

RESEARCH COMMUNICATION

Does a Positive Family History Influence the Presentation of Breast Cancer?

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Abstract

Introduction: An important risk factor for developing breast cancer is a positive family history of breast cancer. In Malaysia, there is no population-based breast screening programme, but the clinical practice guidelines suggest increased surveillance for those with a positive family history ie mammography for those 40 years old and above, breast self-examination and clinical breast examination yearly. **Objective:** To determine if women with a family history of breast cancer present with earlier stages of disease. **Methodology:** From Jan 2001 to Dec 2006, 1553 women with breast cancer presenting to the University Malaya, where family history was recorded, were eligible for this study. Women with a first or second degree relative with breast cancer were compared with those who have no family history with regard to their race, age, stage, size and duration of symptoms. The Chi Square test of significance was used for analysis. **Results:** Out of 1553 patients, 252 (16.2%) were found to have a relative with breast cancer out of which 174 (11.2%) had at least one affected first degree relative. There were no significant difference in the incidence of positive family history between the Malays, Chinese and Indians. 20% below the age of 40 years old had a positive family history compared with 12.6% in women with no family history. ($p < 0.05$). There was no significant difference in stage at diagnosis between those with and without family history, ie 24.2% late stages (Stage 3 and 4) in the group with no family history compared with 21.8% in the group with family history. ($p > 0.05$). The mean size in the group with no family history was 4.4 cm compared to 4.1 cm in the group with family history. There was a significant difference in screen-detected cancers in the women with family history, 10.7% compared with 5.1% of screen-detected cancers in the group without a family history. However there was no difference in the duration of symptoms between the 2 groups – 25.8% in the women without a family history presented after 1 year of symptoms compared with 22.4% in the group with a family history ($p > 0.05$). **Conclusion:** Having a family history of breast cancer does not appear to have much impact on the health-seeking behavior of women. Even though there were more screen detected cancers, these comprised only 10% of the group with family history. Public education should target women at risk ie with family history to encourage these women to present earlier and to undergo screening for breast cancer.

Key Words: Breast cancer - family history - stage at presentation

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Introduction

The three greatest risk factors for developing breast cancer are female sex, increasing age, and a family history of the disease. In Malaysia, there is no population-based breast screening programme, but the clinical practice guidelines suggest increased surveillance for those with a positive family history ie mammography for those 40 years old and above, breast self-examination and clinical breast examination yearly (Management of Breast Cancer: Clinical Practice Guidelines, Ministry of Health Malaysia; Academy of Medicine Malaysia, 2002). Some studies have shown that women with a positive history of breast cancer are more likely to adhere to screening guidelines (Petrissek et al., 2000; Halbert et al., 2006), but others have shown that women with breast cancer who have a positive family history do not appear to present with earlier stages or smaller tumours (Russo et al., 2002). The aim of this study is to determine if women in Malaysia with a family

history of breast cancer present with earlier stages of disease.

Materials and Methods

From Jan 2001 to Dec 2006, 1,946 women were diagnosed with breast cancer in the University of Malaya Medical Centre. After exclusion of foreigners, Eurasians and those in whom a family history was not recorded in the case protocol, 1,553 women (79.8%) were eligible for the study. Women with a first or second degree relative with breast cancer were compared with those having no family history with reference to their race, age, stage, and duration of symptoms. The size of tumour and the method of detection ie whether they were detected by screening was also recorded. The Chi Square test of significance was used for the analysis.

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Table 1. Family History in Relation to Race and Age

		No Family History		With Family History		Total	P value
Race	Chinese	865	(83.8%)	167	(16.2%)	1032	>0.05
	Malays	274	(83.1%)	52	(16.9%)	326	
	Indians	162	(84%)	33	(16%)	195	
Age	Less than 40	164	(80%)	41	(20%)	205	<0.05
	40 and above	1137	(84.4%)	211	(15.6%)	1348	

Results

Out of 1553 patients, 252 (16.2%) were found to have a relative with breast cancer out of which 174 (11.2%) had at least one affected first degree relative. 31 patients (12.3%) had more than 1 relative with breast cancer. There were a total of 130 affected sisters, 62 aunts, 49 mothers, 27 cousins, 7 daughters, 12 grandmothers, and 7 nieces among the 252 women with family history of breast cancer.

There were no significant difference in the incidence of positive family history between the Malays, Chinese and Indians. 20% below the age of 40 years old had a positive family history compared with 12.6% in women with no family history. ($p < 0.05$). 34.8% of women with a family history presented with Stage 1 cancer compared with 23.9% in women without a family history. ($p < 0.05$). (Table 1) However when we compared early stage (Stage 0-2) with late stage (Stage 3-4), there was no significant difference between the two groups, ie 24.2% late stage in the group with no family history compared with 21.8% in the group with family history. ($p > 0.05$). There was no difference in the duration of symptoms between the 2 groups – 25.8% in the women without a family history presented after 1 year of symptoms compared with 22.4% in the group with a family history ($p > 0.05$). (Table 2)

The mean size in the group with no family history was 4.4 cm compared to 4.1 cm in the group with family history. There was also a significant difference in screen-detected cancers in the women with family history, 10.7% compared with 5.1% of screen-detected cancers in the group without a family history.

Discussion

Breast cancer is the commonest cancer in women in most parts of the world. Besides female gender and advancing age, the other most important risk factor is family history. It is estimated that the relative risk of getting breast cancer with a mother with breast cancer is 2.0, 2.3 if a sister is involved, and 3.6 if both mother and sister is affected (Pharoah et al., 1997). Depending on classification of family history ie whether first or second

or third degree relative, the rate of positive family history in women with breast cancer ranges from 10 to 35% (Adami et al., 1980; Wobbes et al., 1987; Collaborative Group on Hormonal Factors in Breast Cancer, 2001; Russo et al., 2002; Margolin et al., 2006). Our study is similar, with 16.2% of patients having a first or second-degree relative with breast cancer, and 11.2% of patient having a first-degree relative with breast cancer. There is no difference in the incidence of a positive family history in Malays, Indians and Chinese in this study (Table 1).

Hereditary forms of breast cancer account for only 7% of all breast cancers, and germline mutations in the inherited breast cancer susceptibility genes BRCA1 and BRCA2 are responsible for most of the familial breast cancer. Genetic risk assessment, as interdisciplinary subspecialty, has been practiced in developed countries for many years, and genetic testing and counseling has become a standard of care for appropriately selected patients. However in developing countries, little information is available on breast cancer genes and breast cancer family clinics rarely exist (Li et al., 2007).

Knowing that a relative, especially a first-degree relative, has breast cancer should affect the screening practice of a woman. Surveillance should include regular expert clinical examination and teaching of “breast awareness” as well as mammography. Hence, theoretically a woman with a family history of breast cancer should present with smaller tumours and in earlier stages. However this is often not the case. In our study, only 10.7% of tumours in the women with family history were detected on screening. Although this was significantly more than the 5.1% in the group without family history that was detected on screening, the small number indicates that women with a family history of breast cancer are not going for routine breast screening. A study by Møller found that the majority of cancers arising in women at increased genetic risk of breast cancer can be detected by planned screening, and 75% of tumours in women with family history are detected on screening even in those under age 50 (Møller et al., 1999). In Malaysia, there is no population-based mammography screening programme, and hence only a small proportion of breast cancers are screen detected in women with or without a

Table 2. Family History in Relationship to Stage and Duration of Symptoms

		No Family History		With family History		Total	P value
Stage	Stage 0-2	985	(75.8%)	197	(78.2%)	1182	>0.05
	Stage 3-4	315	(24.2%)	55	(21.8%)	370	
Duration of symptoms	< 3 months	487	(48.9%)	83	(46.7%)	570	>0.05
	3 months to < 1 year	286	(28.7%)	49	(27.5%)	335	
	1 year and more	224	(22.4%)	46	(25.8%)	270	

positive family history.

One of the features of familial breast cancer is the younger age of onset (Pharoah et al., 1997). In this study, 20% of women under 40 had a positive family history compared with 15.6% of women 40 years and above. ($p < 0.05$). However, a study on a population-based cohort of breast cancer cohort in Sweden found no difference in age with and without a positive family history (Margolin et al., 2006).

Some studies have shown no difference in size of tumour, stage at diagnosis, and lymph node involvement (Wobbes et al., 1987; Russo et al., 2002). A study by Gavrilov et al actually found that women with family history presented with more advanced stages of disease (2002). On the other hand, some studies also found that women with family history presented with less node positivity (Fukutomi et al., 1993; Margolin et al., 2006). Similarly some studies showed an improved survival (Fukutomi et al., 1993, Malone et al., 1996) while others showed no difference in survival (Eccles et al., 2001; Verkooijen et al., 2006).

Our study found no difference in size, stage, and duration of symptoms between the women with a positive family history and those without, meaning that having a positive family history does not mean that the women present with smaller tumours or earlier stages of disease (Table 1).

Why is it that women at risk of breast cancer, where mammography screening is recommended, do not appear to present with significantly earlier stages of disease? Studies on the screening behaviour of women with a positive history of breast cancer has been studied and it is found that at least 25-30% of such women do not report screening (Antill et al., 2006; Lemon et al., 2006), and in one study on Israeli women with a family history, over 60% of women aged 40-49 year old, and 55% of women aged 50 years and above, are inadequately screened for breast cancer (Keinan-Boker et al., 2007).

Hence an education programme targeting women at risk of breast cancer because of a positive family history to encourage such women to undergo counseling on breast cancer screening and to present with earlier stages of disease. Breast cancer family history clinics need to be developed for this purpose.

Conclusion

Having a family history of breast cancer does not appear to have much impact on the health-seeking behavior of women in Malaysia. Even though there were more screen detected cancers, these comprised only 10% of the group with family history. However, there was not much difference in the size of the tumour, the stage at presentation, or the duration of symptoms before presentation. Public education should target women at risk ie with family history to encourage these women to present earlier and to undergo screening for breast cancer.

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