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Risk factors for breast cancer

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Risk factors for breast cancer*

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An unmatched case-control study of 275 breast cancer patients and 503 controls was conducted at Chulalongkorn Hospital and the National Cancer Institute during October 1984 to September 1986. The objective was to study the risk factors for breast cancer in Thai women. The result of this study suggests that the risk factors include women aged > 60 years, women educated for \leq 12 years, women of low socio-economic class, single - status women (in those \geq 45 years). separated/divorced/widowed status among premenopausal women, and nulliparous or women whose parity was < 4. However, women whose frist pregnancy occurred at \geq 25 years or whose use of the oral untrauphive pills was \geq 5 years seems to be associated with an increased risk but is not significant. Obesity, fondness of fatty foods and family history of breast cancer do not show any increased risk of breast cancer. The study also shows that the appropriate knowledge and understanding, as well as regular self - examination have some protective effects against breast cancer.

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ทศสนี นุชประยูร, เต็มศรี ชำนิจารกิจ, บรรเททอง รัชตะปิติ, กิติ จินดาวงษ์, พรณรงค์ โชติวรรณ, สมรัตน์ เลิศมหาฤทธิ์. ปัจจัยเสี่ยงของมะเร็งเต้านม. จุฬาลงกรณ์เวชสาร 2533 เมษายน; 34(4) : 287-295

การศึกษาหาปัจจัยเสี่ยงของมะเร็งเต้านมในหญิงไทย โดยออกแบบการศึกษาชนิด *Unmatched case-control* ผู้ป่วยมะเร็งเต้านม (*cases*) 275 ราย และ *controls* 503 ราย ได้จากภาควิชาศัลยศาสตร์ โรงพยาบาลจุฬาลงกรณ์ และแผนกศัลยกรรม สถาบันมะเร็งแห่งชาติ ระหว่าง ตุลาคม 1984 ถึงกันยายน 1986 โดยการซักประวัติย้อนหลังถึงปัจจัยต่าง ๆ ที่อาจเป็นสาเหตุ การตรวจร่างกายทั่วไป การตรวจเต้านม รวมทั้งการทำ *mammogram* และการตรวจชิ้นเนื้อจากเต้านมทางพยาธิวิทยาหลังการผ่าตัด สรุปได้ว่าปัจจัยเสี่ยงของมะเร็งเต้านมจากการศึกษานี้ ได้แก่ หญิงอายุสูงกว่า 60 ปี การศึกษาสูงสุดไม่เกินระดับมัธยมศึกษา (≤ 12 ปีการศึกษา) รายได้ของครอบครัวต่ำ ($\leq 10,000$ บาท/เดือน) หญิงโสดที่อายุตั้งแต่ 45 ปีขึ้นไป หญิงหย่า/แยก/หม้าย ในขณะที่ประจำเดือนยังไม่หมด และหญิงที่มีบุตรน้อยกว่า 4 คน ส่วนหญิงที่มีลูกคนแรกเมื่ออายุตั้งแต่ 25 ปีขึ้นไป และหญิงที่กำลังใช้ยาเม็ดคุมกำเนิดติดต่อกันตั้งแต่ 5 ปี ขึ้นไป แม้จากการศึกษาจะแสดงว่าเสี่ยงต่อการเกิดมะเร็งเต้านมแต่ไม่มีนัยสำคัญทางสถิติ

ความอ้วน ความชอบอาหารประเภทมัน ๆ และประวัติการเป็นมะเร็งเต้านมในครอบครัว จากการศึกษานี้ไม่ปรากฏว่าเสี่ยงต่อการเกิดมะเร็งเต้านม นอกจากนี้ยังพบว่าความรู้ที่ถูกต้องและการตรวจมะเร็งเต้านมด้วยตนเองจะช่วยลดการเสี่ยงต่อการเป็นมะเร็งเต้านมได้ด้วย

ได้รับทุนอุดหนุนการวิจัย สถาบันวิจัยวิทยาศาสตร์การแพทย์ จุฬาลงกรณ์มหาวิทยาลัย

Breast cancer is the second most common cancer found in Thai women.⁽¹⁾ Morbidity and mortality rates of breast cancer in 1984⁽²⁾ were 4.6 and 0.8 per 100,000 population respectively. Previous epidemiological studies in western countries have shown a relationship between breast cancer and the reproductive factors,⁽³⁻⁵⁾ That is, age at first pregnancy, number of parity, early menarche, late menopause etcetera. Buell P. 's study showed that Japanese women, following their migration to USA, had an increase in incidence of breast cancer compared with Japanese women living in their own country.⁽⁶⁾ the WHO⁽⁷⁾ concluded that 80% of the risk factors were due to environmental factors. The purpose of our investigation was to study the risk factors of breast cancer in Thai women and to compare the results of this study to the previous studies.

subjects and Methods

The study was an unmatched case control study, conducted at Chulalongkorn Hospital and at the National Cancer Institute.

Cases were women who attended the surgical clinic and were admitted for work up and treatment at Chulalongkorn Hospital and the National Cancer Institute Clinic during October 1, 1984 to September 30, 1986. They had to meet the following criteria:

(1) newly diagnosed breast cancer, comprising the following criteria:

- palpable mass in either one or both breasts.
- axillary lymph glands may or may not be enlarged.
- Suspicion of CA by mammography.
- pathologically confirmed histology after operation.

(2) Aged 30-70 years.

Controls were defined as women, aged 30-70 years, who sought the medical services at either Chulalongkorn Hospital or the National Cancer Institute during the same period of Cases' hospitalization but were diagnosed by the attending physician as healthy women or ill with minor ailments, not associated with breast diseases. Most of the controls came for check up and were not limited to any single illness.

Data was obtained from cases and controls by trained interviewers, using structured questionnaires which comprised personal characteristics, medical and reproductive history, contraceptive use, family history, of breast cancer general knowledge and whether self examination of breasts was practiced and fondness for fatty foods. In addition to weight and height recordings, the physical examination of breast tissue was performed by the attending physician. the women who had a suspected mass in breast were sent for mammography and operation. The section of the mass was confirmed pathologically.

Sample size :

By using the formula, $n = 2 \frac{\bar{p}\bar{q}}{pq} (Z_{\alpha} + Z_{\beta})^2 / (P_1 - P_0)^2$

Assumption : $P_0 = .20$ $RR = 2.0$

$\alpha = .05$ $\beta = .10$

Calculation : $P_1 = \frac{P_0 R}{1 + P_0(R - 1)}$
 $= \frac{.20 \times 2}{1 + .20(2 - 1)}$
 $= .333$

$\bar{p} = \frac{1}{2} (P_1 + P_0)$
 $= \frac{1}{2} (.33 + .20)$
 $= .27$

$n = 2 \frac{\bar{p}\bar{q}}{pq} (Z_{\alpha} + Z_{\beta})^2 / (P_1 - P_0)^2$
 $= 2 (.27) (.73) (1.96 + 1.28)^2 / (.33 - .20)^2$
 $= .39 \times 10.50 / .02$
 $= 232$

Cases : controls = 1 : 2

Results

A total of 275 cases and 503 controls were recruited in this study which was conducted between

October 1984 - September 1986. 46% of cases and 58.3% of controls were from Chulalongkorn Hospital; the remainder were from the National Cancer Institute. (Table 1)

Table 1. SOURCE OF DATA AMONG BREAST CANCERS (CASES) AND CONTROLS.

| | CASES | CONTROLS |
|------------------------------|-------------|-------------|
| Source of data (Total) | 275 (100%) | 503 (100%) |
| - Chulalongkorn Hospital | 126 (45.8%) | 293 (58.3%) |
| - National Cancer Institute | 149 (54.2%) | 40 (41.7%) |
| Area of Residence | | |
| - Bangkok Metropolis | 105 (38%) | 249 (49.5%) |
| - Other parts of the country | 171 (62%) | 254 (50.5%) |

Cases and controls were similar in various aspects, i.e. nationality, religion and the median age (cases 47.2, controls 46.2). Women with 4 years of education constituted about 50% in each group. Differences found among the groups were marital status, occupation, family income, menstrual history and fondness for fatty food (Table 2). The most striking finding was that apart from marital status, all the other differing factors were shown to be associated risk factors of breast cancer. For example; women who has ≤ 12 years education had a crude risk of having breast cancer 1.68 times higher than that of women who had > 12 years education. The risk of developing

breast cancer in women whose occupation was agricultural or manual labour was twice higher than that of housewives. The spouses' occupation also mattered, those who were agricultural workers or labourers also had a crude risk of breast cancer of 1.78 relative to 1.0 of those who were officers, traders and firm workers. Interestingly, those women whose spouses were unemployed also had higher risk of developing breast cancer (RR = 1.96). Those with a family income of less than 10,000 B/month, and those with no definite income or very, very low income had 1.9 and 2.8 times the risk of breast cancer respectively. (Table 3)

Table 2. General characteristics of breast cancers (cases) and controls.

| Characteristics | Cases | Controls |
|--|----------------|----------------|
| 1. Present age (years) $\bar{X} \pm SD$ | 47.2 \pm 8.6 | 46.2 \pm 8.5 |
| 2. Nationality : Thai (%) | 86.5 | 84.7 |
| 3. Religion : Buddhist (%) | 97.1 | 96.8 |
| 4. Marital status : married (%) | 67.6 | 74.4 |
| 5. Education : grade 4 (%) | 50.5 | 50.5 |
| 6. Occupation : Housewife (%) | 38.0 | 30.0 |
| 7. Family income < 10,000 B/month (%) | 78.5 | 69.5 |
| 8. Menstrual status - Menopause (%) | 42.2 | 36.6 |
| 9. Quetelet's index : ≥ 25 (%) | 21.5 | 20.9 |
| 10. Fondness for fatty, foods (%) | 34.2 | 38.6 |

Table 3. Age, education, occupation, family income among cases & controls.

| Variables | Cases | Controls | RR | 95% CI RR |
|---|-------|----------|------|------------|
| 1. Age at diagnosis (years) | | | | |
| ≤ 45 | 126 | 258 | 1.0 | — |
| 46 – 60 | 125 | 217 | 1.2 | 0.9-1.7 |
| > 60 | 25 | 28 | 1.8 | 1.03-3.1* |
| 2. Education (years) | | | | |
| 2.1 their own | | | | |
| ≤ 12 | 242 | 398 | 1.68 | 1.21-2.03* |
| > 12 | 33 | 105 | 1.05 | — |
| 3. Occupation | | | | |
| 3.1 their own | | | | |
| - housewife | 77 | 151 | 1.0 | — |
| - agricultural workers/labourers | 98 | 97 | 1.98 | 1.3-2.9* |
| 3.2 of spouse | | | | |
| - waiting for work | 18 | 22 | 1.96 | 1.02-3.8* |
| - Agricultural workers/labourers | 75 | 101 | 1.78 | 1.2-2.6* |
| - officers/traders/firm workers | 108 | 259 | 1.0 | — |
| 4. Family income (฿/month) No definite income | 15 | 20 | 2.83 | 1.1-4.9* |
| < 10,000 | 216 | 352 | 1.90 | 1.29-2.81* |
| ≥ 10,000 | 40 | 124 | 1.0 | — |

In this study, age at menarche, age at first pregnancy, marital status and age at menopause were not shown to be associated with an increased risk of breast cancer (Table 4). Single women in the ≥ 45 age group had 2.1 times of the risk of breast cancer compared to those who were married. In the premenopausal group, it was found that women who were separated/divorced/widowed were 2.3 times the risk of developing breast cancer compared to that of married women with statistical significance (Table 4).

Women who had borne no child were at higher risk (1.6 times) while those who had 1 to 4 children (1.4 times) compared to women who had more than 4 children (Table 4). The crude risk of breast cancer for current OC. users of > 5 years was 2 times higher than that of current non OC. users but with no statis-

tical significance (Table 5).

there was no difference in risk status between women who were obese (Quetelet's index ≥ 25) and those who were not (Quetelet's index < 25). Fondness for fatty foods was not shown an increased risk of breast cancer (Table 6).

Women who had the right knowledge and practiced self examination of the breasts had a crude risk of breast cancer of 0.38 and 0.53 relative to 1.0 of those without knowledge and who did not self-examine respectively (Table 7).

Cases who had a family history of breast cancer in this study appeared to have a similar risk of developing breast cancer as did those with no family history (Table 8).



Table 4. Reproductive History Among Cases and Controls,

| Variables | Cases | Controls | RR | 95% CIRR |
|---|----------------|----------------|------|-------------|
| 1. Age at menarche (years) | | | | |
| $\bar{X} \pm SD$ | 14.7 \pm 1.7 | 14.8 \pm 1.7 | | |
| Range | 11 - 20 | 10 - 20 | | |
| \leq 12 | 18 | 30 | 1.03 | 0.5 - 1.9 |
| 13 - 15 | 176 | 302 | 1.0 | — |
| $>$ 15 | 73 | 147 | 0.85 | 0.6 - 1.2 |
| 2. Marital status | | | | |
| 2.1 total women | | | | |
| single | 42 | 52 | 1.43 | 0.93 - 2.20 |
| married | 186 | 374 | 1.00 | — |
| separated/divorced/widowed | 47 | 70 | 1.35 | 0.90 - 2.03 |
| 2.2 only among women aged \geq 45 years | | | | |
| single | 21 | 18 | 2.1 | 1.1 - 3.9* |
| married | 93 | 174 | 1.0 | — |
| separated/divorced/widowed | 36 | 53 | 1.0 | 0.8 - 2.2 |
| 2.3 only among premenopausal group | | | | |
| single | 28 | 44 | 1.5 | 0.8 - 2.7 |
| married | 112 | 255 | 1.0 | — |
| separated/divorced/widowed | 20 | 20 | 2.3 | 1.2 - 4.4* |
| 3. Age at first pregnancy | | | | |
| $\bar{X} \pm SD$ | 22.6 \pm 7.9 | 21.8 \pm 7.2 | | |
| $<$ 25 years | 109 | 254 | 1.0 | — |
| 25 - 29 years | 64 | 113 | 1.32 | 0.83 - 2.13 |
| \geq 30 years | 24 | 36 | 1.55 | 0.89 - 2.70 |
| 4. Numbers of pregnancy | | | | |
| $\bar{X} \pm SD$ | 3.7 \pm 2.6 | 4.3 \pm 4.0 | | |
| 0 | 57 | 85 | 1.6 | 1.4 - 1.8* |
| 1 - 4 | 144 | 242 | 1.4 | 1.3 - 1.5* |
| $>$ 4 | 74 | 176 | 1.0 | — |
| 5. Age at menopause (years) | | | | |
| $\bar{X} \pm SD$ | 47.2 \pm 5.0 | 48.1 \pm 5.1 | | |
| $<$ 40 | 6 | 8 | 1.0 | — |
| 40 - 44 | 17 | 23 | 0.99 | 0.37 - 2.65 |
| 45 - 49 | 43 | 51 | 1.12 | 0.37 - 3.40 |
| \geq 50 | 37 | 77 | 0.64 | 0.21 - 1.96 |

* statistical significance at $\alpha = .05$ **Table 5.** Duration of current use of oral contraceptives among cases and controls.

| Duration of current OC users | Cases | Controls | RR | 95% CIRR |
|------------------------------|-------|----------|-----|-------------|
| $<$ 5 years | 3 | 16 | 0.5 | 0.4 - 1.78 |
| \geq 5 years | 9 | 12 | 2.0 | 0.81 - 4.91 |
| 0 | 51 | 137 | 1.0 | — |

Table 6. Nutritional status by Quetelet's index (wt/ht²) and fondness of fatty foods.

| | Cases | Controls | RR | 95% CIRR |
|---|-------|----------|------|-------------|
| 5.1 Quetelet's index (Kg/m ²) | | | | |
| < 25 | 142 | 226 | 1.0 | — |
| ≥ 25 | 59 | 105 | 0.89 | 0.59 - 1.32 |
| 5.2 Fondness of fatty foods | | | | |
| yes | 94 | 194 | 0.85 | 0.61 - 1.17 |
| no | 165 | 291 | 1.0 | — |

Table 7. Knowledge and practice in self examination of breast.

| | Cases | Controls | RR | 95% CIRR |
|---------------------------|-------|----------|------|--------------|
| 6.1 Appropriate Knowledge | | | | |
| Yes | 71 | 192 | 0.38 | 0.27 - 0.53* |
| No | 203 | 209 | 1.0 | — |
| 6.2 Practice | | | | |
| Yes | 69 | 194 | 0.53 | 0.38 - 0.73* |
| No | 206 | 307 | 1.0 | — |

* statistical significance at $\alpha = .05$

Table 8. Family history of breast cancy

| Family history | Cases | Controls | RR | 95% CIRR |
|----------------|-------|----------|------|-------------|
| Yes | 6 | 11 | 0.99 | 0.18 - 5.23 |
| No | 270 | 492 | 1.0 | — |

* Statistical significance at $\alpha = 0.05$ หรือ

* $P < .05$

Discussion

Among 275 cases of breast cancer, 38% lived in Bangkok while the other 62% came from different parts of the country. This information suggests that both studied institutions are well known and well-equipped with a high referral rate for diagnosis and treatment of breast cancer. Hence they are ideal places for this study.

The mean age at menarche as well as the mean age at menopause for both with cases and controls were nearly equal despite the fact that 38% of cases and 50% of controls were from Bangkok Metropolis.

Although the mean age of cases (47.2 years) and controls (46.2 years) were very close, there was quite a difference in the distribution of cases and controls in each age group categories (Table 3). The risk of developing breast cancer in women aged 46-60 years was 1.2 times that of women aged ≤ 45 years, but was not of statistical significance, while the risk of breast cancer in women aged over 60 is 1.8 times significantly higher than that of women ≤ 45 years. This finding supports the previous studies of Adami Ho et al⁽⁸⁾ and Jerzy Staszewski⁽⁹⁾ but is different from Jennifer L Kelsy's⁽¹⁰⁾

According to the socio-economic status shown in Table 3, it is suggested that low socio-economic status is one of the risk factors of breast cancer. Although the result of this study is quite different from that by Jennifer L Kelsy⁽¹⁰⁾ and other previous studies done in Western countries⁽¹¹⁻¹⁴⁾ it can be explained that this may only reflect the main picture of developing countries where this study was conducted. Lin T.M. et al's study in Taiwan also showed similar results regarding the risk of breast cancer due to low socio-economic status⁽¹⁵⁾.

In the present study, early menarche and late menopause do not appear to influence the risk of breast cancer which is contrary to the study of Staszewski⁽⁹⁾ but agree with others^(5,8,16,17) Higher rate of breast cancer was found in women having 1-4 pregnancies (RR 1.4), with progressively higher (RR 1.6) among zero number of pregnancy. This finding agrees with a previous study which showed excessive risk of breast cancer in nuns⁽¹⁹⁾ and the conclusion of Stock⁽²⁰⁾ in 1957 indicated that multiple pregnancies might be protective against breast cancer.

It has been documented that single versus married differential is a post menopausal phenomenon. Our finding also showed that only among women aged ≥ 45 years who were single was these a 2.1 times the risk of breast cancer compared to married women with

statistical significance. Disregarding age as a confounding factor, although women of single as well as separated/divorced/widowed status seem to have an increased risk of breast cancer, it was of no statistical significance. In addition, premenopausal women of separated/divorced/widowed status have a significant increase in the risk of breast cancer.

The present study showed that women whose duration of current use of oral contraceptives was 5 years or more had twice the risk of breast cancer but was of no statistical significance. We do not have adequate data to evaluate the risk among different age groups using oral contraceptives. Thus, this study cannot substantiate earlier doubt that OC increases the risk in certain groups of women.

Family history as well as a dietary practice^(5,11,14,24-26) did not influence the risk of breast cancer. Since this data consisted of a small number of study subjects it was not possible to classify the relationships into particular family subgroups.

Nevertheless, it is noteworthy that appropriate knowledge and self-examination of the breasts appear to be associated with a protective effect against breast cancer.

Conclusion

The mean age at menarche of Thai female subjects in this study was 14.8 ± 1.7 (range 10-20 years). and the mean age at menopause was 47.7 ± 5.1

The risk factors of breast cancer from this study can be summed up as follows:

- (1) Women aged over 60 years.
- (2) Women whose education was only for 12 years or less.
- (3) Low socio-economic status of family.
- (4) Single women, only among women aged 45 years.
- (5) Separated/divorced/widowed status, in the premenopausal group.
- (6) Number of pregnancies ≤ 4 ; in particular if no previous pregnancy.

Age at first pregnancy ≥ 25 years, current OC users ≥ 5 years seem to be associated with an increased risk of breast cancer but of no statistical significance.

Obesity, Fondness of fatty foods do not show the increase risk of breast cancer.

Positive family history of breast cancer appears not to be an associating risk factor.

Appropriate knowledge and Self examination of the breasts gives protective effect against breast cancer.

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