

## RESEARCH COMMUNICATION

# Physiological, Reproductive Factors and Breast Cancer Risk in Jiangsu Province of China

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### Abstract

To evaluate the relationship between physiological, reproductive factors and risk of breast cancer, we conducted a case-control study with 669 cases and 682 population-based controls in Jiangsu Province of China. A structured questionnaire was used to elicit detailed information. All subjects completed an in-person interview. Unconditional logistic regression analysis was performed to calculate odds ratios (ORs) and 95% confidence intervals (CIs) as measures of risk for breast cancer. The results have revealed that there was an increasing risk of breast cancer, include early age at menarche ( $\leq 13$  year), late age at menopause ( $> 50$  year) and older age at first pregnancy ( $\geq 30$  year). Breastfeeding was associated significantly with a reduced risk of breast cancer. Women who had history of breastfeeding were at significantly decreased OR (0.44, 95% CI: 0.27-0.73). The protective effects of breastfeeding for breast cancer seemed greater for women who had extended duration of breastfeeding during their lifetime (p for linear trend: 0.0095). These results suggested that physiological and reproductive factors may play important roles in the development of breast cancer among Jiangsu' women of China.

**Keywords:** Breast cancer - physiological and reproductive factors - Chinese women

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### Introduction

Previous studies suggested that physiological and reproductive factors, particularly early age at menarche, late age at menopause, early age at first pregnancy, parity and breastfeeding may reduced breast cancer risk in women, although results were inconsistent (Yavari et al., 2005; Iwasaki et al., 2007; Naieni et al., 2007; Huo et al., 2008; Ozmen et al, 2009; Costarelli et al, 2010).

Breast cancer is the commonest cancer in women of worldwide. Although the incidence rate of breast cancer in China is much lower than those in Western countries, there has been a marked increase in recent years, cancer registries in China are recording annual increases in incidence of 3% to 4% (Parkin et al., 2005). From 2000 to 2005, very large increases in the number of cases of female breast cancers (+38.5%) are predicted (Yang et al., 2005). This large increase in cancer risk is responsible for a 27.5% increase in the number of cases, whereas population growth and aging contribute a further 11% increase (Yang et al., 2005). For seeking the cause of increasing incidence of breast cancer in Jiangsu' women of China, we conducted a case-control study on physiological, reproductive factors and risk of breast cancer.

### Materials and Methods

#### Study Subjects

Breast cancer cases were recruited from data of the Cancer Registries in Taixing, Wuxi, Jintan and Huian Cities of Jiangsu Province of China, and also from who visited Jiangsu Province Cancer Hospital from these cities from June 2004 to December 2007. All cases were histopathologically diagnosed as having a primary breast cancer. Physicians at the hospital asked eligible cases to participate in this study, and doctors or nurses interviewed the subjects after obtaining informed consent.

Population-based controls were selected from healthy residents in eleven villages or towns of Taixing, Wuxi, Jintan and Huian Cities. Doctors of the public health centers randomly selected one or two controls for each case, after matching for ethnicity and age within 2 years using the records of residents at the local governmental office, and then asked eligible residents for their participation. Interviews were performed as far as the cancer cases. Total 669 cases and 682 controls completed interview. A few patients and residents refused to participate in our study, but the response rates were 98% for cases and 99% for controls. The ethics committee of

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Jiangsu Province Institute of Cancer Research approved this study.

#### Data Collection and Statistical Analysis

A structured questionnaire was used to elicit detailed information on demographic background, socioeconomic status, occupational history, height and weight, menstrual and reproductive history. All subjects completed an in-person interview. The body mass index (BMI) was calculated based on weights and heights. Tertile distributions of mean income every person per month in family, weight and height among controls were used to categorize the variables.

Odds ratios (ORs) and 95% confidence intervals (CIs) were estimated by unconditional logistic regression analysis adjusted for potential confounders. All the analyses were performed in SAS 8.02 (SAS Institute Inc., Cary, NC). All tests were two-sided, with the significance level of 0.05.

**Table 1. Comparison of Cases and Controls by Selected Descriptive Characteristics**

	Cases(n=669)	Controls(n=682)	$\chi^2$	P
Age(year)				
<40	76 (11.4)	87 (12.8)	0.978	0.807
40-49	226 (33.8)	229 (33.6)		
50-59	227 (33.9)	234 (34.3)		
≥60	140 (20.93)	132 (19.4)		
Menarche age (years)				
≤13	180 (26.9)	141 (20.7)	8.449	0.038
at 14	211 (31.5)	216 (31.7)		
at 15	191 (28.6)	219 (32.1)		
≥16	87 (13.0)	106 (15.5)		
Marriage status				
spinster	2 (0.30)	0	13.758	0.017
married	590 (88.2)	629 (92.2)		
married again	38 (5.68)	16 (2.35)		
divorced	4 (0.60)	2 (0.29)		
widowed	34 (5.08)	35 (5.13)		
other	1 (0.15)	0		
Educational level				
illiterate	118 (17.6)	133 (19.5)	8.067	0.089
primary	201 (30.0)	232 (34.0)		
junior high	198 (29.6)	198 (29.0)		
senior high	111 (16.6)	80 (11.7)		
college	41 (6.13)	39 (5.72)		
Occupation				
workers	175 (26.2)	110 (16.1)	64.085	0.001
peasants	299 (44.7)	377 (55.3)		
professional*	48 (7.17)	65 (9.53)		
administration	48 (7.17)	21 (3.08)		
finance	45 (6.73)	22 (3.23)		
housework	26 (3.89)	67 (9.82)		
other	28 (4.19)	20 (2.93)		
Body mass index (BMI)				
<22	225 (33.6)	244 (35.8)	4.875	0.087
22-24.9	256 (38.3)	282 (41.4)		
≥25	188 (28.1)	156 (22.9)		
Income/month				
Low	171 (25.6)	259 (38.0)	30.790	0.001
Middle	230 (34.4)	232 (34.0)		
High	268 (40.1)	191 (28.0)		

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## Results

#### Characteristics of Cases and Controls

A total of 669 cases (309 premenopausal and 360 postmenopausal) and 682 controls (292 premenopausal and 390 postmenopausal) were included in the study. The comparison of cases and controls by selected descriptive characteristics are summarized in Table 1. There were no significant differences between cases and controls in distribution of age, menopausal status, educational level and BMI., whereas significant differences were observed for menarche age, marriage status, occupation and mean income every person per month in family. Group of case had an earlier menarche age and higher income comparison with controls.

#### Physiological, Reproductive Factors and Risk

ORs and their 95% CIs adjusted for age, menopausal status, marital status, educational level, occupations,

**Table 2. Physiological, Reproductive Factors and Breast Cancer Risk**

	Cases(n=669)	Controls(n=682)	OR ( 95% CI)
Age at menarche (years)			
≥14	479 (73.1)	541 (79.3)	1.00
≤13	180 (26.9)	141 (20.7)	1.47 (1.12-1.92)
Age at menopause (years)			
≤50	216 (60.0)	305 (78.2)	1.00
≥50	144 (40.0)	85 (21.8)	2.17 (1.55-3.03)
Childbirth			
Never	25 (3.7)	13 (1.9)	1.00
Have	644 (96.3)	669 (98.1)	0.54 (0.27-1.06)
Age at first childbirth			
≤25	454 (67.9)	530 (77.7)	1.00
26-29	169 (25.3)	127 (18.6)	1.46 (1.10-1.94)
≥30	30 (4.5)	18 (2.6)	1.68 (0.90-3.14)
Never	16 (2.4)	7 (1.0)	2.61 (1.05-6.50)
P for trend			<0.0001
No. of full-term childbirths			
0	32 (4.9)	14 (2.1)	1.00
1	337 (50.4)	340 (49.9)	0.47 (0.24-0.92)
2	181 (27.1)	177 (26.0)	0.53 (0.26-1.06)
3	66 (9.9)	80 (11.7)	0.55 (0.25-1.25)
≥4	53 (7.9)	71 (10.4)	0.23 (0.07-0.71)
P for trend			0.0206
No. of non full-term childbirths			
0	630 (94.2)	648 (95.0)	1.00
≥1	39 (5.8)	34 (5.0)	1.23 (0.76-1.98)
Oral contraceptive use			
Never	602 (90.0)	619 (90.8)	1.00
Have	67 (10.0)	63 (9.2)	1.12 (0.77-1.62)
Breastfeeding			
Never	56 (8.4)	23 (3.4)	1.00
Have	613 (91.6)	659 (96.6)	0.44 (0.27-0.73)
Duration of breast feeding (months)			
0	56 (8.4)	23 (3.4)	1.00
1-11	214 (32.0)	216 (31.7)	0.46 (0.27-0.80)
12-23	225 (33.6)	250 (36.7)	0.41 (0.24-0.71)
≥24	174 (26.0)	193 (28.3)	0.72 (0.38-1.35)
P for trend			0.0095

OR were adjusted for age, menopausal status, marital status, educational level, occupations, body mass index and income/month

BMI and income are shown in Table 2. It indicated that an increasing risk of breast cancer was associated with early age at menarche ( $\leq 13$ ) and late age at menopause ( $\geq 50$ ), the OR of younger than 14 age at menarche was 1.47 (95%CI: 1.12-1.19) and the OR of older than 50 age at menopause was 2.17 (95%CI 1.55-3.03).

Women who had childbirth history were at lowered OR (0.54, 95%CI:0.27-1.06), although no statistical significance. The age at first pregnancy was related with the risk of breast cancer. As compared with those with  $\leq 25$  years old at first pregnancy, women with 26-29 years old at first pregnancy had an OR of 1.46 (95%CI 1.10-1.94), those with  $\geq 30$  years old at first pregnancy had an OR of 1.68 (95%CI 0.90-3.14), while women who no history of pregnancy had an OR of 2.61 (95%CI 1.05-6.50). Larger number of full-term births were related with decreased OR for breast cancer and with a dose-response relationship (p-value for linear trend: 0.0206). The number of non full-term births and the oral contraceptive use were not related with breast cancer risk.

Breastfeeding displayed significantly protective effects against breast cancer. Women who had history of breastfeeding were at significantly decreased OR (0.44, 95%CI: 0.27-0.73). The protective effects of breastfeeding for breast cancer seemed greater for women who had extended duration of breastfeeding during their lifetime (p-value for linear trend: 0.0095).

## Discussion

Breast cancer is a common malignancy for women in most parts of the world. A lot of studies about the association with etiology and risk factors of breast cancer were conducted, particularly physiological and reproductive factors. Various physiological and reproductive factors, including age at menarche, age at menopause, age at first pregnancy and parity have been shown to modify the risk of breast cancer (Oran et al, 2004; Anderson et al, 2007; Iwasaki et al, 2007). Our results in this study also demonstrated that early age at menarche ( $\leq 13$  years old), later age at menopause ( $> 50$  years old) and later age at first pregnancy were associated with an increased risk for breast cancer, and childbirth was associated with a decreased risk for breast cancer. In this study, we also found the number of full-term births were related with risk of breast cancer. Larger number of full-term births decreased breast cancer risk, it maybe similar to the effect of parity to breast cancer risk. Early menarche and late menopause are associated with increased lifetime exposure to estrogens, the protective effects of pregnancy-related against breast cancer are associated with the changes of estrogen and pregnancy hormones (Russo et al, 1987; Russo et al, 1990; Russo et al, 1991; Blakely et al, 2006; Bernstein et al, 1985; Dorgan et al, 1995; Garcia-Closas et al. 2002; Bernstein et al, 1995). Therefore these consistent results suggested that estrogen, pregnancy hormones exposure and deprivation were important in the etiology of breast cancer.

In present study, we found that breastfeeding was related to decreased risk of breast cancer and the protective effects of breastfeeding for breast cancer seemed greater

for women who had extended duration of breastfeeding during their lifetime. This result is similar to that of other authors (Lai et al, 1996; Olaya-Contreras et al., 1999; Tryggvadottir, 2001; Collaborative Group on Hormonal Factors in Breast Cancer, 2002; Okobia et al, 2005; Huo et al., 2008). Shema et al. (2007) found that short duration of lifetime breastfeeding, late age at first breastfeeding and experience of insufficient milk increase breast cancer risk. Kelsey et al. (1993) think the effect of breastfeeding appeared to be more protective in Asian countries. The mechanisms of breastfeeding protective action on breast cancer remains uncertain. Several hypotheses have been proposed to account for the protective effects of breastfeeding. These include that breastfeeding promoting the terminal differentiation of breast tissue, caused long-term endogenous hormonal changes, possibly reduced estrogen and increased prolactin production to decrease cumulative exposure to estrogen, inhibiting the initiation or growth of breast cancer cells, and suppressing ovulation, as well as attributing to the excretion of carcinogenic agents from breast ductal tissue through breastfeeding (Freudenheim et al., 1997; Enger et al., 1998; Ursin et al., 2004).

In conclusion, our study revealed roles for some modifiable determinants of breast cancer that can be focused by public health intervention in Jiangsu province of China. Accordingly, public awareness should be increased regarding the protective effect of age at first pregnancy, childbirth and longer duration of breastfeeding in developing breast cancer. More studies are recommended to explore the determinant of breast cancer in Jiangsu province of China.

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