UNIVERSITI PUTRA MALAYSIA

NUTRITIONAL AND LIFESTYLE RISK FACTORS FOR BREAST CANCER AMONG MALAYSIAN WOMEN: A CASE-CONTROL STUDY

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FPSK(M) 2004 10

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Thesis Submitted to the School of Graduate Studies, Universiti Putra Malaysia, in Fulfilment of the Requirements for the Degree of Master of Science

March 2004

Abstract of thesis presented to the Senate of Universiti Putra Malaysia in fulfilment of the requirement for the degree of Master of Science.

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Chairman: **Associate Professor Mirnalini a/p V.S. Kandiah, Ph.D.**

Faculty: **Medicine and Health Sciences**

Breast cancer is the most common incident cancer in women worldwide, accounting for 9% of all new cancers. While the exact causes of breast cancer are unknown, the risks are higher among older women (50 years and above) than those less than 35 years. Dietary factors that have been linked to breast cancer include saturated fat, meat, vegetables and fruits. Other factors that have been linked to breast cancer include age at menarche, age at first and last birth, smoking, use of oral contraceptives and body mass index. This case-control study was carried out to determine the nutritional and lifestyle risk factors of breast cancer among Malaysian women. A total of 162 pre- and post-menopausal women (81 cases and 81 controls) was included in the study, which was carried out between 1 January to 31 December, 2000. Cases were selected from the Breast Cancer Clinics in Hospital Kuala Lumpur (HKL) and Universiti Malaya Medical Centre (UMMC). All cases were newly diagnosed and

have not undergone any treatment or surgery. Controls were women staff and wives of staff of Universiti Putra Malaysia (UPM). They were matched by age (± 5 years) and ethnicity with the cases. Additional Chinese controls (17 women) were selected from the Malaysian-Chinese Association (MCA) from Ampang Jaya by invitation to the group's leader. Data collection was carried out in four main parts: the interview (to obtain socio-demographic and lifestyle data); anthropometric measurements; dietary information, using semi-quantitative food frequency questionnaire; and biochemical data (to obtain serum lipid profile). Majority of the respondents were pre-menopausal women with the mean age of 46.63 in cases and 47.58 in controls. Half of the breast cancer patients were seen at UMMC while the other half in HKL, and most of them (43.1%) presented with a second stage of cancer. Smoking, exercise, breast-self examination and breastfeeding practices were not significantly different between the two study groups. However, there was a significant difference in the duration of exercise between cases and controls. Reproductive history like age at menarche, age at first marriage, age at first birth and parity were also not significantly different between cases and controls. Anthropometric indicators like height, weight, waist and hip measurements, as well as body mass index and waist-hip ratio did not show any association with breast cancer, and neither were they significantly different between case and control subjects. Intakes of micronutrient were not significantly different between the two study groups with the exception of sodium. Blood lipid profiles also did not show any difference between groups. Preliminary data showed that women who

have four to five children were 1.32 times more at risk for breast cancer as compared to those who never had any children (95% CI=1.32-1.47). Multiple logistic regression model showed that menarche at higher age and increased BMI decreased breast cancer risk while higher age at last birth increased breast cancer risk. The relatively small sample size of this study could have resulted in this results. Furthermore, there could have been recall bias and under-reporting of energy intake among case subjects due to the occurrence of the disease. Larger cohort and interventional studies should be carried out to further explore this factors with relation to breast cancer.

Abstrak tesis yang dikemukakan kepada Senat Universiti Putra Malaysia sebagai memenuhi keperluan untuk Ijazah Master Sains.

FAKTOR RISIKO PEMAKANAN DAN CARAGAYA HIDUP DALAM KANSER PAYUDARA DI KALANGAN WANITA DI MALAYSIA: SATU KAJIAN KES-KAWALAN

Oleh

JUSTINA TAN PIK CHOO

Mei 2004

Pengerusi: **Profesor Madya Mirnalini a/p V.S. Kandiah, Ph.D.**

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Kanser payudara adalah kanser yang paling kerap di kalangan wanita, sehingga mewakili 9 % daripada jumlah kanser. Walaupun sebab-sebab kejadian kanser payudara tidak diketahui, namun risikonya adalah lebih tinggi di kalangan wamita yang lebih tua (50 tahun ke atas) dibandingkan dengan wanita yang lebih muda (kurang daripada 35 tahun). Faktor pemakanan yang dikaitkan dengan kanser payudara termasuk lemak tepu, daging, sayur-sayuran dan buah-buahan,. Faktor-faktor lain yang juga dikaitkan dengan kanser payudara termasuk umur baligh, umur semasa melahirkan anak yang pertama dan terakhir, merokok, penggunaan pil perancang keluarga dan indeks jisim tubuh. Kajian kes-kawalan ini telah dijalankan untuk mengenalpasti factor-faktor pemakanan dan caragaya hidup di kalangan wanita di Malaysia. Kajian ini melibatkan 162 wanita yang sudah mencapai dan belum mencapai tahap menopausa (81 kes dan 81 kawalan), dan dijalankan di antara 1 Januari dan 31

Disember, 2000. Kes telah dikenalpasti di Kilinik Payudara di Hospital Kuala Lumpur (HKL) dan Pusat Perubatan Universiti Malaya (PPUM). Kesemua kes adalah baru didiagnosakan sebagai menghidapi kanser payudara, dan belum menjalani sebarang rawatan atau pembedahan. Kawalan merupakan staf wanita dan isteri staf Universiti Putra Malaysia (UPM). Mereka telah dipadankankan mengikut umur (±5 tahun) dan bangsa. 17 wanita Cina tambahan telah dipilih daripada kumpulan Pertubuhan Cina-Malaysia (MCA) dari Ampang Jaya setelah diberi jemputan daripada ketua pertubuhan. Data yang dikumpul merangkumi empat bahagian utama: temuramah (untuk mendapat data sosio-demografi dan caragaya hidup); ukuran antropometri; maklumat mengenai pemakanan menggunakan soal-selidik frekuensi makanan semi-kuantitatif; dan data biokimia (untuk mendapatkan profail lipid). Majoriti responden adalah wanita pra-menopausa dengan min umur 46.63 tahun bagi kes dan 46.63 tahun bagi kawalan. Setengah daripada pesakit kanser payudara ditemui di PPUM manakala setengah lagi di HKL, dan kebanyakan mereka (43.1%) adalah di peringkat kanser kedua. Merokok, bersenam, menguji payudara sendiri dan menyusu badan tidak menunjukkan perbezaan yang signifikan di antara dua kumpulan kajian. Namun, terdapat perbezaan signifikan dalam tempoh bersenam di antara kumpulan kes dan kawalan. Sejarah reproduktif seperti umur semasa baligh, umur pada perkahwinan pertama, umur pada kelahiran pertama dan jumlah anak kesemuanya tidak menunjukkan perbezaan signifikan di antara kumpulan kes dan kawalan. Indikator antropometrik seperti tinggi, berat, lilitan pinggang, lilitan punggung, serta indeks jisim tubuh dan

nisbah lilitan pinggang-punggung kesemuanya juga tidak menunjukkan sebarang perbezaan signifikan di antara kumpulan kes dan kawalan. Di antara kesemua micronutrien, hanya pengambilan natrium sahaja yang menunjukkan perbezaan yang signifikan di antara dua kumpulan kajian. Profail lipid juga tidak berbeza di antara kumpulan kajian. Keputusan awal telah menunjukkan bahawa wanita yang mempunyai empat hingga lima orang anak mempunyai risiko 1.32 kali lebih tinggi berbanding dengan mereka yang tidak mempunyai anak (95% CI=1.32-1.47). *Multiple logistic regression* menunjukkan bahawa umur kedatangan haid pertama yang lebih rendah, IJT yang lebih tinggi dan umur pada kelahiran terakhir yang lebih tinggi kesemuanya meningkatkan risiko mendapat kanser payudara. Kesemua factor caragaya hidup dan pemakanan tidak menunjukkan sebarang kaitan dengan kanser payudara, dan juga tidak menunjukkan sebarang perbezaan yang signifikan di antara kumpulan kes dan kawalan. Sampel saiz kajian yang kecil mungkin telah mempengaruhi keputusan keseluruhan kajian ini. Mungkin juga terdapat bias di dalam pengingatan kumpulan kes terhadap pemakanan mereka. Malah, kemungkinan juga terdapat laporan yang rendah terhadap pengambilan tenaga di kalangan kumpulan kes disebabkan oleh kejadian kanser. Kajian kohort dan intervensi yang lebih besar harus dijalankan untuk mengkaji dengan lebih mendalam faktor-faktor yang berkaitan dengan kanser payudara.

ACKNOWLEDGEMENTS

First and foremost, I thank God for all the strength that He has granted me, in completing what I have started. My thanks also goes out to my parents and family members including my husband and daughter, who have given me support, encouragement and motivation throughout these years.

I would like to take this opportunity to thank the most wonderful person, my mentor, my supervisor and my friend, Assoc. Prof. Dr. Mirnalini Kandiah. Your friendship is most treasured and will be forever remembered; your tutorship and guidance are most appreciated.

My sincere thanks also goes out to all members in the supervisory committee: Prof Dr Khor Geok Lin, Dr Mohd Nasir Mohd Taib and Dr Jothimalar. Your contributions have made a significant change in my life.

A note of thanks goes to all lecturers and staff of Fakulti Perubatan dan Sains Kesihatan, who have extended their friendship throughout my years in UPM. I would like to say a big thanks to Loh Su Peng, who has journeyed and shared much with me, and most of all, who has become a true friend, indeed. To Ruslina, Shalini, Sharon Wong, Lalitha - thank you for your sincere friendship and your assistance in this project.

I would like to extend my deepest gratitude to the many doctors, nurses and staff of Universiti Malaya Medical Centre, UMMC and Hospital Kuala Lumpur, HKL for their support in my research. My heartfelt thanks goes out especially to Prof Yip Cheng Har, Dr Patricia Gomez and Dr Fuad Ismail (and the clinic staff) for their assistance and friendship throughout the course of my visits to the respective hospitals. Also many thanks to Prof Lee Hin Peng and all the staff of the Department of Community and Family Medicine in the National University of Singapore for their advice and in sharing their experiences.

Many thanks to all those who have helped in making my data collection a success, Mr Tai Beng Hoe and Mdm Marie Yong (MCA-Ampang Jaya), S/N YC Ong (HUKM), Annam (UH), S/N Biro (GH) and S/N Azizah (GH).

I would also like to say a note of thanks to all the respondents of this research. Half of them are breast cancer patients, whom I have learnt much about life. I have also made lots of friends from the Breast Cancer Welfare Association (BCWA), from whom much of my inspiration is derived. I will always remain your friends dearly in my heart.

Thank you also to many other individuals who have helped me in one way or another, in making this study a success. We have become friends, and for me, friends remain forever.

Justina Tan

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CHAPTER ONE

Introduction

The word "cancer" originated from Hippocrates (460-370 B.C.), considered the "Father of Medicine." He used the terms "carcinos" and "carcinoma" to describe non-ulcer forming and ulcer-forming tumours (American Cancer Society, 2001). Normal body cells grow, divide, and die in an orderly fashion. Cancer cells, however, continue to grow and divide, and can spread to other parts of the body. These cells are then accumulated to form tumours or lumps that may destroy normal tissues. Benign tumours are not cancer, in that they can be removed and often, they do not come back. Malignant tumours, on the other hand, become cancerous. They contain abnormal tumours in which cell division is not controlled, thus they can invade and damage nearby tissues and organs.

Breast cancer is a malignant tumour that has developed from cells of the breast. There are many types of breast cancer such as adenocarcinoma, ductal carcinoma *in situ* and invasive ductal carcinoma (Appendix A). When a cancer has spread to other sites outside the breast, it is said to have metastasized. In this situation, the cancer cells are often found in the lymph nodes. If the cancer has reached these nodes, it means that cancer cells may have spread to other parts of the body, ie the bones, liver or lungs. If breast cancer has spread to the lung, the

cancer cells in the lung are actually breast cancer cells. This disease will then be called metastatic breast cancer (not lung cancer).

Breast cancer is the third most common cancer in the world, and the most common incident cancer in women worldwide (American Cancer Society, 2001), accounting for 9% of all new cancers (WCRF/AICR, 1997). In the United States, breast cancer ranks second among the leading causes of death after lung cancer, making up 23.3% of the total deaths in the country (American Cancer Society, 2001). In 1998, the World Health Organisation (WHO) reported that the incidence of breast cancer in developed countries is 505,000 women while the incidence in developing countries is 390,000 women (WHO, 1998).

The American Cancer Society (2001) reported that the worldwide incidence rate for breast cancer has been increasing by 4% per year since the 1980's and is at the level of 110.6 cases per 100,000 women. The Centre for Disease Control (CDC, 2001) estimated 192,200 new cases of invasive breast cancer to occur among women in the United States during the year of 2001 (CDC, 2001). Out of this total, an expected 40,600 deaths will occur (40,200 among women and 400 among men). Between 1973 and 1989, incidence rates increased nearly 40% for women aged above 65 years (Sondik, 1994). Between the 70's and the 90's, the incidence of breast cancer increased by 117% while mortality increased by 50%.

The increase in the detection rate of breast cancer has been very significant since the 80s with the introduction of the mammogram. With mammography, breast cancer can be detected at an earlier stage where treatment is likely to have significant effects resulting in the increase in average length of life as well as improvement in the quality of life.

Death rates due to breast cancer also significantly declined with this early detection and improved treatment (CDC, 2001). Kerlikowski *et al.* (1995) found that mammography screening could reduce deaths by 20 to 30% among women aged 50 to 74 years and about 17% among women aged between 40 and 49 years. The UK Trial of Early Detection of Breast Cancer (TEDBC) was carried out in 1979 to investigate the effect of screening and education about breast self-examination (BSE) on breast cancer mortality in eight centres in England and Scotland. Moss *et al.* (1999) carried out a follow-up study of 16 years, and compared the observed number of deaths from breast cancer in each centre with the expected number, calculated by Poisson regression model. Mortality due to breast cancer was 27% lower (RR=0.73, 95% CI 0.63-0.84) in the screening centres. This showed that a reduction in breast cancer mortality could be achieved from early detection by screening.

Incidence rates in countries like Japan and Singapore are also increasing due to the increase in the elderly population. The increase in breast cancer incidence in these two countries is more than two times in women born in the 1915 and 1940 birth cohorts (Lee, 1998). In 1980, the

incidence rate in Singapore was 27 per 100,000 women, but increased to 39.3 per 100,000 women in 1990, while the rate stood at 47.1 per 100,000 women in 1995 (Yip and Ng, 1996). This incidence rate, however, is most likely to increase even further in the future (Seow *et al.*, 1998).

Figure 1 shows the incidence rate of breast cancer in selected Asian countries as reported in the publication by the World Cancer Research Fund and American Institute for Cancer Research (1997). These rates were based on the years between 1983 and 1987. Women in Manila, the urban city of Philippines, were reported to have an incidence of up to more than three times higher than that of Thailand. Meanwhile, Figure 1 also shows that breast cancer incidence is highest among Indian Singaporeans (34.0 per 100,000 women) as compared to Chinese (31.6 per 100,000 women) and Malays (23.2 per 100,000).