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Risk Factors for Breast Cancer in Hong Kong women: a case control study

Editor's message

This issue intends to complement the "Hong Kong Breast Cancer Registry Report No. 10" on the identification of factors associated with risk of getting breast cancer. Our findings suggested that both non-modifiable and modifiable factors are associated with increased risk of breast cancer. Our study aims to provide insights into breast cancer management to encourage more research and discussion conducive to policy change in synch with our mission to mitigate the threat and sequelae of breast cancer.

Introduction

Over the past two decades, there has been an increase in new cases of female breast cancer (BC) in Hong Kong. According to the Hong Kong Cancer Registry, female BC cases tripled from 1,266 in 1994 to 3,900 in 2015, making it the most common cancer among women in Hong Kong since 1994.[1] Identifying the risk factors for BC development in the local context help understand the reasons for such a rising trend in the incidence, thereby provide evidence for local BC control. Previous literature has suggested that BC is a multifactorial disease that is caused by genetic and environmental factors, and the interactions between the two. Many studies have been conducted to investigate potential risk factors for developing BC for women in Western and East Asian countries.[2-7] Some modifiable lifestyle and behavioural factors, non-modifiable hormonal, reproductive and intrinsic factors have been assessed, and some of the variables are identified as risk factors. According to the Hong Kong Breast Cancer Registry Report No. 10,[8] potentially strong relationships between these risk factors and BC were observed among the BC patients in Hong Kong (Table 1). However, there has been no comprehensive epidemiological study to scientifically examine the relationships of these factors and the risk of developing BC among Hong Kong women. Furthermore, Chinese BC patients are usually younger suggesting that the factors contributing to BC development may be different from those for Western women.[3] The objective of this study is to examine the potential attributes that may have linkage to BC among local Chinese women.

Table 1 **Prevalence of risk factors among 16,743 breast cancer patients in Hong Kong**

Risk factor	%
Non-modifiable	
no childbirth / first live birth after age 35	26.4
early menarche (<12 years old)	13.9
first-degree relative with breast cancer	10.8
late menopause (> 55 years old)	2.8
Modifiable and lifestyle-related	
lack of exercise (<3 hours / week)	77.6
high levels of stress (>50% of time)	37.1
night shift	2.0
Modifiable and behavioural-related	
no breastfeeding	65.8
diet rich in meat / dairy products	14.1
habit of drinking alcohol	5.0
habit of smoking	4.8
Modifiable and medical-related	
use of hormonal contraceptives	30.6
being obese	21.5
use of hormone replacement therapy	3.8

Methodology

The study participants consisted of BC cases and age-matched (within 10 years) controls recruited during 2014-2017. The cases consisted of prevalent and incident cases of BC who registered with the Hong Kong Breast Cancer Registry during the study period. The controls were women without history of any cancers and were recruited at different time and venue throughout the territory by systematic random sampling method. All the cases and controls were Chinese women aged 18 years or more who have been living in Hong Kong for at least 5 years prior to cancer diagnosis (for cases) or interview (for controls).

The potential 15 factors being studied were grouped into the four categories: i) non-modifiable (family history, age at menarche, menopausal status, reproductive history and age at menopause); ii) modifiable and lifestyle-related (physical activity, stress and night shift); iii) modifiable and behavioural-related (breastfeeding, diet, smoking and alcohol drinking); and iv) modifiable and medical-related (weight status, use of hormonal contraceptives and hormone replacement therapy). Chi-square test was used to compare the distribution of the selected sociodemographic characteristics between the cases and controls. All the potential factors were studied using the unconditional multiple logistic regression controlled for age. Adjusted odds ratio (aOR) and corresponding 95% confidence intervals (CI) were presented. Model fitness was assessed using likelihood ratio test and Hosmer & Lemeshow goodness-of-fit test. Stratified analyses by menopausal status were conducted to further examine the relevance of the risk factors among pre- and postmenopausal women.

Results of study

A total of 10622 subjects (5102 cases) who completed the whole survey were included in the subsequent analyses. Majority of the study subjects were aged 40 to 59, lived in the New Territories, were married or cohabitating and have completed secondary or higher education. The cases and controls were not statistically different in terms of age, area of residence and education level (Table 2). Slightly less proportion of the cases were married or cohabitating than the controls (75.9 vs. 79.5%; p<0.005). The distribution of the potential risk factors for BC among the cases and controls are presented in Table 3.

Table 2 **Characteristics of cases and controls**

Characteristic	Cases, n (%) (n = 5102)		Controls, n (%) (n = 5520)	
Age				
< 40	590	(11.6)	631	(11.4)
40-49	1978	(38.8)	2151	(39.0)
50-59	1846	(36.2)	2020	(36.6)
60-69	558	(10.9)	564	(10.2)
≥ 70	130	(2.5)	154	(2.8)
Area of residence				
Hong Kong Island	740	(14.5)	817	(14.8)
Kowloon	1116	(21.9)	1215	(22.0)
New Territories	3246	(63.6)	3488	(63.2)
Marital status				
Married / cohabitating	3871	(75.9)	4388	(79.5)
Widowed / divorced	474	(9.3)	410	(7.4)
Never married	757	(14.8)	722	(13.1)
Education level				
Primary or below	994	(19.5)	1061	(19.2)
Secondary	2864	(56.1)	3153	(57.1)
Matriculation or above	1244	(24.4)	1306	(23.7)

A. Overall

Table 4 shows the results of the multiple logistic regression model adjusted for age. Fourteen out of the 15 factors being studied were found to be associated with BC in various directions. Among them, 11 factors were associated with an increased risk of BC, while three of them were associated with a decreased risk. Menopausal status was the only factor that was not found to have relationship with BC risk. The following sections describe the relationships of these factors in four categories.

i Non-modifiable factors

Results indicated that women having first-degree relative(s) suffering from BC (aOR=2.88; 95%CI, 2.43-3.41) or having early menarche (aOR=1.35; 95%CI, 1.19-1.52 comparing <12 years old vs. ≥12 years old) were associated with an increased risk of BC. Compared to women who had their first live birth at or before the age of 35, women who had first live birth after the age of 35 had a significantly higher risk of BC (aOR=2.06, 95%CI, 1.66-2.55), while nulliparous women were also at increased risk, but the increase was not statistically significant (Table 4).

Table 3 **Distribution of potential breast cancer risk factors between cases and controls**

Factor	Cases, n (%) (n = 5102)		Controls n (%) (n = 5520)	
Non-modifiable				
First-degree relative with breast cancer				
No	4533	(88.8)	5301	(96.0)
Yes	569	(11.2)	219	(4.0)
Age at menarche				
≥ Age 12	4238	(83.1)	4881	(88.4)
< Age 12	864	(16.9)	639	(11.6)
Age at menopause				
≤ Age 55	1982	(94.9)	2158	(97.1)
> Age 55	107	(5.1)	65	(2.9)
Reproductive history				
First live birth at age ≤ 35	3435	(67.3)	4102	(74.3)
First live birth at age > 35	266	(5.2)	156	(2.8)
No childbirth	1401	(27.5)	1262	(22.9)
Modifiable and lifestyle-related				
Physical activity				
≥ 3 hours per week	996	(19.5)	1574	(28.5)
< 3 hours per week	4106	(80.5)	3946	(71.6)
Stress				
Less than half the time	3018	(59.2)	4597	(83.3)
More than half the time	2084	(40.8)	923	(16.7)
Night duties (52 days or more in the past 12 months)				
No	5006	(98.1)	5358	(97.1)
Yes	96	(1.9)	162	(2.9)
Modifiable and behavioural-related				
Breastfeeding				
No	3559	(69.8)	3376	(61.2)
Yes	1543	(30.2)	2144	(38.8)
Diet				
Balanced diet	3535	(69.3)	4177	(75.7)
Vegetarian / vegetable rich	770	(15.1)	928	(16.8)
Meat or dairy product rich	797	(15.6)	415	(7.5)
Ever smoked				
No	4826	(94.6)	5308	(96.2)
Yes	276	(5.4)	212	(3.8)
Alcohol drinking				
Non-regular drinker	4849	(95.0)	5142	(93.2)
Regular drinker	253	(5.0)	378	(6.8)
Modifiable and medical-related				
Weight status				
Non-obese (BMI < 25)	3873	(75.9)	4621	(83.7)
Obese (BMI ≥ 25)	1229	(24.1)	899	(16.3)
Ever use of hormonal contraceptives				
No	3557	(69.7)	4202	(76.1)
Yes	1545	(30.3)	1318	(23.9)
Ever use of hormone replacement therapy				
No	4889	(95.8)	5352	(97.0)
Yes	213	(4.2)	168	(3.0)

ii Modifiable and lifestyle-related factors

Compared to women who had physical activity for three hours or more per week, those who had physical activity for less than three hours per week were more likely to be diagnosed with BC (aOR=1.53; 95%CI, 1.39-1.69) (Table 4). Stress is also a significant risk factor associated with BC in which women who self-reported having higher levels of stress were at higher risk (aOR=3.40; 95%CI, 3.09-3.73 comparing having stress for more than half of the time vs. less than half of the time). In contrast, women who had night shift duties for at least 52 nights in the past 12 months were associated with a lower risk of BC (aOR=0.48; 95%CI, 0.37-0.64).

iii Modifiable and behavioural-related factors

Regardless of the duration of breastfeeding, women who had ever breastfed had a 27% lower risk of BC than those who had never breastfed (aOR=0.73; 95%CI, 0.67-0.81). Results suggested that women who consumed diets which were rich in meat or dairy products had higher risk of getting BC than those who consumed balanced diets (aOR=1.80; 95%CI, 1.57-2.07) (Table 4). Ever smoking was found to increase a woman's risk of BC significantly (aOR=1.28, 95%CI, 1.04-1.56). On the other hand, women who regularly drank alcohol had decreased risk (aOR=0.57, 95%CI, 0.47-0.68) (Table 4).

iv Modifiable and medical-related factors

Obesity and ever use of hormonal contraceptives were both associated with increased risk of BC (Table 4). Obesity has been associated with a 46% increase in the risk of BC (aOR=1.46, 95%CI, 1.32-1.62). Without considering the duration of hormonal contraceptive use, women who had ever used hormonal contraceptives had 37% increased risk (aOR=1.37; 95%CI, 1.25-1.51).

B. Stratified by menopausal status

Further analyses were conducted for pre- and postmenopausal women separately (data not shown). Our analyses showed that the results obtained in the overall analyses also applied to premenopausal women. On the contrary, for postmenopausal women, in addition to the risk factors identified in the overall analyses, some additional factors were found to be associated with an increased or decreased risk of BC. Postmenopausal women who were vegetarian or had a vegetable rich diet had 21% reduced risk of BC (aOR=0.79, 95%CI, 0.66-0.93). Night shift was not found to be a significant risk factor for BC among postmenopausal women. In addition, nulliparous postmenopausal women had 38% increased risk of BC when compared to those who had fist live birth at or before the age 35 (aOR=1.38; 95%CI, 1.13-1.68). Furthermore, women who experienced menopause after the age of 55 was associated with an increased risk of BC (aOR=1.71; 95%CI, 1.21-2.41) while use of hormonal replacement therapy was not found to be associated with BC risk.

Table 4 **Associating factors of breast cancer by multiple logistic regression**

Factor	n	Adjusted Odds Ratio (95%CI)	p value
Non-modifiable			
First-degree relative with breast cancer			
No	9834	1	
Yes	788	2.88 (2.43, 3.41)	<0.001
Age at menarche			
≥ Age 12	9119	1	
< Age 12	1503	1.35 (1.19, 1.52)	<0.001
Menopausal status			
Premenopausal	6310	1	
Postmenopausal	4312	1.12 (0.98, 1.28)	0.089
Reproductive history			
First live birth at age ≤ 35	7537	1	
First live birth at age > 35	422	2.06 (1.66, 2.55)	<0.001
No childbirth	2663	1.10 (0.99, 1.23)	0.090
Modifiable and lifestyle-related			
Physical activity			
≥ 3 hours per week	2570	1	
< 3 hours per week	8052	1.53 (1.39, 1.69)	<0.001
Stress			
Less than half the time	7615	1	
More than half the time	3007	3.40 (3.09, 3.73)	<0.001
Night duties (52 days or more in the past 12 months)			
No	10364	1	
Yes	258	0.48 (0.37, 0.64)	<0.001
Modifiable and behavioural-related			
Breastfeeding			
No	6935	1	
Yes	3687	0.73 (0.67, 0.81)	<0.001
Diet			
Balanced diet	7712	1	
Vegetarian / vegetable rich	1698	0.97 (0.87, 1.09)	0.602
Meat or dairy product rich	1212	1.80 (1.57, 2.07)	<0.001
Ever smoking			
No	10134	1	
Yes	488	1.28 (1.04, 1.56)	0.019
Alcohol drinking			
Non-regular drinker	9991	1	
Regular drinker	631	0.57 (0.47, 0.68)	<0.001
Modifiable and medical-related			
Weight status			
Non-obese (BMI < 25)	8494	1	
Obese (BMI ≥ 25)	2128	1.46 (1.32, 1.62)	<0.001
Ever use of hormonal contraceptives			
No	7759	1	
Yes	2863	1.37 (1.25, 1.51)	<0.001

Discussion

This is the first large-scale case-control study to examine the factors associated for BC in Hong Kong women. Our study has provided local evidence that BC was associated with both non-modifiable and modifiable factors among local Chinese women.

In 2015, it was found that one in every four women suffering from cancers was diagnosed with breast cancer. Given that breast cancer is the most common cancer among women in Hong Kong and there is an increasing trend of incidence over the past two decades,[1] women should be aware of the significant risk factors for BC and take necessary actions for reducing their risk of BC. Our findings further support the Cancer Expert Working Group's (CEWG) recommendation on the primary prevention of BC: women should maintain a healthy lifestyle, especially by doing more physical activity, having a balanced diet, maintaining a healthy weight / body mass index, and avoiding stress, in order to reduce their risk of getting BC.[9] Our data supported these strategies in the hope of reducing the incidence of BC in Hong Kong.

To mitigate the threat and sequelae of BC, simply taking primary preventive actions to reduce the risk of breast cancer development is not enough. Secondary prevention such as breast screening should also be deployed in order to detect cancer early. Currently, the CEWG only recommends local women having family history of BC (regarded as "high risk") to undergo regular breast screening.[9] However, our study provided evidence that other factors were also significantly associated with an increased risk of BC. These identified factors are often common behaviours among women in the local community such as having high levels of stress, lack of exercise, or having diets rich in meat / dairy products. In addition, a recent Taiwan study[10] revealed that universal biennial mammography screening was associated with a 41% mortality reduction and 30% reduction of stage II+ BC, much more efficient than risk-based mammography screening, when both were compared with annual clinical examination. Therefore, secondary preventive measures such as breast screening should not be confined to women having family history of breast cancer, those who harbour the significant risk factors should also undergo regular breast screening in order to detect cancer early and reduce mortality by shifting of staging.

Unexpectedly, our study found that night shifts and alcohol drinking were both associated with decreased risk of BC. The possible explanation for this is that our sample size were not large enough to observe the associations of these two factors with BC. We found that only a small proportion of subjects reported having these two risk factors (around 3% for night shift and 7% for alcohol drinking).

Various BC risk assessment tools / models have been developed worldwide to estimate the risk of developing BC for a women incorporating with known risk factors.[11-14] Validation of these models have predominantly been done in Western countries, but the BC risk using these models was consistently overestimated in Asian countries, such as Singapore,[15] Korea[16] and China.[17] Using the results obtained from this study, future studies aiming to develop a predictive model for BC among local Chinese women will be conducted.

The strength of the current study is our BC patients are recruited from both private and public healthcare centres throughout the territory, therefore data of a wide array of patients with varying demographics are collected and analyzed. Similarly, our controls are recruited at different time and venue throughout the territory by systematic random sampling method. Therefore, we believe that the results of this study is applicable to represent the female population in Hong Kong in making relevant decision on breast cancer control.

One of the limitations of this study is that some of the factors are reported subjectively and are difficult to be quantified, e.g. stress. The level of stress reported by a particular woman may not be equal to that reported by another woman, though they are regarded as having the same level of stress in the study. Further quantitative study is warranted to look into the relationships between stress and BC. Furthermore, our study investigated the relationships of the 15 factors with BC only. The factors affecting a woman's risk of BC in real life can be more complex and the factors may have interactions with each other.

Conclusion

The study has provided local evidence that BC is associated with both non-modifiable and modifiable factors among local Chinese women. Women should be encouraged to take primary preventive actions, i.e. maintaining a healthy lifestyle, in order to reduce their risk of BC, which in turn may reduce the incidence of BC in Hong Kong. In addition, women should be breast aware and seek medical help promptly if they found abnormalities in their breasts. Women who harboured the significant non-modifiable and/or modifiable risk factors should undergo regular breast screening in order to detect cancer early and reduce mortality by shifting of staging.

References

(Please refer to Chinese version)

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