Risk factors of breast cancer in women in Kelantan, Malaysia

B Norsa'adah, B N Rusli, A K Imran, I Naing, T Winn

ABSTRACT

Introduction: Breast cancer is the commonest cancer for females in Malaysia, with a prevalence of 86.2 per 100,000 women in 1996. Breast cancer mortality rate shows an increasing trend in Malaysia from 0.61 in 1983 to 1.8 per 100,000 women in 1992. The aim of this study was to identify the risk factors for breast cancer in women in Malaysia.

Methods: A matched case-control study was carried out at referral hospitals in Kelantan from July 2000 to June 2001. A standardised questionnaire that comprised socio-demographical factors, obstetrical and gynaecological histories, anthropometric measurements, and other potential risk factors for breast cancer, was used to interview 147 histologically-confirmed breast cancer patients and 147 controls. Controls were non-breast cancer patients who were matched for age and ethnicity, and excluded those with malignancies, or having gynaecological, hormonal or endocrine problems. Simple and multiple conditional logistic regressions were used for analyses.

Results: Factors contributing toward increased risk of breast cancer were nulliparity (odds ratio [OR] of 15.3; 95 percent confidence interval [CI] of 3.2, 72.4), overweight (OR of 2.1; 95 percent CI of 1.1, 3.9), family history of breast cancer (OR of 4.3; 95 percent CI of 1.3, 14.1) and previous use of oral contraceptives (OR of 2.5; 95 percent CI of 1.3, 4.8).

Conclusion: This study reconfirmed that similar risk factors identified in Western populations were responsible for the occurrence of breast cancer in Kelantan. It also supported the theory that breast cancer occurrence was related to oestrogen exposure and familial factors. It suggested the importance of having children, maintaining ideal body weight and caution for oral contraceptive users and women with a family history of breast cancer.

Keywords: breast cancer, cancer risk factors, oestrogen exposure, oral contraceptive

Singapore Med J 2005; 46(12):698-705

INTRODUCTION

Breast cancer is the commonest cancer among women in Malaysia, with a prevalence of 86.2 per 100,000 women in 1996[1]. The incidence rate of breast cancer in 1996 was 23.8 per 100,000[2]. Chinese had the highest age-standardised rate (70.1 per 100,000), compared to Malays (41.0 per 100,000) and Indians (61.7 per 100,000)[3]. Breast cancer comprised 30.4% of all female cancers in Malaysia in 2002[3]. This was higher compared to previous reports in Sabah with 18%[4], Kuala Lumpur (10.7% to 13.8%), and Singapore with 13%[5]. The trend in breast cancer mortality in Malaysia had been increasing from 0.6 in 1983 to 1.8 per 100,000 women in 1992[6]. Data from population-based Singapore Cancer Registry revealed an average increase of 3.6% incidence rate over the 25-year period[7].

The risk factors for breast cancer in Western populations had been extensively investigated, and it has been suggested that lifestyle-related and reproductive factors were strongly associated with breast cancer. In contrast, less information exists regarding factors that are associated with breast cancer in Asian women. In Singapore, Ng et al[8] found the same risk factors that were responsible for the higher incidence of breast cancer in Western populations, and also explained the rise of breast cancer incidence in Singapore.

The aim of this study was, therefore, to identify risk factors of female breast cancer in Malaysia. Determining the risk factors in breast cancer offers hopeful promise of modifying those factors, thus preventing breast cancer occurrence. Some of the breast cancer risk factors could be modified either through behavioural or environmental changes.

Unit of Biostatistics and Research Methodology
School of Medical Sciences
Universiti Sains Malaysia
Kubang Kerian
16150 Kota Bharu
Malaysia

B Norsa'adah, MBBS, MComMed
Medical Lecturer

School of Dental Sciences
Universiti Sains Malaysia

B N Rusli, MPH, PhD
Professor

L Naing, MPH, MMedStats
Medical Lecturer

Department of Surgery
Kota Bharu Hospital
15586 Kota Bharu
Malaysia

A K Imran, MBBS, FRCP
Surgeon

Department of Community Medicine
School of Medical Sciences
Universiti Sains Malaysia

T Winn, MPH, DrPH
Medical Lecturer

Correspondence to:
Dr Norsa'adah Binti Bachok
Tel: (60) 9766 4896
Fax: (60) 9765 3370
Email: norsaadah@kb.usm.my

Table I. Socio-demographical characteristics of the subjects.

Socio-demographic characteristics	Cases (n=147)		Controls (n=147)		p-value[a]
	No.	%	No.	%	
Age at diagnosis (in years)					0.6536
26-40	37	25.2	40	27.2	
41-55	88	59.9	83	56.5	
56-70	22	15.0	24	16.3	
Education level					0.3601
None	24	16.3	15	10.2	
Primary school	34	23.1	40	27.2	
Lower secondary (form 1-3)	16	10.9	23	15.6	
Upper secondary (form 4-6)	62	42.2	58	39.5	
Diploma/degree	11	7.5	11	7.5	
Occupation					0.3006
Housewife/unemployed	84	57.1	91	61.9	
Self-employed	11	7.5	11	7.5	
Civil servant	40	27.2	35	23.8	
Private sector	12	8.2	10	6.8	
Marital status					0.0141
Single	10	6.8	1	0.7	
Married	113	76.9	129	87.8	
Divorced	5	3.4	4	2.7	
Widowed	19	12.9	13	8.8	
Monthly household income (in Malaysian ringgit)					0.5329
0-1,000	90	61.2	87	59.2	
1,001-2,000	35	23.8	31	21.1	
≥2,001	22	15.0	29	19.7	

[a] LR test, simple conditional logistic regression.

METHODS

The study design was matched hospital-based case-control study. Cases were female patients with histologically-confirmed primary breast cancer according to the International Classification of Diseases for Oncology[9]. Cases were recruited from inpatients and outpatients at oncology and radiotherapy clinics or surgical clinics in two referral hospitals in the east coast of Malaysia, diagnosed between 1991 and 2000. Exclusion criteria for cases were male patients and those who had cognitive problems.

Control subjects were matched one for one with age (within 5 years) and same ethnicity. They were patients attending the same hospitals. Exclusion criteria for controls were those with known malignant, hormonal, gynaecological or endocrine diseases. Standardised structured questionnaires were developed and used for the interview. The questionnaires were divided into several sections comprising socio-demography, anthropometric measurements, reproductive history and established and potential risk factors for breast cancer.

Age at menarche was defined as the chronological age when the woman first had her menses. Age at menopause was defined as the chronological age at which the woman developed amenorrhoea of at least six months duration prior to the date of interview. Age at first full-term pregnancy was defined as the age of the woman at the last date of her first pregnancy that extended into completed 28 weeks, regardless of the outcome of the pregnancy. First-degree relatives included sister, mother or daughter while distant relatives include other than first-degree relative, i.e. grandmother, granddaughter, aunt or niece, who has had breast cancer. The women were considered to have previously used oral contraceptives (OC), hormone replacement therapy (HRT), traditional herbal medication, vitamins, or mineral supplement if they took them regularly for at least a month. Traditional herbal medication was defined as the usage of crude plant-based products or roots or leaves to prevent or cure a disease or ailment[10].

All data entry and analyses were conducted using STATA 7[11]. Means and standard deviations (SD) for continuous variables and frequencies and percentages for categorical variables were calculated. Differences of proportions between cases and controls for categorical variables were analysed by simple conditional logistic regression. The p-values of the likelihood-ratio (LR) test were used. Crude odds ratios (OR) for variables in the model were also drawn from simple conditional logistic regression. The level of significance was set at p less than 0.05 for all hypotheses tests in this study.

Significant predictors for breast cancer were determined using multiple conditional logistic regression analysis in order to control possible confounders, test interactions and take into account the matched sampling. All variables were included in the saturated model of multivariate analysis. All possible risk factors were independent variables and cases and controls were the dichotomous binary outcomes. The analysis was started by removing the largest p-value one at a time and tested for their significance using the LR test to confirm that they were truly significant in the model. If the LR test was significant, the variables will be put back in the model. After confirming the main-effect model, possible two-way interactions were checked by using the LR test. The final model was tested for fitness by using Hosmer-Lemeshow goodness-of-fit test. The adjusted odds ratios were estimated with 95% confidence intervals (CI).

RESULTS

A total of 147 female patients with histologically-confirmed primary breast cancer were interviewed. The most common histological type was infiltrative

ductal carcinoma (73%). Presentation of breast cancer at stage III or IV was 60%. The age of breast cancer patients ranged from 28 to 70 years. The mean age was 46.3 (SD 9.3) years. Table I shows the socio-demographical characteristics of the subjects. There were no significant differences in age, education level, occupation and monthly household income between cases and controls. Breast cancer patients had significantly more single women (6.8%) and less married women (76.9%) compared to controls (0.7% and 87.8%, respectively) (p=0.0141).

Table II shows the reproductive characteristics of the subjects. There was no significant difference between cases and controls in the number of abortions, age attained at menarche, menopausal status, age attained at menopause, and menstrual cycle. However, number of children (p<0.0001), parity status (p<0.0001) and breastfeeding practice (p<0.0001) were found to be highly significant. Table III shows the anthropometrical measurements of the subjects. There was no significant difference between cases and controls in relation to height and weight. However, there was a significant difference between cases and controls in relation to their body mass index (BMI) (p=0.0212).

The univariate analyses of risk factors of female breast cancer are shown in Table IV. There were significant differences between cases and controls in terms of family history of breast cancer (p=0.0018), regular use of OC (p=0.0208) and history of bilateral oophorectomy (p=0.0245). There were no significant differences between cases and controls in regular use of HRT, vitamins, micronutrient supplements or traditional medication, smoking cigarettes, alcohol intake, previous histories of benign breast disease and breast biopsy.

Table V shows the results of multiple conditional logistic regression analysis of risk factors of female breast cancer. The odds of having breast cancer for nulliparous women were 15.3 times higher (95% CI: 3.2-72.4) than those of women who had more than two children. The odds of having breast cancer for women who had BMI of 25 or more were 2.1 times higher (95% CI: 1.1, 3.9) than the odds of women whose BMI of less than 18.5. The odds of having breast cancer for women with family history of breast cancer were 4.3 times higher (95% CI: 1.3, 14.1) than those of women with no family history. The odds of having breast cancer for women who had regularly used OCs were 2.5 times higher (95% CI: 1.3, 4.8) than those of women who had not regularly used OCs.

Table II. Reproductive characteristics of the subjects.

Reproductive characteristics	Cases (n=147)		Controls (n=147)		p-value[a]
	No.	%	No.	%	
Number of abortions					0.1555
0	96	65.3	95	64.6	
1	38	25.9	30	20.4	
≥2	13	8.8	22	15.0	
Number of children					<0.0001
0	22	15.0	2	1.4	
1-2	30	20.4	21	14.3	
>2	95	64.6	124	84.8	
Parity status (in years)					<0.0001
Parous ≤30	112	76.2	137	93.2	
Parous >30	13	8.8	8	5.4	
Nulliparous	22	15.0	2	1.4	
Average duration of breastfeeding (in years)					<0.0001
0	35	23.8	8	5.4	
>0-≤1	21	14.3	28	19.0	
>1	91	61.9	111	75.5	
Age at menarche (in years)					0.3157
≤11	10	6.8	6	4.1	
12-16	133	90.5	136	92.5	
>16	4	2.7	5	3.4	
Menopausal status					0.8185
Pre-menopause	107	72.8	108	73.5	
Post-menopause	40	27.2	39	26.5	
Age at menopause (in years)					0.2817
≤50	25	62.5	21	53.8	
>50	15	37.5	18	46.2	
Menstrual cycle					0.6802
Regular	115	78.2	118	80.3	
Irregular	32	21.8	29	19.7	

[a] LR test, simple conditional logistic regression.

Table III. Anthropometrical measurements of the subjects.

Anthropometrical measurement	Cases (n=147)		Controls (n=147)		p-value[a]
	No.	%	No.	%	
Height at diagnosis (in metres)					0.0583
≤1.55	97	66.0	81	55.1	
>1.55	50	34.0	66	44.9	
Weight at diagnosis (in kg)					0.5639
30-54	60	40.8	52	35.4	
55-79	80	54.4	85	57.8	
80-104	7	4.8	10	6.8	
Body mass index at diagnosis (kg/m^2)					0.0212
Underweight (<18.5)	18	12.2	9	6.1	
Normal (18.5-24.9)	56	38.1	79	53.7	
Overweight/obese (≥25.0)	73	49.7	59	40.1	

[a] LR test, simple conditional logistic regression

Table IV. Univariate analyses of risk factors for breast cancer.

Risk factor	Cases (n=147)		Controls (n=147)		p-value[a]
	No.	%	No.	%	
Family history of breast cancer					0.0018
None	123	83.7	141	95.9	
First degree relative	9	6.1	1	0.7	
Distant relative	15	10.2	5	3.4	
Oral contraceptive pills					0.0208
Ever use	53	36.1	36	24.5	
Never use	94	63.9	111	75.5	
Hormone replacement therapy					0.1480
Ever use	2	1.4	6	4.1	
Never use	145	98.6	141	95.9	
Regular intake of vitamin/ supplement					
Yes	41	27.9	45	30.6	0.5928
No	106	72.1	102	69.4	
Regular intake of traditional medication					0.7179
Yes	71	48.3	74	50.3	
No	76	51.7	73	49.7	
Ever smoke cigarettes					0.7386
Yes	6	4.1	5	3.4	
No	141	95.9	142	96.6	
Regular intake of alcohol					0.7050
Yes	5	3.4	4	2.7	
No	142	96.6	143	97.3	
Previous benign breast disease					1.0000
Yes	10	6.8	10	6.8	
No	137	93.2	137	93.2	
Had bilateral oophorectomy					0.0245
Yes	7	4.8	1	0.7	
No	140	95.2	146	99.3	
Had previous breast biopsy					0.1650
Yes	4	2.7	1	0.7	
No	143	97.3	146	99.3	
Practising low-fat diet					0.8026
Yes	103	70.1	105	71.4	
No	44	29.9	42	28.6	
Exercise at least 3 times/week					0.4304
Yes	50	34.0	44	29.9	
No	94	66.0	103	70.1	
Ever practised breast self examination (BSE)					0.6308
Yes	126	85.7	123	83.7	
No	21	14.3	24	16.3	
Practised BSE once per month					0.7053
Yes	26	17.7	28	19.0	
No	121	82.3	119	81.0	

[a] LR test, simple conditional logistic regression

DISCUSSION

Among well-established risk factors of breast cancer, only nulliparity, overweight/obesity, family history of breast cancer and OC usage were significantly associated with higher risks of breast cancer in this study. Although several variables, such as marital status, parous after 30 years old, breastfeeding, height and bilateral oophorectomy, were significant in univariate analyses, they were found not significant in multivariate analysis.

Nulliparity was identified as a risk factor for breast cancer in other studies as well[12-15]. Increasing parity was inversely associated with the risk of breast cancer[12]. The protective effect of parity was noted especially in multiparity of five or more and among women of 40 years or older[12]. Other studies showed that having many children[16] and having the first child before the age of 30 years[12] were inversely related to the risk of breast cancer. This study did not find significant association between breast cancer and age of the first full-term pregnancy.

Changes in the reproductive behaviours of Malaysian women were closely related to the women's educational level and socio-economic status. Urbanisation and technological revolution play a part in these changes. Changes in living standards and lifestyles have affected age at first pregnancy and numbers of children produced[17]. Traditionally, women in Malaysia would marry in their mid-teens; bear children at earlier ages and breastfeed their children for long periods, which were protective lifestyles against breast cancer. There is an increasing trend to abandon these traditional habits of reproduction. There are increasing occupational and tertiary educational opportunities for women that influence their marital status and childbearing. Many have postponed marriages or having children and some may not be able to get partners at all and remained childless.

More female students were reported to be pursuing a higher education with a female to male ratio at Malaysian public universities standing at 65:35[18]. The labour force participation rate of women in Malaysia had increased from 44% in 1980 to 47.8% in 1990. The population census also showed that there was an increasing mean age of women at first marriage from 23.5 years in 1980 to 24.7 years in 1991[19]. The number of children the women had and the age they had their first child were related closely to each other. Those who had their first child at earlier ages tend to have more children than those who had their first child at later ages. The marrying age of women has an influence on their fertility, namely the number of children and age at first birth of these women. If this pattern of reproductive behaviour is not monitored, there will be an increasing proportion of women with reproductive risk factors of breast cancer that will lead to a higher incidence of breast cancer in Malaysia.

A higher proportion of women in the breast cancer

Table V. Multiple conditional logistic regression analysis of risk factors for female breast cancer.

Risk factors	Crude odds ratio[a]	Adjusted odds ratio[b]	95% CI[c]	p-value[d]
Number of children				<0.001
>2	1.0	1.0		
1-2	2.2	1.6	0.8-3.2	
Nulliparous	26.4	15.3	3.2-72.4	
Family history				0.0074
No	1.0	1.0		
Yes	4.0	4.3	1.3-14.1	
Oral contraceptive pills				0.0031
Never use	1.0	1.0		
Ever use	1.9	2.5	1.3-4.8	
Body mass index at diagnosis (kg/m^2)				0.0105
Normal (18.5- 24.9)	1.0	1.0		
Underweight (<18.5)	2.7	3.9	1.3-11.9	
Overweight/obese (≥25.0)	1.6	2.1	1.1-3.9	

[a] Simple conditional logistic regression; [b] Multiple conditional logistic regression; [c] 95% confidence interval of the adjusted odds ratio; [d] LR test, multiple conditional logistic regression

group were childless due to being single or infertile. It was postulated that the significant association between nulliparity and the risk of breast cancer was related to their infertility conditions or the subsequent treatment taken[20]. However, instead of an increased risk of breast cancer among infertile women, Garland et al[13] found that ovulatory infertility provided a protective effect against breast cancer due to lower exposure to ovulatory cycles. Furthermore, it was found that clomiphene citrate, an ovulation-inducing agent which was an oestrogen antagonist, similar to tamoxifen, was associated with a lower risk of breast cancer among infertile women[13].

This study disclosed that subjects with a family history of breast cancer had a significantly higher risk of breast cancer compared to those without a similar family history, which was consistent with other studies[17,21]. Subjects with a family history of breast cancer exhibit a four-fold excess risk (OR=4.3), compared to 1.5-2.1 in a meta-analytical study[21]. Recall bias in this case-control design whereby breast cancer patients are more likely to remember a positive family history than controls, resulted in an overestimation in the effect size.

The extent of breast cancer risk depends on the nature of the family history, such as the type of relative affected, age at which the relative developed breast cancer, and the number of relatives affected. The involvement of several first-degree relatives of several generations, younger age and pre-menopausal at diagnosis and bilateral breast cancer suggested the role of genes BRCA1 and BRCA2[14]. The risk of breast cancer in women with a family history was higher in younger women, especially those under 40 years of age[21].

This study detected a significant association between OC use and breast cancer, consistent with another local study by Lokman et al[15]. However, most studies found no or weak association of OC use with the risk of breast cancer[22]. OC intake among nulliparous women was moderately associated with breast cancer[20]. This association became stronger if the women had first-degree relatives with breast cancer and especially women with an inherited predisposition towards breast cancer such as those with BRCA1 and BRCA2 gene carrier[23]. However, OC should not be considered a contraindication in women with a family history of breast cancer[24]. The association of OC use with breast cancer is related to the duration, dosage, pattern of usage, type of OC and the age of first use[25]. This study could not measure the relationship of breast cancer with duration, type, dosage and pattern of OC usage because most of the subjects did not know or could not recall the details. The association between breast cancer and other types of hormonal contraceptives via other routes, such as injection or implant also needs further research. Shapiro et al[26] found that injectable hormonal contraceptives did not increase the risk of breast cancer.

Our study also found no significant association between HRT and breast cancer, contrary to those in other studies[27]. The failure to detect the association may be related to the low uptake of HRT among post-menopausal women in Malaysia, as was similarly observed in the Italian study[20]. Only 1.4% of women with breast cancer and 4.1% of controls had ever taken HRT. In contrast, Ross et al[27] found that 54% of breast cancer patients had ever taken HRT in a population-based case-control study.

The use of HRT is usually associated with higher socio-economic status and ethnic groups. Women in Malaysia are still reluctant to take HRT and many lack knowledge regarding its benefit in preventing heart diseases, osteoporosis and reducing menopausal symptoms.

Obese post-menopausal women were at higher risk of developing breast cancer[14,28]. The excessive body fat stores lead to peripheral conversion of lipocytes to oestrogen, hence promoting the growth of cancer cells[29]. On the other hand, there was an inverse relationship between obesity and pre-menopausal breast cancer. Obese pre-menopausal women tended to have irregular menstrual cycles and greater tendencies for anovulatory cycles, thus lowering the oestrogen influence on the target breast cells[29]. This study found a significant association between the risk of breast cancer and overweight, as well as underweight women. A possible reason for these findings was we did not stratify our subjects according to the menopausal status, because of the small sample size of post-menopausal women, consisting only 27% of the cases. Although a majority of the subjects was pre-menopausal, our results did not show a significant inverse association with breast cancer.

There was no significant association between the breastfeeding practices and breast cancer in this study, which was similar to those in another prospective study by Michels et al[30], but contrary to findings in a local study in Kuala Lumpur[15]. The failure to find an association between breastfeeding and breast cancer in this study may be related to the prolonged breastfeeding practised by most women in Malaysia, especially Malays, which was the major ethnic group in this study. Prolonged breastfeeding was a tradition and culture to many Asian women and related to socio-economic status, education, employment and marital status of the women. The national prevalence of breastfeeding was 88.6%, which was highest in Kelantan and among Malays[1]. In contrast, a review by Lipworth et al[31] failed to find an inverse association between breastfeeding and breast cancer due to the low prevalence of prolonged breastfeeding. Further study is needed by taking into account detailed information, such as lifetime duration of breastfeeding, number of children breastfed, ages at first and last lactation, and duration of amenorrhoea during breastfeeding[32].

The major drawback of this study was the reliance on recall and self-reported information. Recall bias was unavoidable, especially for elderly women recalling past events such as age at menarche[12]. However, recall bias of reproductive history was less likely, since factors such as breastfeeding and taking OC were related closely to major events in a woman's life. Women tended to remember accurately pregnancy-related events and were unlikely to under-report such occasions. A study found that there was a significant correlation between maternal recall and actual duration of breastfeeding eight to nine years later, with a correlation coefficient of 0.95[33]. The cases tended to recall exposure better than the population at large, but since controls were also drawn from the same hospital population, it was presumed that both cases and controls had similar recall bias. Hospital-based controls may improve the comparability of recall, thus produce similar misclassification errors as the cases[14].

As this study was a hospital-based study, there was selection bias in hospital utilisation and the intake of cases, which might not be representative of all women with breast cancer. There is an increased probability of hospitalisation among severe and advanced cases, compared to those with less complications and those at an early stage of breast cancer. This might be the reason that 60% of cases in this study were at advanced stages. Cases drawn from hospital populations would probably also suffer from other conditions than would be cases drawn from the general population[34]. Hospital-based cases represent a selective population because going to a hospital is culturally influenced and dependent upon perception of hospital facilities, reputation, policies and staff competency. Cases in this study were identified in major teaching and general hospitals in east coast Malaysia. One of the hospitals is the only centre in east coast Malaysia that offers radiotherapy and oncology services. Furthermore, factors that might influence hospitalisation at a particular facility tend to be balanced between cases and controls within a hospital-based case-control study.

However, the exposure of hospital-based controls to risk factors of breast cancer may not represent exposure distribution of source population from which the cases were derived. For example, hospital-based controls may be less likely to take OC because of contraindication related to their underlying medical problems. On the other hand, hospital-based controls may also be more likely to take OC because of the association of OC with conditions requiring hospitalisation, thereby changing the risk estimates[35]. Inoue et al[36] compared the lifestyle of hospital non-cancer outpatients with those in the general population and found no significant differences in their lifestyles. Cases and controls were from the same source of population that may have the same

probability of exposure, thus improving comparability. Careful criteria were applied to eliminate patients with conditions that shared the same known or potential exposure for breast cancer.

We had considered two different models of multiple conditional logistic regression analyses. One was the final model as a result of selection of univariate analyses of p-value less than 0.2 and another was the final model as a result of using all variables in the full saturated model regardless of their p-values in order to avoid missing significant variables in the final model. The latter model, which was used as our result, showed the same variables as in the former model (number of children, family history and OC pills) with an addition of body mass index at diagnosis.

In conclusion, significant risk factors of breast cancer disclosed in this study include nulliparity, overweight/obesity, family history of breast cancer and the use of OC. Nulliparity and family history of breast cancer are well-established risk factors for breast cancer, while the association of OC and obesity with breast cancer are still controversial. There were non-significant associations between breast cancer and socio-economic status, marital status, age at menarche, age at menopause, breastfeeding and intake of HRT, although they were well-established risk factors in most studies. This study reconfirmed that similar risk factors identified in Western populations were responsible for the occurrence of breast cancer in Kelantan, although some risk factors were not significantly associated with the risk of breast cancer due to some study limitations. These findings further supported the theory that breast cancer occurrence was related to oestrogen hormone exposure, either endogenous or exogenous, and familial factors. It suggested the importance of bearing children, having ideal BMI, caution for OC users and women with a family history of breast cancer.

Taking OC should be avoided, especially among nulliparous, older women and those who have a family history of breast cancer. These women have other choices of contraceptives, such as barrier methods and intrauterine contraceptive devices. Women are also encouraged to practise healthy lifestyles, such as healthy diet and regular physical activity to maintain ideal BMI. It is recommended that obese, childless women, previous OC users and those with a family history of breast cancer, perform regular breast cancer screening, including monthly breast self-examinations, half-yearly clinical breast examinations and annual mammograms after the age of 40 years. Surveillance of women at high risk is useful in detecting breast cancer at an early stage.

ACKNOWLEDGEMENT

The authors would like to thank the Dean and the School of Medical Sciences of Universiti Sains Malaysia for the encouragement and support.

REFERENCES

1. Ministry of Health Malaysia. Report of the Second National Health and Morbidity Survey Conference. Kuala Lumpur, Malaysia: Public Health Institute, 1997.
2. Penang Cancer Registry. 1996 Statistical Report. Penang: State Health Department, 1999.
3. Lim GCC, Halimah Y, Lim TO, eds. First Report of the National Cancer Registry: Cancer Incidence in Malaysia 2002. Kuala Lumpur: National Cancer Registry, 2003.
4. Ganesan J, Pillai SS, Gudum HR. The spectrum of histologically diagnosed malignant neoplasms in Sabah, 1983-1988. Med J Malaysia 1991; 46:116-22. Erratum in: Med J Malaysia 1991; 46:297.
5. Lim HH. The epidemiology of cancers in the University Hospital, Kuala Lumpur. Med J Malaysia 1982; 37:52-9.
6. Kementerian Kesihatan Malaysia. Overview of Prevention and Control Programme for Breast Cancer. Kursus mempertingkatkan perkhidmatan pengesanan awal barah payudara di peringkat kebangsaan. Kuala Lumpur: Ministry of Health Malaysia, 1994.
7. Seow A, Duffy SW, McGee MA, et al. Breast cancer in Singapore: trends in incidence 1968-1992. Int J Epidemiol 1996; 25:40-5.
8. Ng EH, Gao F, Ji CY, et al. Risk factors for breast carcinoma in Singaporean chinese women: the role of central obesity. Cancer 1997; 80:725-31.
9. World Health Organization. International Statistical Classification of Diseases and Related Health Problems. 10th revision. Vol 1. Geneva: World Health Organization, 1992.
10. Glisson J, Crawford R, Street S. Review, critique, and guidelines for the use of herbs and homeopathy. Nurse Pract 1999; 24:44-69.
11. STATA 7. USA: Stata Corporation, 1984-2001.
12. Kelsey JL, Gammon MD, John EM. Reproductive factors and breast cancer. Epidemiol Rev 1993; 15:36-47.
13. Garland M, Hunter DJ, Colditz GA, et al. Menstrual cycle characteristics and history of ovulatory infertility in relation to breast cancer risk in a large cohort of US women. Am J Epidemiol 1998; 147:636-43.
14. Tavani A, Gallus S, La Vecchia C, et al. Risk factors for breast cancer in women under 40 years. Eur J Cancer 1999; 35:1361-7.
15. Lokman R, Dayang AA, Hasni MJ, Noor Hassim I. Selenium blood level and other risk factors of breast cancer among patients in HKL. VIII National Public Health Qolloquium. Kuala Lumpur: Community Health Department, Medical Faculty UKM, 2001.
16. Magnusson CM, Persson IR, Baron JA, et al. The role of reproductive factors and use of oral contraceptives in the aetiology of breast cancer in women aged 50 to 74 years. Int J Cancer 1999; 80:231-6.
17. Stephans FO. Breast cancer: aetiological factors and associations. (a possible protective role of phytoestrogens). Aust N Z J Surg 1997; 67:755-60.
18. Chok SL, Hayatudin H. Gender gap in varsities. The New Straits Times 2001 May 25; 1.
19. Department of Statistics. General Report of the Population Census 1991. Vol 1. Kuala Lumpur: Department of Statistics, Malaysia, 1995.
20. Fioretti F, Tavani A, Bosetti C, et al. Risk factors for breast cancer in nulliparous women. Br J Cancer 1999; 79:1923-8.
21. Pharoah PD, Day NE, Duffy S, et al. Family history and the risk of breast cancer: a systematic review and meta-analysis. Int J Cancer 1997; 71:800-9.
22. Breast cancer and hormonal contraceptives: further results. Collaborative Group on Hormonal Factors in Breast Cancer. Contraception 1996; 54 (3 suppl):1S-106S.
23. Grabrick DM, Hartmann LC, Cerhan JR, et al. Risk of breast cancer with oral contraceptive use in women with a family history of breast cancer. JAMA 2000; 284: 1791-8.
24. Burke W. Oral contraceptives and breast cancer. A note of caution for high-risk women. JAMA 2000; 284:1837-8.

25. McPherson K, Steel CM, Dixon JM. ABC of breast diseases. Breast cancer – epidemiology, risk factors, and genetics. BMJ 2000; 321:624-8.
26. Shapiro S, Rosenberg L, Hoffman M, et al. Risk of breast cancer in relation to the use of injectable progestogen contraceptives and combined estrogen/progestogen contraceptives. Am J Epidemiol 2000; 151:396-403. Erratum in: Am J Epidemol 2000; 151:1134.
27. Ross RK, Paganini-Hill A, Wan PC, et al. Effect of hormone replacement therapy on breast cancer risk: Estrogen versus estrogen plus progestin. J Natl Cancer Inst 2000; 92:328-32.
28. Lam PB, Vacek PM, Geller BM, et al. The association of increased weight, body mass index, and tissue density with the risk of breast carcinoma in Vermont. Cancer 2000; 89:369-75.
29. Hirose K, Tajima K, Hamajima N, et al. Effect of body size on breast-cancer risk among Japanese women. Int J Cancer 1999; 80:349-55.
30. Michels KB, Willett WC, Rosner BA, et al. Prospective assessment of breastfeeding and breast cancer incidence among 89,887 women. Lancet 1996; 347:431-6.
31. Lipworth L, Bailey LR, Trichopoulos D. History of breast-feeding in relation to breast cancer risk: a review of the epidemiologic literature. J Natl Cancer Inst 2000; 92:302-12.
32. Furberg H, Newman B, Moorman P, et al. Lactation and breast cancer risk. Int J Epidemiol 1999; 28:396-402.
33. Vobecky JK, Vobecky J, Froda S. The reliability of the maternal memory in a retrospective assessment of nutritional status. J Clin Epidemiol 1988; 41:261-5.
34. Lasky T, Stolley PD. Selection of cases and controls. Epidemiol Rev 1994; 16:6-17.
35. Malone KE, Daling JR, Weiss NS. Oral contraceptives in relation to breast cancer. Epidemiol Rev 1993; 15:80-97.
36. Inoue M, Tajima K, Hirose K, et al. Epidemiological features of first-visit outpatients in Japan: comparison with general population and variation by sex, age, and season. J Clin Epidemiol 1997; 50:69-77.