A STUDY OF THE PROFILE, RISK FACTORS AND KNOWLEDGE, ATTITUDE AND PRACTICE OF WOMEN WITH BREAST CANCER IN KELANTAN

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GLOSSARY

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Definition of Terms

Age at first full-term pregnancy is 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 (Ng *et al.*, 1997).

Age at menarche is defined as the chronological age when the woman first had menstruation.

Age at menopause is defined as the chronological age when the woman developed amenorrhoea of at least 6 months duration prior to the date of interview (Ng *et al.*, 1997).

Alcohol drinker includes former and current regular alcohol drinker of at least a glass per week for a month in duration.

Breast self-examination refers to the systematic examination of one's own breasts by a woman who believes she to be healthy for the purpose of preventing disease or detecting asymptomatic disease.

Body mass index is calculated by using the formula, "W/H^{2}" where W is weight in kilogram and H is height in metres.

Cases refer to all breast cancer patients in this study who fulfilled the selection criteria.

Cigarette smoker includes former and current regular and occasional smokers of at least a month in duration.

Controls refer to non-breast cancer patients in this study that fulfilled the selection criteria.

Ever taken regular oral contraceptive, hormone replacement therapy, traditional herbal medication, vitamins or micronutrient supplements include those who ever took these preparations regularly for at least one month and include current and former users.

First-degree relatives include the mother, sisters or daughters while **distant relatives** include those other than first-degree relatives like cousins, the

grandmother, granddaughters, aunts or nieces who has had breast cancer. Family history denotes either first degree or distant relatives.

Parity is the number of pregnancy of more than 28 weeks duration with outcome of a single or multiple live births or stillbirths.

Practising low fat diet intake includes subjects who deliberately limited high fat intake in their diet.

Practising regular exercise is defined as having physical activity of at least for 20 minutes 3 times per week.

Risk factors are factors that increase a person's chance of getting breast cancer.

Subjects refer to all participants in this study (cases and controls).

Traditional herbal medication includes the usage of crude plant-based products or roots or leaves to prevent or cure a disease or an ailment (Glisson *et al.*, 2000).

Abbreviations

BMI	Body Mass Index
BSE	Breast Self-Examination
CBE	Clinical Breast Examination
95% CI	95% Confidence Interval
CIS	Carcinoma In-Situ
cm	centimetre
HKB	Hospital Kota Bharu
HRT	Hormone Replacement Therapy
HUSM	Hospital Universiti Sains Malaysia
kg	kilogram
m	metre
NS	Non-significant
OC	Oral Contraceptives
OR	Odds Ratio
PSP	Pemeriksaan Sendiri Payudara
SEER	Surveillance Epidemiology End Result
SGH	Singapore General Hospital
TNM	Tumour, Node and Metastasis
UHKL	University Hospital Kuala Lumpur
USA	The United States of America

ABSTRACTS

ABSTRAK

KAJIAN PROFIL, FAKTOR RISIKO DAN PENGETAHUAN, SIKAP DAN AMALAN DI KALANGAN WANITA KANSER PAYUDARA DI KELANTAN

Kanser payudara adalah kanser wanita paling kerap di dunia dengan prevalens di Malaysia seramai 86.2 per 100,000 wanita pada 1996. Terdapat peningkatan kadar kematian disebabkan oleh kanser payudara di Malaysia dari 0.6 pada 1983 kepada 1.8 per 100,000 penduduk pada 1992. Tujuan kajian adalah untuk mengenalpasti profil, faktor risiko dan membandingkan tahap pengetahuan, sikap dan amalan mengenai kanser payudara di antara pesakit kanser payudara dan kawalan. Kajian kes kawalan di hospital telah dijalankan di Kelantan. Soalselidik piawai digunakan untuk menemuduga 147 pesakit kanser payudara yang disahkan melalui histologi. Kumpulan kawalan seramai 147 dipadankan dengan umur dan kumpulan etnik kes dikalangan bukan pengidap penyakit kanser, sakit puan, gangguan hormon atau endokrin. Faktor risiko dan jumlah markah dianalisa menggunakan "simple conditional logistic regression" dan ujian berpasang *t*. Model "multiple conditional logistic regression" kemudian digunakan untuk mengawal "confounders". Min umur pesakit kanser payudara adalah 46.3 $\pm$ 9.3 tahun. Jenis histologi paling kerap ialah "infiltrative ductal" (73%). Kanser

payudara di peringkat III and VI adalah 60%. Faktor-faktor risiko kanser payudara adalah nullipara (nisbah ods (OR) 42.6, 95% julat kepercayaan (95% CI) 4.8-380.8), mempunyai satu atau dua anak (OR 2.2, 95% CI 1.0-5.0), sejarah keluarga pengidap kanser payudara (OR 4.2, 95% CI 1.4-12.8) dan pernah mengamal ubat perancang keluarga (OR 2.8, 95% CI 1.4-5.8). Pesakit kanser payudara mempunyai tahap pengetahuan yang lebih baik dengan perbezaan bererti berbanding dengan kawalan (ujian berpasang t =4.9, $p<0.001$). Tiada perbezaan bererti antara kes dan kawalan bagi jumlah markah sikap (ujian berpasang t =0.6, $p>0.05$) dan amalan (ujian berpasang t = -0.7, $p>0.05$). Kurang dari 20% kes dan kawalan mengamalkan pemeriksaan sendiri payudara bulanan. Kajian ini melibatkan pesakit kanser payudara yang lebih muda sebelum menopos. Profil kanser payudara dikajian ini berbeza daripada kajian lain seperti taburan umur dan etnik. Kajian ini mengesahkan faktor risiko yang sama seperti kajian di barat bertanggungjawab kepada kejadian kanser payudara di Kelantan. Ia juga menyokong teori yang kanser payudara berkaitan dengan pendedahan kepada estrogen hormon dan faktor keturunan. Ia menekankan kepentingan untuk mempunyai anak terutama lebih daripada dua, amaran kepada wanita yang pernah menggunakan ubat perancang keluarga dan yang mempunyai sejarah keluarga kanser payudara. Tahap pengetahuan yang lebih baik tidak menjamin sikap positif dan amalan yang lebih baik. Pengajaran kesihatan diperlukan terutama untuk wanita berisiko tinggi supaya dapat menukar sikap mereka dan meningkatkan amalan pemeriksaan saringan yang berkala dan betul bagi kanser payudara.

ABSTRACT

Breast cancer is the commonest female cancer in the world with Malaysian prevalence of 86.2 per 100,000 women in 1996. There was an increasing trend of breast cancer mortality rate in Malaysia from 0.61 in 1983 to 1.8 per 100,000 populations in 1992. This study was aimed to identify profile, risk factors of breast cancer and to compare the level of knowledge, attitude and practice regarding breast cancer between cases and controls. A matched case-control study was carried out at hospitals in Kelantan. A standardized questionnaire 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 of cases and non-malignant, non-gynaecological, non-hormonal and non-endocrinological patients. Potential risk factors and score of knowledge, attitude and practice were initially analysed by simple conditional logistic regression and paired *t* test. Multiple conditional logistic regression modelling was later used to control potential confounding factors. The mean age of breast cancer patients was 46.3 $\pm$ 9.3 years. The most common histological type was infiltrative ductal carcinoma (73%). Presentation at stage III and VI was 60%. Factors contributing towards increased risk of breast cancer were nulliparity (Odds Ratio (OR) 42.6, 95% Confidence Interval (95% CI) 4.8-380.8), having one

or two children (OR 2.2, 95% CI 1.0-5.0), family history of breast cancer (OR 4.2, 95% CI 1.4-12.8) and ever taken oral contraceptives (OC) (OR 2.8, 95% CI 1.4-5.8). Cases had significantly better score of knowledge than controls (paired *t* test =4.9, $p<0.001$). There were no significant differences between cases and controls in total scores of attitude (paired *t* test =0.6, $p>0.05$) and practice (paired *t* test = -0.7, $p>0.05$). Less than 20% of cases and controls practised monthly Breast Self-Examination (BSE). This study included younger pre-menopausal women. The profile of breast cancers such as age and ethnic distributions was different from other studies. This study reconfirmed that similar risk factors identified in western population 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 especially more than two and caution for OC users and women with family history of breast cancer. Significant higher level of knowledge did not ensure positive attitude and better practice. Health education is needed especially for high-risk women in order to change their attitude and facilitate regular correct method of screening for breast cancer.

INTRODUCTION

CHAPTER ONE

INTRODUCTION

Global trend suggests an epidemiological transition from the improvement of communicable diseases through immunization, environmental sanitation and socio-economic status of population, to the increasing trend of non-communicable, degenerative and life-style related diseases (Linet, 2000).

One of the degenerative, non-communicable and life-style diseases is cancer. Cancer is a public health problem in developing as well as developed countries. In developed countries, cancer was the second most common cause of death, while in developing countries it was responsible for about one in 20 deaths (Ministry of Health Malaysia, 1997a). It was expected that cancer incidence would increase by 25% in the developed and 100% in the developing world in the next 25 years (Ministry of Health Malaysia, 1997a).

Cancer was the fifth leading cause of death in government hospitals in 1996 compared to 1978 where cancer was not even in the top ten of the list (Ministry of Health Malaysia, 1997a). The emergence of cancer as one of the ten leading causes of death in Malaysia warrants a serious consideration towards its

prevention and control. The incidence rate for all types of cancer in Malaysia was 150 per 100 000 population in 1996, compared to 95.1 per 100 000 population in 1978 (Ministry of Health Malaysia, 1997b). The prevalence rate of all types of cancer in males and females were 153.1 and 301.3, respectively, per 100 000 population. Breast cancer was the commonest cancer among females (45.9 per 100 000 population) in 1996, followed by cervical and stomach cancer (Ministry of Health Malaysia, 1997b).

1.1 OVERVIEW OF BREAST CANCER

Breast cancer results from an anomaly of uncontrolled growth and division of breast cells. The breast cancer cells will destroy normal nearby tissues by local invasion and may break away from the primary site and enter the bloodstream and lymphatic system, thus spreading to other organs such as bone, lung, liver and brain. The diagnosis of breast cancer can only be made by histological examination of breast tissue. The breast tissue may be obtained by fine needle aspiration biopsy, core needle biopsy, incisional or excisional biopsy or stereotactic image guidance of needle biopsy for unpalpable masses.

Breast tissue is a tubuloalveolar gland that consists of ductal and lobular units. The development and growth of breast tissue is under the influence of oestrogen, progesterone, adrenal hormones, pituitary hormones, and trophic effects of insulin and thyroid hormone.

Oestrogen is the primary hormone responsible for rapid proliferation of breast cells during puberty and pregnancy; that signals changes during the menstrual cycle and maintains the female structure of the breast. During puberty, oestrogens cause arborisation of the ductal system while progesterones induce development of terminal ducts with the presence of growth hormone and insulin (Farrar *et al.,* 1995). During hormonal changes of menstrual cycle, the lobular units undergo histologic alteration. Similarly, the lobular units undergo marked proliferation and enlargement during pregnancy. Furthermore, there is loss of hormonal stimulation during post-menopause, hence a decrease in absolute number and diffuse atrophy of the residual lobular units (Kuhns and Ackermenn, 1995).

Besides being responsible for the growth of normal breast tissues, oestrogens also play important role in stimulating the growth of cancer cells of the breast. Oestrogens have direct effect on tumour cells by stimulating the release of mitogenic growth factors and facilitate the invasion and metastases of the tumour (Spratt *et al.,* 1995, Clemons and Goss, 2001).

Oestrogen and progesterone receptors status is important to determine in breast cancer. The positive receptors test means the breast cancer cells grow under the influence of hormone, thus predicts whether the cancer is sensitive to hormones. The treatment option is dependent upon the hormone receptor tests and staging of breast cancer.

Tumour, Nodal and Metastasis (TNM) classification for staging of breast cancer is based on clinical examination of the tumour (T), regional lymph nodes involvement (N) and distant metastases (M). It is introduced to predict prognosis, determine the choice of treatment and compare the results of different treatment approaches. Table 1.1 shows the TNM classification for the staging of breast cancer, while table 1.2 shows the grouping of theTNM staging of breast cancer.

Table 1.1 TNM classification for staging of breast cancer*

Primary Tumour		
Tx		Primary tumour cannot be assessed.
T0		No evidence of primary tumour.
T1s		Carcinoma-in-situ: intraductal carcinoma, lobular carcinoma, or Paget's disease of nipple with no tumour.
T1		Tumour ≤ 2 cm in greatest dimension.
	T1a	≤ 0.5 cm in greatest diameter.
	T1b	> 0.5 cm, but not > 1 cm in greatest diameter.
	T1c	> 1 cm, but not > 2 cm in greatest diameter.
T2		Tumour > 2 cm but not > 5 cm in greatest dimension.
T3		Tumour > 5 cm in greatest dimension.
T4		Tumour of any size with direct extension into chest wall or skin.
	T4a	Extension to chest wall.
	T4b	Edema (including peau d'orange) or skin ulceration or satellite skin nodules confined to same breast.
	T4c	Inflammatory carcinoma.

Table 1.1 Continued

Regional Lymph Node Involvement			
Nx			Regional Lymph node cannot be assessed.
N0			No regional lymph node involvement.
N1			Metastasis to movable ipsilateral axillary lymph node(s).
	N1a		Only micrometastasis (none larger than 0.2cm).
	N1b		Metastasis to lymph node(s), any larger than 0.2 cm.
		N1bi	Metastasis in 1 to 3 lymph nodes, any > 0.2cm and all < 2 cm in greatest dimension.
		N1bii	Metastasis in 1 to 4 lymph nodes, any > 0.2cm and all < 2 cm in greatest dimension.
		N1biii	Extension of tumour beyond the capsule of a lymph node, any metastasis in 1 to 5 lymph nodes, > 0.2 cm and all < 2 cm in greatest dimension.
		N1biv	Metastasis to a lymph node ≥ 2 cm in greatest dimension.
N2			Metastasis to ipsilateral axillary lymph node(s) fixed to one another or to other structures.
N3			Metastasis to ipsilateral internal mammary axillary lymph node(s).
Distant Metastasis			
Mx			Presence of distant metastasis cannot be assessed.
M0			No distant metastasis.
M1			Distant metastasis present (including ipsilateral supraclavicular lymph nodes).

* Beahrs *et al.*, 1992.

Table 1.2 TNM stage grouping*

Stages	TNM classification
Stage 0	TIS, N0, M0
Stage I	T1, N0, M0
Stage IIA	T0-1, N1, M0 T2, N0, M0
Stage IIB	T2, N1, M0 T3, N0, M0
Stage IIIA	T0-2, N2, M0 T3, N1-2, M0
Stage IIIB	T4, N1-2, M0 Any T, N3, M0
Stage IV	Any T, any N, M1

*Beahrs *et al.*, 1992.

1.2 PREVALENCE OF BREAST CANCER

Breast cancer is an important public health problem and contributes toward significant morbidity and mortality among Malaysian women. It was the most common female cancer in the world (McPherson *et al.*, 2000) and in Malaysia (Ministry of Health Malaysia, 1997b) but the second commonest cancer after cervical cancer in Kelantan (Department of Health Kelantan, 1996).

There were geographical and ethnic variations in breast cancer incidence rates. The highest rates were in North America and Europe and lowest in Asia and

Africa. The age-adjusted incidence of invasive breast cancer was highest among white, Hawaiian and black women, while the lowest rates were reported among Korean, American Indian, and Vietnamese women (National Cancer Institute, 1999). Surveillance Epidemiology End Result (SEER) Cancer Statistics Review 1973-1997 reported that the incidence rate of breast cancer in USA in 1997 was 115.4 and the mortality rate was 23.3 per 100 000 women (National Cancer Institute, 1999). Japanese, Chinese and Filipino women, who migrated to the USA, had elevated risk of breast cancer after several generations and their incidence rate of breast cancer was approaching the rate of American whites (National Cancer Institute, 1999).

Breast cancer incidence rates in the USA had been 4-7 times higher than those reported in China or Japan (National Cancer Institute, 1999). The incidence rate of breast cancer in Malaysia was also very much lower compared to those in the west. The incidence rate of breast cancer in Peninsular Malaysia in 1982 was 28 per 100 000 women compared to 69 per 100 000 women in the United States in the same year (Chan, 1982). Penang Cancer Registry (1999), the only reliable regional cancer registry in Malaysia reported that the incidence rate of breast cancer in 1996 was 23.8 per 100 000 women. The second National Health and Morbidity Survey showed that the breast cancer prevalence in Malaysia was 86.2 per 100 000 women in 1996 (Ministry of Health Malaysia, 1997b). Chinese women had a higher incidence (34 per 100 000 women) compared to Malays (24 per 100 000 women) (Chan, 1982).

Breast cancer was the commonest malignancy among women that contributed 10.7% of female cancer cases in University Hospital, Kuala Lumpur from 1972 to 1974, 13% of Singaporean cancers from 1968 to 1970 and 13.8% of cancers diagnosed by the Institute of Medical Research, Kuala Lumpur from 1969 to 1971 (Lim, 1982). Ganesan *et al.* (1991) found that breast cancer contributed 18% of all female cancers in Sabah. Furthermore, McPherson *et al.* (2000) also reported that breast cancer contributed 18% of all female cancers in the world.

The National Cancer Institute of the United States reported an overall decline in cancer incidence and mortality rates. The age-adjusted breast cancer mortality rate for white females in the USA dropped 6.8% between 1990 and 1995 (Chu *et al.*, 1996). This was reverse from the earlier reports. The decline might be due to the better cancer prevention and control efforts that included healthy life-style changes, educational efforts and regular cancer screening. Similarly, there were changes in the incidence and mortality rates of breast cancer in England and Wales since the introduction of screening programs, although other factors like better treatment may play a role (Quinn & Allen 1995). There was a reduction of up to 21% in mortality rate from breast cancer from 1990 to 1998 in the United Kingdom (Blanks *et al.*, 2000). Furthermore, SEER program of the USA also noted that there were increasing incidence rates of stage I and II breast cancer, while stage III and IV breast cancer incidence rates were decreasing (National Cancer Institute, 1999).

In contrast, the trends in incidence and mortality rates of breast cancer in Malaysia were increasing. The under-reported mortality rate from breast cancer increased from 0.61 in 1983 to 1.8 per 100 000 women in 1992 (Kementerian Kesihatan Malaysia, 1994). The age-adjusted mortality rate of Peninsula Malaysia showed an increase from 3.7 in 1982 to 5.8 per 100 000 women in 1990 (Yip and Ng, 1996). Data from population-based Singapore Cancer Registry between 1968 and 1992 revealed an average increase in the incidence rate of 3.6% over the 25 year period; 20.2 per 100 000 women between 1968 and 1972 to 38.8 per 100 000 women between 1988 and 1992. It was projected that the rates would reach 55 per 100 000 women by 1995 (Seow *et al.,* 1996).

1.3 RISK FACTORS OF FEMALE BREAST CANCER

It is important to identify women at high-risk of breast cancer, in order to improve understanding of factors associated with breast cancer. This information is important for preventive and diagnostic purposes. It may also explain the low incidence rates in Asian women and the upward trend in the incidence in developing countries.

Table 1.3 summarises the risk factors of female breast cancer (Kelsey, 1993).

Table 1.3 Summary of risk factors of female breast cancer*

Factors	High risk group
Established risk factors (relative risk more than 4.0)	
Age	Old
Family history of breast cancer	Higher if having mother or sister with breast cancer
Established risk factors (relative risk 2.1 – 4.0)	
History of cancer in one breast	Yes
Previous biopsy of benign proliferative	Yes
Radiation to chest	Yes
Established risk factors (relative risk 1.1 – 2.0)	
Socio-economic status	High
Marital status	Never married
Place of residence	Urban
Ethnic group	Chinese Malaysian¥
Bilateral oophorectomy before 40 years old	No
Nulliparity	Yes
Age at first full term pregnancy	After 30 years of age
Age at menarche	At 11 or younger
Age at menopause	After 55 years of age
Obesity	For post-menopausal
Uncertain risk factors	
Parity	High
Breastfeeding	Never
Long term exposure to oral contraceptive (OC)	Yes
Long term exposure to hormone replacement (HRT)	Yes
Height	Tall
Alcohol consumption	Yes
Cigarette smoking	Yes

*Adapted from Kelsey, 1993

¥Chan (1982), Yip and Ng (1996)

The risk factors of breast cancer in Western populations had been extensively investigated and suggested that life-style and reproductive factors were strongly

related to breast cancer. In contrast, less information exists regarding factors that are associated with breast cancer in Asian women. A study by Ng *et al.* (1997) suggested that the same risk factors responsible for the higher incidence of breast cancer in western population, might explain the rise of breast cancer incidence in Singapore.

A positive family history of breast cancer is among the most significant predictors of breast cancer risk (Pharoah *et al.*, 1997, Floretti *et al.*, 1998, Tavani *et al.*, 1999, McPherson *et al.*, 2000). Details of the family history are important, such as the relation of family members to patients, the age at which breast cancer is diagnosed, whether they are at pre- or post-menopausal or if one or both breasts are involved. The combination of multiple primary relatives, multiple generations, multiple occurrences of bilateral breast cancer or the occurrence during pre-menopausal period suggests a genetic predisposition. Autosomal dominant genes BRCA-1 and BRCA-2 are related to the breast cancer occurrence (Tavani *et al.*, 1999).

Breast cancer has been shown to be associated with oestrogen exposure (Bernstein and Ross, 1993, Stephans, 1997). Oestrogen is responsible for the growth and proliferation of breast tissues. It is also responsible for the initiation of breast cancer cells (Clemons and Goss, 2001). Further evidence of the effect of oestrogen is from the effect of tamoxifen, an anti-oestrogen chemotherapeutic agent, in the reduction of breast cancer risk. However, Wiseman (2000) argued

that oestrogen is not the sole cause of breast cancer but only acting as a promoter of carcinogenesis since not many pregnant women have breast cancer and men also get breast cancer too. It is suggested that breast cancer has a single, unknown aetiology and not due to multiple causes.

Increased or prolonged exposure to oestrogen is associated with a higher risk of developing breast cancer. Reproductive factors that increase the number of menstrual cycle such as early menarche, nulliparity, late onset of menopause and late age of having the first child, contribute toward higher risk of breast cancer (Helmrich *et al.*, 1983, Kelsey *et al.*, 1993, Stephans, 1997, Garland *et al.*, 1998, Tavani *et al.*, 1999, McPherson *et al.*, 2000). On the other hand, factors that reduce the number of ovulatory cycles are associated with lower risk of breast cancer such as moderate exercise, longer lactation and higher parity. Women who give birth to their first child before 30 years of age are at lower risk of developing breast cancer compared to those give birth for the first time after age 30 or those who never bear children. Women who underwent oophorectomy before the age of 35 years and did not take replacement oestrogen have a reduction in their breast cancer risk (Parazzini *et al.*, 1997). Even hysterectomy alone is protective against breast cancer because it modifies ovulation through ovarian blood flow (Parazzini *et al.*, 1997). Women who have had irregular menstrual cycles are prone toward anovulatory cycles, thus having lower risks for breast cancer (Garland *et al.*, 1998). Furthermore, having an abortion is related to a higher risk of breast cancer, regardless of whether it is spontaneous or

induced, due to the interruption of pregnancy (Melbye *et al.*, 1998 Tavani *et al.*, 1999, Floretti *et al.*, 2000). Having an abortion also resulted in an incomplete differentiation of mammary gland cells making the tissue more susceptible to carcinogenesis (Kelsey *et al.*, 1993).

There is an inverse relation between breastfeeding and breast cancer risk regardless of duration (Furberg *et al.*, 1999). It was postulated that lactation reduced the woman's exposure to ovarian hormones by suppressing ovulation. There is reduced oestrogen production during lactation and changes in epithelial cells of mammary ductules during lactation. Furthermore, breastfeeding may remove oestrogen or carcinogens through breast milk and delay reestablishment of ovulation. On the other hand, many Western studies found no protective effect of breastfeeding on breast cancer (Kelsey *et al.*, 1993, Michels *et al.*, 1996). The failure to detect the association was due to the low prevalence of prolonged breastfeeding in western population (Lipworth *et al.*, 2000).

Exogenous oestrogen such as those obtained through hormone replacement therapy (HRT) and oral contraceptives (OC) also has roles in the development of breast cancer.

Use of OC is weakly associated with breast cancer (Collaborative Group on Hormonal Factors in Breast Cancer, 1996, Tavani *et al.*, 1999, McPherson *et al.*, 2000). Collaborative analysis of data from 54 epidemiologic studies of breast

cancer in 25 countries showed only small increase in the risk of breast cancer for the current or previous users of combined OC (Collaborative Group on Hormonal Factors in Breast Cancer, 1996). The association of OC with breast cancer were related to the duration, dosage, pattern of usage, type of OC and the age of first using it. On the other hand, a meta-analysis study showed no increased risk for ever users of OC even for long duration (Romieu *et al.*, 1990).

All types of study designs showed an association of ever users of HRT with breast cancer occurrence (McPherson *et al.*, 2000, Clemons and Goss, 2001). It was closely related to the duration of intake, type and dosage of preparation used. The risks associated with continuous combined HRT were tended to be substantially less than those associated with sequential combined regime. The risks associated with combined HRT were higher than that in oestrogen replacement alone (Ross *et al.*, 2000). Progestogens did not protect breast from carcinogenic effect of oestrogen but increased the oestrogen-related risk of breast cancer. It was reported that even one year of HRT could increase the chances of breast cancer by 2.3% for each additional year (Collaborative Group on Hormonal Factors in Breast Cancer, 1997). The effect however, would disappear after 5 years of cessation of intake.

Obese, post-menopausal women are at high risk of developing breast cancer (Helmrich *et al.*, 1983, Haybittle *et al.*, 1996, Tavani *et al.*, 1999, Lam *et al.*, 2000). It is related to the hormonal influences of obesity. The increased body fat

stores can lead to higher circulating levels of oestrogen with peripheral conversion of lipocytes, hence promoting the growth of breast cancer cells (Hirose *et al.*, 1999, Clemons and Goss, 2000). Obesity is also associated with advanced stage of breast cancer at initial diagnosis. On the other hand, there is an inverse relationship between body mass index (BMI) and pre-menopausal breast cancer (Trentham-Dietz *et al.*, 1997, Hirose *et al.*, 1999). The proposed mechanism is that obese, pre-menopausal women tend to have longer menstrual cycles and greater tendencies for anovulatory cycles, thus lowering the net oestrogen influence on the target breast cells. Before menopause, the excess fat has little influence on the level of oestrogen due to the overriding influence of ovarian oestrogen production. The timing of gaining weight during adulthood, especially after menopause, is also critical in determining the association between weight changes and breast cancer (Ng *et al.*, 1997). Women who gain weight throughout adulthood are at an increased risk for developing breast cancer after menopause (McTiernan, 2000). Ng *et al.* (1997) also found that central obesity was more relevant in increasing the risk of breast cancer.

While it has been clearly established that smoking increases the risk of developing lung cancer, it is suggested that smoking may contribute towards increased risk of breast cancer as well. Tobacco smoke is thought to interfere with oestrogen metabolism and a carcinogen itself. Timing of exposure and duration of smoking are related to the breast cancer risk. Smoking increased the

risk of developing breast cancer for women who had smoked for more than 30 years (Bennicke *et al.*, 1995).

Dietary factors have been linked to breast cancer development. It is noted that breast cancer is less common in countries where the typical diet is low in total fat especially polysaturated fat (Yuan *et al.*, 1995). Cross cultural studies demonstrated that women from low risk countries like Asia and Africa acquired the same high risk of breast cancer as their American counterpart when they migrated to the US and adopted western diet (Yuan *et al.*, 1995). A study on the effect of diet on breast cancer in Singapore suggested that soya products containing phyto-oestrogen, which suppresses endogenous oestrogenic activity of breast cells, were responsible for the low rates of breast cancer in Asian countries (Lee *et al.*, 1991). Consuming less saturated animal fat may reduce the risks of breast cancer as well as other diseases. Meanwhile, Knekt *et al.* (1990), in a longitudinal study, found that there was no significant association between absolute fat intake and the occurrence of breast cancer. Meta-analysis of 23 studies on dietary fat association with breast cancer had shown that only case-control studies showed significant associations while cohort studies did not (Boyd *et al.*, 1993).

Vitamin C, E and beta-carotene have anti-oxidant properties while vitamin A is a regulator of cellular differentiation that may reduce the risk of breast cancer. A study by Hunter *et al.* (1993) showed that large intakes of vitamin C and E did not

protect women from breast cancer and low intake of vitamin A may increase the risk of breast cancer. Another study found that vitamin E, dietary fibre and supplements did not significantly related with breast cancer (Verhoeven *et al.*, 1997). Furthermore, there were significant inverse relationships between the risk of breast cancer and carotenoids and vitamin A from foods but not supplement of vitamin A, C or E (Zhang *et al.*, 1999). A case-control study in Greece found that only beta-carotene was inversely associated with breast cancer in pre-menopausal women whereas other micronutrients were not significantly related (Bohlke *et al.*, 1999). High intake of dietary fibres, especially vegetables, fruits and whole grains, was significantly reduced the risk of breast cancer (Yuan *et al.*, 1995).

In addition to other general health benefits, exercise may alter body's hormonal environment thereby possibly reducing the risk of breast cancer. Women who exercised at least 4 hours per week had a 37% reduction in the risk of breast cancer (Thune *et al.*, 1997). Exercise is associated with increased frequency of anovulatory cycles or if the ovulation does occur, the levels of serum oestrogen and serum progesterone in the cycles are much decreased (Floretti *et al.*, 1998). Intensive exercise can cause amenorrhoea. The benefits were greatest among women who had borne children and were physically active in their teens and early twenties. The effect of physical activity is also related closely to the BMI of the women. Excessive BMI was related to higher risk of breast cancer in post-menopausal women (Tavani *et al.*, 1999).

There was an association between benign breast diseases and breast cancer. Women, who have had breast biopsies for any reason, had higher risks of developing subsequent breast cancer. A study by Jacobs *et al.* (1999) found that radial scars present in benign breast biopsies were significantly associated with increased risks of subsequent breast cancer. An overall incidence of breast cancer in patients with palpable cysts was 2.81 times greater than that of the general population (Dixon *et al.*, 1999). It was suggested that the occurrence of a cyst is a marker of epidermal activity that has a higher concentration of oestrogen, thus related with an increased risk of breast cancer.

1.4 BREAST CANCER SCREENING

Only half of women with breast cancer have identifiable risk factors (Linet, 2000). Some of the breast cancer risk factors are not readily modifiable through either behavioural or environmental changes. The extent of prevention of breast cancer achieved by healthy lifestyles, such as dietary control and exercise, is not known. Thus, secondary prevention of early detection and prompt treatment, with the goal of reducing breast cancer mortality, should be targeted in order to halt the increasing trend of breast cancer among Malaysian women.

The National Program of Breast Cancer Prevention was launched by Ministry of Health in 1995 as part of its Healthy Life-Style Campaign. It has a broad risk

target group and is mainly an opportunistic screening tied to the Family Health Development Program of the Ministry of Health. Educational BSE (Breast-self Examination) is taught mainly during antenatal visits at health centres, which is not frequent. Furthermore, CBE (Clinical Breast Examination) is done during family planning program and whenever is indicated or requested. Mammography, which is expensive and requires well-trained staff, is not used at all as a screening tool in Malaysia. Mammography cannot be considered as an ideal screening method since it is technically complex, relatively expensive and has poor accessibility and availability in Malaysia. Besides not cost-effective, mammography has limited usefulness in women under the age of 40 years (Overmoyer, 1999). Thus, BSE and CBE are the obvious choices as screening methods for breast cancer.

Effective breast cancer screening detects disease during the pre-clinical phase before the development of symptoms and thereby has a favourable impact on the mortality rate (Overmoyer, 1999). Screening programs should be aimed at reducing mortality as well as the incidence of breast cancer, and targeted at high-risk women. Only mammogram has been shown to be capable of reducing breast cancer mortality (Chu *et al.*, 1996).

The benefit of BSE is somewhat controversial. Monthly BSE is safe, easy and potentially beneficial because of its non-invasive method of detection. BSE provides an opportunity to detect breast problem early, thus facilitating

consultation and early management. Besides that, early stage detection of a disease is associated with better treatment options and less morbidity compared with those presenting at an advanced stage. With adequate education and training, women can be expected to be able to care for their own breasts. Although it is the least sensitive method of breast cancer screening (sensitivity ranging 12-25%) (Fletcher *et al.*, 1993) and has a high false positive rate, BSE has the potential in detecting smaller tumours with better histological grade and lesser lymph node involvement (Locker *et al.*, 1989).

Most studies indicated a positive association between the practice of BSE and CBE and early detection of breast cancer. A meta-analysis reported that those who had BSE at least once before their illness had lesser lymph node involvement and smaller tumour diameter compared to those who did not practised (Hill *et al.*, 1988). Studies have shown that early stage of detection is associated with better survival rates. A study of pT1N0M0 breast cancer found the 10-year and 20-year survival rates, corrected for intercurrent deaths, were 93% and 81% respectively (Joensuu *et al.*, 1999). Breast cancer commonly presented late in Malaysia. Information from the Ministry of Health, Malaysia revealed that only 5.8% presented in stage I where the disease is confined to the breast only, 66.7% presented in stage II and III where the disease has extended to lymph nodes and 27% presented in stage IV with distant metastasis (Ministry of Health Malaysia, 1994). Based on this information, there is good evidence to encourage women to practise BSE regularly.

The efficacy of BSE in reducing breast cancer mortality has conflicting results. A randomised trial of 267,040 women in Shanghai showed no significant difference in breast cancer mortality between those who were given intensive training in BSE compared to controls after 5 years follow-up (Thomas *et al.,* 1997). However, a non-randomised study in UK showed a reduction in breast cancer mortality resulting from screening and education about BSE after 16 years of intervention (UK Trial of Early Detection of Breast Cancer Group, 1999).

BSE can detect changes and differences rather than in the interpretation of self-examination findings. By doing monthly BSE, women will become familiar with the normal appearance, configuration and texture of their breasts and may be able to identify any changes. BSE is a preventive strategy that could be applicable and acceptable to all women regardless of their current biological life phases, reproductive desires, hormonal needs, cultural and financial constraints and risk levels.

There are various methods of doing BSE. The Health Education Unit of Ministry of Health, Malaysia has produced a standardized guideline for BSE, in order to gain maximum benefit from practising it (Appendix 2).

1.5 KNOWLEDGE, ATTITUDE AND BELIEFS

Health screening behaviour is closely related to the individual's knowledge, attitude and beliefs. Although better knowledge on breast cancer does not necessarily translate into actual practice of BSE, women who have better knowledge are more likely to practice it. The second National Health and Morbidity Survey found that those who practised screening methods of breast cancer were those who had higher educational level that in turn influenced their knowledge and awareness on breast cancer (Ministry of Health Malaysia, 1997b). It is very important to understand the extent of people's knowledge, attitude and beliefs in relation to breast cancer in order to develop an effective intervention and prevention programs on breast cancer. Lack of regular cancer screening practice, which is related to poor knowledge and negative attitude, has been blamed to the late presentation of breast cancer at advanced stages.

Poor knowledge regarding breast cancer and its screening methods may be due to the unavailability of information in the absence of regular educational campaign. Some women may be unaware of the need for BSE. Women who have specific breast complaints may not know where to go.

Cultural values with respect to modesty and sexuality partly account for the lack of attention to breast health. Some women are not comfortable when talking about breasts or sexuality. Many may feel that breast examination is an intimate

examination. Some may feel upset or surprised if their physicians requested to examine their breasts. Many women prefer female physicians when examining their breasts and may actually postpone or delay consultation out of embarrassment.

The women's knowledge, attitude and beliefs regarding breast cancer are closely related to previous life experiences with illnesses and medical systems, religious beliefs, socio-economic factors and the impact mass media and healthy life-style campaigns mounted by the Ministry of Health.

1.6 CONCEPTUAL FRAMEWORK

The conceptual framework of this study is shown as figure 1.1. It was postulated that oestrogen and genetic play important roles in the occurrence of breast cancer (Martin and Weber, 2000). Oestrogens are produced endogenously by ovaries and adrenals. Conversion of androgen to oestrogens may occur in fatty tissues especially in post-menopausal period when ovaries had regressed.

Factors as mentioned before such as nulliparity, having first full-term birth after the age of 30 years, early menarche, late menopause, never breastfeeding and obesity may relatively increased or prolonged the women's exposure to oestrogens, thus increased risk of developing breast cancer. While exogenous oestrogens from OCP and HRT are also related to higher risk of developing breast cancer.

Family history of breast cancer is associated with the occurrence of breast cancer. Women who have genes called BRCA 1 and BRCA 2 are at risk of breast cancer. Besides hormonal and genetic factors, there are other factors that may contribute towards higher risk of breast cancer. Some benign breast diseases have higher risk to develop or progress to breast cancer. Taking high animal fat diet, radiation, alcohol intake and smoking may also contribute to the higher risk of breast cancer.

Breast cancer should be detected at earlier stages via screening methods of breast cancer: mammography, CBE and BSE. The practice of screening methods is related to high level of knowledge and positive attitude and beliefs about breast cancer. High level of knowledge and positive attitude and beliefs are also needed in order for women to have appropriate successful management and thus longer survival.