Consortium; Breast Cancer Res. 2015 Dec;17(1): 535.

CONTACT

Terri Lehman, Ph.D.
 Chief Scientific Officer
 BioServe Biotechnologies, Ltd.
 9000 Virginia Manor Road, Suite 207
 Beltsville, MD 20705
 Tel: (301) 470-3362
 Email: terri@bioserve.com

