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Short Communication

Seasonal variation in breast cancer diagnosis in Singapore

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Summary This study investigates seasonality in the diagnosis of 3219 female breast carcinoma cases reported between 1995–8 in Singapore. There is little evidence of marked seasonal variation. Angular regression suggested that observed differences in peak diagnosis with respect to menopausal status, tumour size, ER and PR status may be chance. © 2001 Cancer Research Campaign http://www.bjcancer.com

Seasonality in the presentation of breast cancer has been claimed in countries with distinct climatic seasons. Thus in northern latitudes, the peak of the seasonal variation in Israel occurred in Spring (Cohen et al, 1983), USA in May (Jacobsen and Janerich, 1977), while Southampton, England it was in June (Kirkham et al, 1985). In contrast, Galea and Blamey (1991) suggest in Nottingham, England there is 'no difference in frequency of tumour detection' – here May to August compared to September to April. On the other hand peaks for those tumours self-detected and requiring surgery occurred in Spring and late Autumn in the USA (Ross et al, 1997) with a similar pattern in Bulgaria (Dimitrov et al, 1998). In southern latitudes the peak of initial detection of breast cancer in Auckland, New Zealand occurred in December (Holdaway et al, 1990).

It has been suggested that the peak presentation may vary with patient characteristics. Thus Kirkham et al (1985) noted that the seasonality is more pronounced in premenopausal than post-menopausal women who peaked 3 months earlier in March. They also suggested that the small tumours (<3 cm diameter) were diagnosed 1 to 2 months earlier than the larger ones.

However, in none of these studies has the possibility been quantified that the seasonal pattern observed is an artifact of the confounding influence of referral patterns.

Singapore is a small island and this, as well as the health care system itself, facilitates open access to care. The 3.7 million population comprises peoples whose origins are mainly Chinese (78%), Malay (14%) or Indian (7%) (Lau, 1993). Being equatorial (latitude 1° north), the tropical climate has a relatively unchanging pattern over the year with daily temperatures ranging from 24 to 32°C. As previous studies have all been conducted in countries with distinct weather patterns and with lower overall health care delivery system performance (WHO, 2000), evidence from Singapore may be particularly useful in examining the influence of any seasonal variation in breast cancer.

The Singapore Breast Cancer Registry identified all permanent residents of Singapore with malignant breast carcinoma from January 1995 to December 1998 and the corresponding medical and histology records were collected and reviewed. The date of diagnosis was taken as the day of surgery or when the malignancy was either clinically or histologically confirmed. These would usually be some days after the date of first presentation.

In addition, ethnicity (Chinese, Malay, Indian or others), date of birth, menstrual, oestrogen and progesterone receptor (ER, PR) status; tumour size and stage were recorded. Menopausal status was considered to be uncertain if patients had bilateral oophorectomy.

Data from each calendar year is standardized to 12 months of equal duration and the date of peak diagnosis is identified using the methods described in Machin and Chong (1998). The associated statistical significance was tested by Mardia χ^2 statistic with 2 degrees of freedom (Mardia, 1972). The bootstrap technique (Fisher, 1993) was used to obtain a 95% confidence interval (CI) for the peak date using 1000 bootstrap samples of the same size as the number of patients under consideration.

The variation in date of peak diagnosis between different patient groups was explored using the methods of Fisher and Lee (1992). They describe how the regression of an angular variable, the day of diagnosis of breast cancer within the year, on a potential explanatory variable such as menopausal or receptor status can be made.

In total 3219 women were diagnosed with breast cancer over the 4 years. Figure 1 shows the frequency distribution of the date of diagnosis, presented as a rose diagram on a half monthly basis. There is no clear cut seasonal pattern although fewer cases are diagnosed in January and February (close to the Western and Chinese New Year festivals) and they appeared more numerous approximately 6 months later over the June to August period. The estimated peak (Table 1) of August 27 (95% CI July 14 to October 07) is statistically significant (P = 0.015) but of small magnitude (R = 0.036).

Table 1 shows the estimated peaks for groups based on patient and tumour characteristics recorded at presentation. It is clear, for example, that the peaks within the 4 ethnic groups are far from strong, and while those for the Chinese and Others coincide in August, that for the Malays is 3 weeks earlier in July whereas for the Indians, it is 2 months later in October. Only that for the Indian women is statistically significant (P = 0.036) but, with R = 0.160, this is not very marked.

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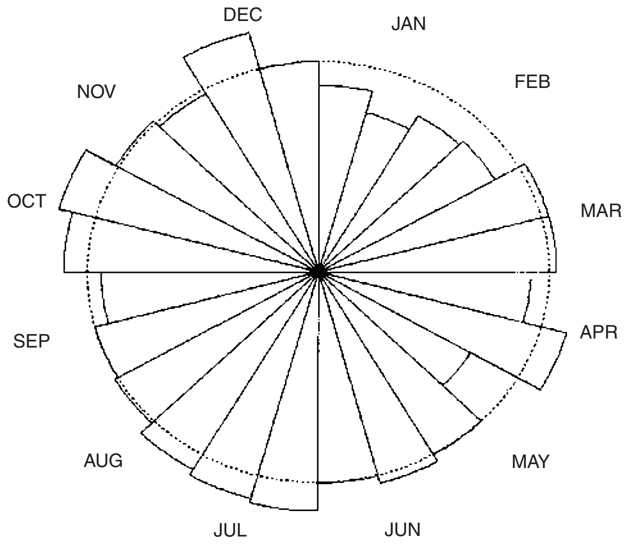

Figure 1 Rose diagram of half-monthly diagnosis of female malignant breast cancer patients

There is only a 4-day difference in the peak dates for pre- and post-menopausal women. The peaks for ER- and PR-negative women essentially coincide in late August and early September respectively and both precede the peaks for the positive tumours by 1 month. These are all statistically significant but of relatively low magnitude. The close agreement in the results for ER and PR status arise since the status is the same for each in 78% of the women for which they are both observed.

The date of peak diagnosis for the women who have large sized tumours (≥1 cm) is late August in contrast to early December in those with the small tumours. However, the only statistically significant peak is for those with the larger tumours (R = 0.049, P = 0.002) but again this is of low magnitude.

Apart from Stage 0 patients who have an estimated peak in early July, the higher the stage the earlier the peak in diagnosis although only that for Stage IIA disease at September 25 is statistically significant (R = 0.061, P = 0.034).

Table 2 summarizes the associated regression analyses for the patient and tumour characteristics that are binary in nature. However, these analyses did not establish any statistically significant differences between the corresponding subgroups. For example, the observed 3-month difference in the peak dates of diagnosis for the different-sized tumours is not established as other than due to chance (β = 1.112, 95% CI: – 0.81 to 3.04, P = 0.26).

A clear drawback of this study (and most others in this area) is the uncertain relationship between date of diagnosis and date of onset of symptoms of breast cancer. The latter is more likely to be aetiologically important as the variable delays from first symptom to presentation and eventual diagnosis may depend on many factors. In our situation, the delay between onset of symptoms and presentation is uncertain but that between presentation and diagnosis is not likely to be great.

Table 1 Summaries of seasonal variation by patient and tumour characteristics at presentation for all women

	Number of cases	Corresponding calendar date	Magnitude of peak, R	95% CI	Mardia χ^2	P
All	3219	Aug 27	0.036	Jul 14–Oct 07	8.41	0.015
Ethnicity						
Chinese	2743	Aug 21	0.031	Jun 21–Oct 10	5.31	0.070
Malay	307	Jul 30	0.060	Apr 04–Oct 21	2.22	0.33
Indian	130	Oct 28	0.160	Sep 09–Dec 13	6.65	0.036
Others	39	Aug 20	0.130	Mar 30–Dec 06	1.31	0.52
Menopause						
Pre	1557	Aug 19	0.026	May 22–Jan 24	2.10	0.35
Uncertain	264					
Post	1398	Aug 23	0.036	Jun 13–Nov 04	3.59	0.17
ER						
Negative	1061	Sep 01	0.084	Jul 27–Sep 30	14.86	0.0006
Not done	732					
Positive	1426	Oct 02	0.056	Aug 26–Nov 15	8.98	0.011
PR						
Negative	1308	Aug 31	0.071	Jul 27–Oct 02	13.07	0.002
Not done	779					
Positive	1132	Oct 04	0.076	Sep 09–Nov 19	12.96	0.002
Tumour (cm)						
<1	338	Dec 06	0.030	Jul 16–May 06	0.60	0.74
≥ 1	2572	Aug 30	0.049	Jul 27–Oct 04	12.20	0.002
Not done	309					
Stage						
0	276	Jul 05	0.036	Feb 10–Dec 08	0.70	0.71
I	770	Sep 12	0.042	Jun 13–Dec 11	2.68	0.26
IIA	922	Sep 25	0.061	Aug 09–Nov 15	6.76	0.034
IIB	662	Aug 04	0.034	Apr 01–Nov 23	1.52	0.47
III	208	Jun 18	0.039	Jan 30–Dec 04	0.63	0.73
IV	199	Apr 16	0.026	Nov 07–Oct 07	0.26	0.88
Not done	182					

Table 2 Regression coefficients for differences in peak date of diagnosis for selected patient and tumour characteristics at presentation for all women

Variable		Date of peak	Number of cases	Regression coefficient, β	Standard error	*P*
Menopause	Pre	Aug 19	1557	0		
	Post	Aug 23	1398	0.030	0.425	0.94
ER	Negative	Sep 01	1061	0		
	Positive	Oct 02	1426	0.275	0.227	0.23
PR	Negative	Aug 31	1308	0		
	Positive	Oct 04	1132	0.302	0.214	0.16
Tumour size (cm)	≥ 1	Aug 30	2572	0		
	<1	Dec 06	338	1.112	0.983	0.26

The overall health care system in Singapore is ranked very highly (WHO, 2000) and provides relatively open access to care although individuals are less likely to self refer during the span of the New Year (December to February) festivities. In addition, the tropical climate is of an essentially unchanging pattern over the year. For both these reasons a major seasonal component in the diagnosis of breast cancer (whether induced by climatic changes or referral) would not be anticipated. Thus the fewer cases in January and February and the consequential peak of small magnitude in August reflect self-referral patterns alone and not the presence of an aetiological determinant. Likewise, the corresponding seasonality reported in other studies may be enhanced (or obscured) by local referral characteristics, perhaps leading to a false indication of an underlying climatic component which might, for example, influence hormone activity as has been conjectured (Cohen et al, 1983; Mason et al, 1985).

When seasonality between patients with different characteristics is compared, our findings are not always consistent with previous studies. Thus while Kirkham et al (1985) reported peak presentation for pre-menopausal women was 3 months earlier than for post-menopausal, they differed by only 4 days in Singapore (Table 1).

The regression methodology introduced, analogous to that used routinely in other areas of clinical research, potentially allows a more detailed investigation of possible seasonal patterns. In this study, these methods suggested observed differences between groups might be no more than chance. This will not necessarily be the case in other geographical locations.

If a climatic component played a major role in the development of breast cancer, then one might anticipate some gradient between studies ranging from northern (and southern) latitudes to the equator and perhaps similarities between those of common latitude but differing longitude. One would anticipate little effect at the equator as we have observed. The findings of certain other studies may have been distorted by different health care delivery systems and other confounding variables. Studies reported to date show no such gradient but the lack of standardization in the identification of case presentation dates and reporting details make the true position unclear. To overcome these shortcomings, a coordinated and prospective study using individual dates of onset, patient specific and health care delivery details encompassing subjects from many latitudes and longitudes is required to reveal the extent of a climatic component, if any, in the aetiology of breast cancer.

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