

## RESEARCH COMMUNICATION

# Breast Cancer in Sabah, Malaysia: A Two Year Prospective Study

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### Abstract

**Introduction:** Malaysian women have a 1 in 20 chance of developing breast cancer in their lifetime. Sabah, formerly known as North Borneo, is part of East Malaysia with a population of 3.39 million and more than 30 ethnic groups. We conducted a 2 year prospective epidemiological study to provide unreported data of breast cancer from this part of the world and to recognise which particular group of patients are more likely to present with advanced disease. **Methods:** All newly diagnosed breast cancers seen at the Queen Elizabeth Hospital, Kota Kinabalu, from January 2005 to December 2006 were included in the study. Patient and tumour characteristics, including age, race, education, socioeconomic background, parity, practice of breast feeding, hormonal medication intake, menopausal status, family history, mode of presentation, histology, grade, stage of disease and hormonal receptors status were collected and analysed. **Results:** A total of 186 patients were seen. The commonest age group was 40 to 49 years old (32.3%). Chinese was the commonest race (30.6%) followed by Kadazan-Dusun (24.2%). The commonest histology was invasive ductal carcinoma (88.4%). Stages at presentation were Stage 0- 4.8%, Stage I- 12.9%, Stage II- 30.1%, Stage III- 36.6% and Stage IV- 15.6%. The estrogen and progesterone receptor status was positive in 59.1% and 54.8% of cases, respectively. 73.7% of Chinese patients presented with early cancer compared to 36.4% of the other races. Patients who presented with advanced disease were also poor, non-educated and from rural areas. 20.4% of patients defaulted treatment; most of them opted for traditional alternatives. **Conclusions:** Sabahan women with breast cancer present late. Great efforts are needed to improve public awareness of breast cancer, especially among those who have higher risk of presenting with advanced disease.

**Key Words:** Breast cancer - late presentation - advanced stage - poor, rural - ethnic groups

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### Introduction

Breast cancer is the commonest cancer among women in Malaysia as well as worldwide. Globally, it was estimated there were 1,150,000 new cases with 410,000 deaths in 2002 (Ferlay et al., 2002). Breast cancer has high incidence rates in USA, Europe, Australia, New Zealand and in some parts of South America, especially Uruguay and Argentina and is relatively less common in Africa and Asia (Stewart and Kleihues, 2003). Overall worldwide Age Standardised Rate (ASR) of breast cancer was estimated to be 37.4 per 100,000 (Ferlay et al., 2002).

In Malaysia, there were 3,738 new cases reported in 2003. Breast cancer made up 31% of all newly diagnosed cancer among Malaysian women with an overall ASR of 46.2 per 100,000 (Lim and Yakaya, 2003). Each Malaysian woman has a 1 in 20 chance to develop breast cancer in her lifetime. Sabah, formerly a British Colony known as North Borneo, is part of East Malaysia and the second

largest state in Malaysia. Sabah has an estimated population of 3.39 million with more than 30 ethnic groups. The largest indigenous ethnic group is Kadazan-Dusun (17.8%), followed by Bajau and Murut. The largest non-indigenous ethnic group is Chinese (9.6%). To date, data on breast cancer from Sabah has been poorly reported and published. National data on breast cancer published in the National Cancer Registry of Malaysia 2002 did not include data from Sabah due to inadequate reporting of cases (Lim and Yakaya, 2003).

Queen Elizabeth Hospital, situated in the capital of Sabah, Kota Kinabalu, is the main public tertiary referral centre in the state. We conducted a prospective epidemiological study in our hospital on breast cancer to provide unreported data on breast cancer in Sabah and, with statistical analysis, to recognise which particular groups of patients who are more likely to present with advanced disease. We hope that a clearer epidemiological picture of breast cancer in Sabah will lead to appropriate

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measures to improve the outcome of management of the disease in Sabah and Malaysia as a whole.

**Materials and Methods**

The subjects of our study were all newly diagnosed breast cancer patients seen in our hospital from January 2005 to December 2006. We included patients who were referred from private institutions for continuation of treatment at different stages of management of the disease. We excluded patients who presented with recurrent breast cancer and those who refused to participate in the study. Patients' data including age, race, place of residence, level of education, religion, income, age of menarche, marital status, parity, age of first child birth, practice of breast feeding, menopausal status, hormonal medication intake, family history, mode of presentation and as well as tumour characteristics including tumour site, type, grade, stage and hormonal receptors status were collected and analysed. Data were collected at the dedicated breast clinic, general surgical clinic and wards of the hospital prospectively for 2 years. Staging of the disease was in accordance to the American Joint Committee on Cancer (AJCC) Cancer Staging Manual, sixth edition. Advanced breast cancer is defined as breast cancer at either stage 3 or 4 of the disease.

Statistical Package for the Social Sciences (SPSS version 15.0) was used for statistical analysis. The Chi

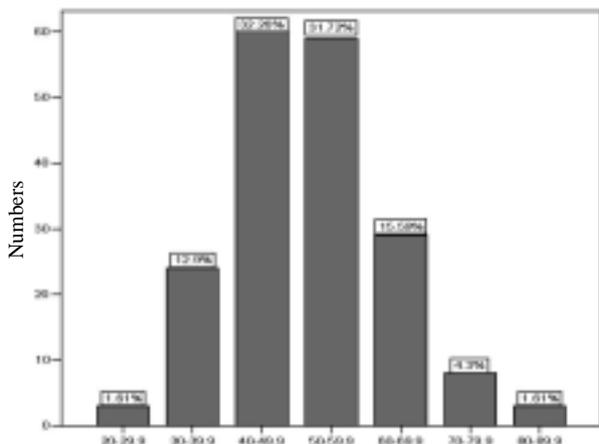
square test was used for associations between categorical variables and the Student's t test for associations between continuous and categorical variables. Logistic regression analysis was used to identify independent covariates predicting patients with advanced breast cancer. The level of statistical significance was set at  $P < 0.05$ .

**Results**

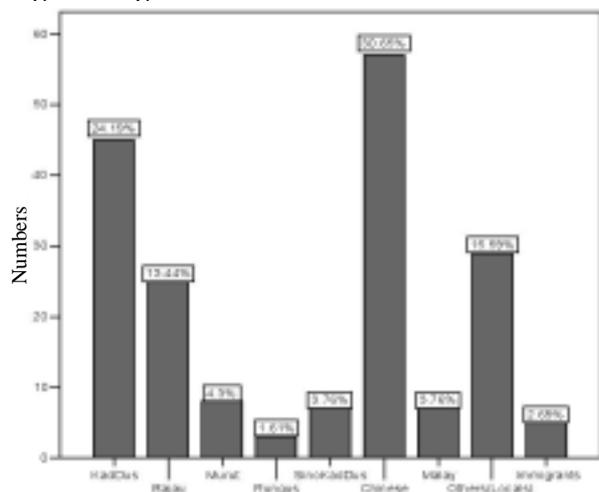
In 2005 and 2006, we saw a total of 186 cases of newly diagnosed breast cancer. 99.5% of them were female and 0.5%, male. The most common age group was 40 to 49 years old (32.3%) (Figure 1), with a mean age of 51.0 (standard deviation, 11.0). The youngest and oldest patients were 24 and 83 year old respectively. 54.8% of them were post-menopausal. The most common race affected was Chinese (30.6%), followed by Kadazan-Dusun (24.2%) and Bajau (13.4%) (Figure 2). Interestingly, our subjects included 5 (2.7%) illegal immigrants (Filipinos and Indonesians). 46.8% of patients were from the rural area (villages) and 30.1% of them had never received any formal education. 56.5% of patients earned less than 1,000 Ringgit Malaysia (RM) per month (330 Australian Dollars). 15.6% of patients were referred from private institutions for continuation of treatment, majority due to financial constraint on chemotherapy and radiotherapy.

The proportion of patients with risk factors are as follows: early menarche (before 13 year old) in 31.7%, unmarried in 9.1%, nulliparity in 16.7%, late first child birth (after 30 year old) in 11.3%, late menopause (after 55 year old) in 4.3%, non-breast feeding in 29.6%, hormonal medication (oral contraceptive pill and hormonal replacement therapy) intake in 32.3% and positive family history in 11.3%.

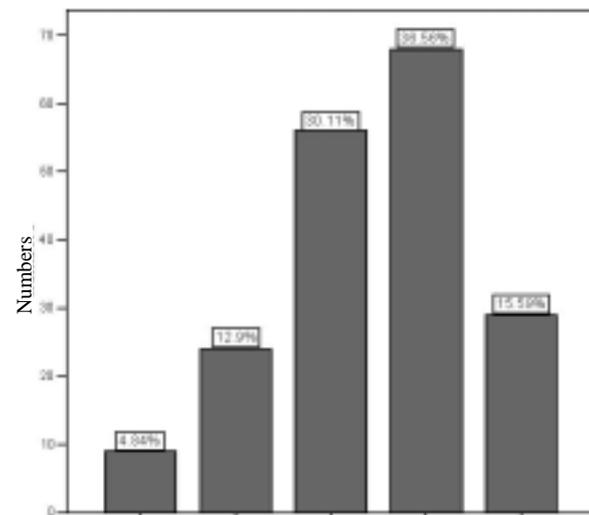
Table 1 presents the proportion of mode of clinical presentations and tumour characteristics. The commonest mode of presentation was with a breast lump, 78.0%. 9.1% of patients presented to us with ulcerative mass and only 2.2% presented with suspicious lesion on mammography. 51.6% of the tumours were on the right side and 46.2% on the left. 2.2% had bilateral disease. The commonest



**Figure 1. Age Distribution of Breast Cancer Cases**



**Figure 2. Race Distribution of Breast Cancer. KadDus: Kadazan-Dusun**



**Figure 3. Stage at Presentation of Breast Cancer**



**Figure 4. A Patient Presenting with an Ulcerative Lesion**

site was the upper outer quadrant with 53.8%. Infiltrating ductal carcinoma was the commonest histological type (88.4%) with grade II the commonest grade (59.4%) according to Bloom and Richardson grading. 59.1% of tumours were estrogen receptor (ER) positive and 54.8% were progesterone receptor (PR) positive. 65.9% of ER-negative tumours presented at advanced stage compared to ER-positive, 42.7% ( $P=0.02$ ). Similar pattern was seen

**Table 1. Clinical Presentations and Tumour Characteristics**

Characteristics	Number	(%)
<b>Presentation</b>		
Breast Lump	145	(78.0%)
Ulcerative Mass	17	(9.1%)
Skin and Nipple Changes	10	(5.3%)
Metastasis	6	(3.2%)
Suspicious Mammography	4	(2.2%)
Nipple Discharge	2	(1.1%)
Others	2	(1.1%)
<b>Tumour Histology</b>		
Invasive Ductal Carcinoma	157	(84.4%)
Invasive Lobular Carcinoma	6	(3.2%)
Medullary Carcinoma	4	(2.2%)
Mucinous Carcinoma	5	(2.7%)
Ductal Carcinoma In Situ	8	(4.3%)
Colloid Carcinoma	2	(1.1%)
Papillary Carcinoma	3	(1.6%)
Apocrine Carcinoma	1	(0.5%)
<b>Tumour Grade</b>		
I	24	(13.3%)
II	107	(59.4%)
III	49	(27.2%)
<b>Tumour Side</b>		
Right	96	(51.6%)
Left	86	(46.2%)
Both	4	(2.2%)
<b>Tumour Site</b>		
Upper Outer	100	(53.8%)
Upper inner	26	(14.0%)
Lower outer	26	(14.0%)
Lower inner	10	(5.4%)
Areolar	20	(10.8%)
More than 1	4	(2.2%)
<b>Hormonal Receptor Status</b>		
ER Positive	110	(59.1%)
PR Positive	102	(54.8%)

with PR-negative and PR-positive tumours where 66.7% and 41.0% respectively presented as advanced disease ( $P=0.0001$ ).

The commonest stage of breast cancer at presentation in our institution was stage III- 36.6%, followed by stage II- 30.1%, stage IV- 15.6%, stage I- 12.9% and only 4.8% presented at stage 0 (Fig. 3). Further sub-staging are as follows: stage 0- 4.8%, stage I- 12.9%, stage IIA- 20.4%, stage IIB- 9.7%, stage IIIA- 17.2%, stage IIIB- 11.3%, stage IIIC- 8.1%, stage IV- 15.65%. Majority of patients (52.2%) presented with advanced disease (Figure 4).

Patient characteristics associated with advanced disease presentation which were statistically significant in univariate analysis were non-Chinese race, patients from rural area, patients with income of less than 1000 RM per month and the non-educated (Table 2). 63.6% of non-Chinese and only 26.3% of Chinese presented with advanced disease ( $P = 0.0001$ ). 70.1% of patients from rural area ( $P = 0.0001$ ), 60.0% of patients who earn less

**Table 2. Correlation between Patient Characteristics and Stage at Presentation**

Patient Characteristics	Stages 0, I & II	Stages III & IV	P Value
Mean age(year)	51.2	50.8	0.822
<b>Race</b>			
Chinese	42 (73.7%)	15 (26.3%)	0.0001
Non-Chinese	47 (36.4%)	82 (63.6%)	
<b>Residence</b>			
Urban	63 (63.6%)	36 (36.4%)	0.0001
Rural	26 (29.9%)	61 (70.1%)	
<b>Income</b>			
< 1000 RM	42 (40%)	63 (60%)	0.015
≥1000 RM	47 (58%)	34 (42%)	
<b>Education</b>			
None	12 (21.4%)	44 (78.6%)	0.0001
Yes	77 (59.2%)	53 (40.8%)	
<b>Religion</b>			
Muslim	28 (42.4%)	38 (57.6%)	0.272
Non-Muslim	61 (50.8%)	59 (49.2%)	
<b>Marital status</b>			
Single	7 (41.2%)	10 (58.8%)	0.563
Married	82 (48.5%)	87 (51.5%)	
<b>Age of first child birth</b>			
≤30	63 (46.7%)	72 (53.3%)	0.035
>30	15 (71.4%)	6 (28.6%)	
<b>Parity</b>			
Nulliparous	11 (35.5%)	20 (64.5%)	0.131
Non-nulliparous	78 (50.3%)	77 (49.7%)	
<b>Breast feeding</b>			
Yes	63 (48.1%)	68 (51.9%)	0.919
No	26 (47.3%)	29 (52.7%)	
<b>Hormonal Medication</b>			
Yes	34 (56.7%)	26 (43.3%)	0.097
No	55 (43.7%)	71 (56.3%)	
<b>Menarche</b>			
<13 year old	33 (55.9%)	26 (44.1%)	0.4
≥13 year old	45 (48.9%)	47 (51.1%)	
<b>Menopause</b>			
Yes	38 (45.2%)	46 (54.8%)	0.518
No	51 (50.0%)	51 (50.0%)	
<b>Family History</b>			
Yes	9 (42.9%)	12 (57.1%)	0.627
No	80 (48.5%)	85 (51.5%)	

**Table 3. Logistic Regression Analysis Predicting Advanced Breast Cancer**

Patient Characteristics	P Value	Odds Ratio (95% confidence interval)
Non-Chinese	0.043	2.35 (1.03 to 5.39)
Rural residence	0.043	2.18 (1.03 to 4.64)
Non-educated	0.020	3.70 (1.62 to 8.45)
Salary < 1000 RM	0.592	0.82 (0.40 to 1.70)

than 1000 RM per month ( $P = 0.015$ ) and 78.6% of patients who had never been to school ( $P = 0.0001$ ) presented with advanced disease. A patient who is non-Chinese, from rural area, has an income of less than RM 1000 and non-educated had a 83.3% likelihood to present with advanced disease in our study ( $P < 0.0001$ ). In multivariate analysis where these four relevant coefficients were put in logistics regression analysis, non-Chinese race ( $P = 0.043$ ), rural residence ( $P = 0.043$ ) and non-educated ( $P = 0.02$ ) were recognized as independent factors predicting advanced breast cancer at presentation (Table 3).

In our study too, 20.4% of patients refused proper recommended treatment or defaulted follow up altogether with majority of them opted for traditional or alternative therapy.

## Discussion

Breast cancer is the commonest cancer among women in Malaysia and despite being the second largest state in the country, data on breast cancer from Sabah has been poorly reported and published. From our study, the commonest affected race was Chinese but they present at earlier stage of the disease compared to other races. Non-Chinese were twice more likely to present with advanced disease (Table 3). A similar picture was also seen in Peninsular Malaysia and Singapore (Greene et al., 2002; Hisham and Yip, 2003; 2004; Lim and Yahaya, 2004; Tan et al., 2005). In our study too, Chinese had less ER-negative tumours compared to non-Chinese (33.3% vs. 44.2%). It has been reported that ER-negative tumours are more aggressive and carry a poorer prognosis compared to ER-positive tumours (Rochefort et al., 2003). In line with the report, our study has shown ER-negative tumours were more likely to present as advanced disease compared to ER-positive tumours (65.9% vs. 42.7%). Commonest age group was 40 to 49 years of age which is similar with Peninsular Malaysia (Lim and Yahaya, 2004). The western world has the peak prevalence in the 50 to 59 year old age group (Greene et al., 2002). There was no significant age difference in patients who presented in early and late disease in our study (Table 2). This is in contrast with several reports that younger patients were more likely to present with advanced and aggressive disease<sup>9</sup>.

52.2% of our patients presented with either stage III or IV disease. This is compared to within Malaysia- Kuala Lumpur Hospital, 50-60%; University Malaya Medical Centre, Kuala Lumpur, 30-40% and Penang State, 37.7% (Penang Cancer Registry, 1999; Hisham and Yip, 2004). Kuala Lumpur Hospital caters mainly to the lower socioeconomic group of patients in Kuala Lumpur which

helped to explain the similar high proportion of advanced disease seen here (Hisham and Yip, 2004). Proportion of patients presented with advanced disease seen in large medical centres in the region such as Tan Tock Seng Hospital in Singapore and Asan Medical Centre in Korea were 21.6% and 12.3-17.4% respectively (Tan et al., 2005; Son et al., 2006). In the USA, only 7% of patients had stage III disease at the time of diagnosis and the Western world in general had 25% of breast cancer patients presented at advanced stage (National Cancer Institute, 2001; Lim and Yahaya, 2004).

Patients with advanced disease seen here were more likely to be non-Chinese, poor- with salary of less than RM 1000 per month, from rural area and non-educated. These four parameters were found to be all statistically significant in univariate analysis and, except for income less than RM 1000, in multivariate analysis (Figures 2 and 3). It is also important to highlight that 9.1% of patients here presented with ulcerative mass and only 2.2% had a suspicious lesion on mammography. This is in great contrast with USA, where 30% to 40% of breast cancers are detected with screening mammography. Besides, 20.4% of patients defaulted proper treatment and follow up, most opted for alternative or traditional therapy. This further delayed appropriate treatment. Most of them came back to us with more advanced disease after a period of time. This figure is in huge contrast even if compared to Kuala Lumpur Hospital where only 5% of patients defaulted treatment (Lim and Yahaya, 2004).

This picture of late presentation and high default rate can be attributed to multiple factors. Lack of awareness of breast cancer among women in Sabah and strong influence of traditional and cultural belief are two main factors. Lack of awareness with wrong social and cultural perception of breast cancer have been associated with advanced disease at presentation (Sandelin et al., 2002; Lim and Yahaya, 2004). Women feel that their role as a wife, mother and female as a whole will be seriously threatened and affected if they have breast cancer. Thus, a strong sense of denial normally developed as a protective mechanism against such threat. Due to strong traditional influence, many women will initially seek traditional or alternative treatment such as 'bomoh' or faith healing before they present to hospital when the initial treatment has failed.

Most parts of Sabah are still very much underdeveloped with limitation of quality education, communication system and health care. An ill patient may take up more than a full day of travelling on foot, by river or gravel road to reach the nearest health centre. Sabah has the poorest health care service in the country with a doctor to patient ratio of 1: 4000, in comparison with Kuala Lumpur, 1: 500 and Malaysia in general, 1: 150,014. Efforts to improve education, communication and health care system have remained a great challenge. There is currently no national mammography screening of breast cancer in Malaysia due to lack of financial funding and resources (Lim and Yahaya, 2004).

Much effort is needed to improve the awareness of breast cancer among women in Sabah. The month of October is dedicated as breast cancer awareness month in

Malaysia where talks, seminars and related activities on breast cancer awareness, detection and treatment are held all over the country. These activities are seen to be effective and beneficial but the effect of which will mainly be among women living in urban areas where such activities are normally held. Effort to involve more rural areas must be multiplied as most patients with advanced cancer in our report were from rural areas. The media and non-government organisations can play an invaluable role in such areas. Hospitals and health clinics in rural areas should also improve efforts to educate and promote breast cancer awareness including breast self examination among the villagers at all times.

The public should also be made aware that alternative and traditional therapy have no role in the management of breast cancer. The practice of alternative and traditional medicine should be regulated and monitored strictly by the authorities. Besides, poor road conditions and communication network to rural areas in the state should be improved to ease referrals and delivery of more effective health care. The discrepancy of doctor-patient ratio with the rest of Malaysia should be addressed to and setting up a national screening programme for breast cancer will be desirable. There should also be a fast tract referral system for patients suspected of breast cancer to be seen earlier at referral hospitals.

In conclusion, the majority of women with breast cancer in the state of Sabah present with advanced disease. Those who presented late in our study were more likely to be non-Chinese, poor, non-educated and from rural areas. A significant portion of them defaulted proper treatment and had a strong belief in alternative and traditional therapies. More effort is needed to increase awareness of breast cancer among women in Sabah, especially among those who are more likely to present with advanced disease.

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