# **ORIGINAL ARTICLE**

# Factors influencing late stage of breast cancer at presentation in a district Hospital - Segamat Hospital, Johor

# Mao Li Cheng, MB BCh BAO, DaoYao Ling, MBBS, Prathibha K P Nanu, MBBS, Hasnizal Nording, MS, Chen Hong Lim, MS

Department of Surgery, Hospital Segamat, Johor.

### SUMMARY

Introduction: In Malaysia, late stage presentation of breast cancer (stage III or IV) has been a healthcare problem that varies geographically throughout the country. This study aims to understand the factors influencing late stage of breast cancer at presentation among Malaysian women in Segamat Hospital, Johor, which is a district hospital.

Methods: A retrospective descriptive study was conducted on secondary data of all newly diagnosed breast cancer women from 1st August 2011 to 28th February 2014. Secondary data includes age, ethnicity, marital status, family history, education level, occupation, presenting symptom, duration of symptom, tumour size, tumour pathology, tumour grading, oestrogen, progesterone and HER-2 receptor status were collected and analysed using SPSS version 20.0.

Result: In total, data from 52 women was analysed and two women were excluded for incompleteness as these women defaulted. Late stage at presentation was 59.6% of all new cases (17.3%, stage III and 42.3%, stage IV). The commonest age group of all women diagnosed with breast cancer was in the 5th decade. Majority of them were Malay, married and housewives with no family history of breast cancer. The statistically significant factors associated with late stage at presentation include Malay ethnicity (p=0.019), presenting symptoms other than breast lump (p=0.047), and duration of breast lump more than 3 months (p=0.009).

Discussion/Conclusion: The study demonstrated presentation at late stage of breast cancer is a major health concern among Malaysian women in district hospital. This may be attributed to different sociocultural beliefs, strong belief in complementary and alternative medicine, lack of awareness, and difficult accessibility to healthcare services.

**KEY WORDS:** Breast Cancer, Cancer Staging, District Hospital, Malaysia

### INTRODUCTION

Breast cancer is the commonest cancer and has the highest cause of cancer death among women worldwide. From 2008 to 2012, the incidence rate of breast cancer increased by more than 20%, while mortality increased by 14%.<sup>1</sup> However, there are disparities between developed and developing countries. The incidence rates remain highest in developed countries, but mortality is relatively higher in developing countries.<sup>1</sup> This is because women presented at late stage of disease (stage III or stage IV) in developing countries.<sup>2</sup>

In 2012, International Agency for Research in Cancer estimated 5,410 new cases of breast cancer with 2,572 mortalities among Malaysian women.<sup>1</sup> In Malaysia, the stage of breast cancer at presentation varies according to geographical distribution.<sup>3-5</sup> However, majority of researches were conducted in tertiary hospitals in the cities. Data from district hospitals that serve the suburban and rural areas was lacking. Therefore, research from suburban and rural areas are important for clinicians to better understand the stage of breast cancer among Malaysian women in these areas. These may provide information needed for early cancer detection and thereby improving the overall survival.

We constructed a retrospective descriptive study of breast cancer among Malaysian women in a district hospital -Segamat Hospital. Segamat Hospital is a 314 bedded hospital in Segamat district, north of Johor, where the female population is 52,657.<sup>6</sup> This hospital neither has mammogram nor a pathologist. These services are provided by the nearest hospital - Hospital Pakar Sultanah Fatimah, Muar, which is 83.5 km away. The study is aimed to understand the distribution of breast cancer and factors influencing late stage at presentation in a district hospital. We believe a better understanding of this group of women will help in early cancer detection and improve the overall survival of breast cancer in these areas.

### MATERIALS AND METHODS

This is a retrospective review of all newly diagnosed breast cancer women who presented to surgical department at Segamat Hospital between 1st August 2011 and 28th February 2014. Non-Malaysians, male, recurrent breast cancer, phyllodes breast tumour and women who defaulted treatment were excluded. Data including stage of disease, socio-demographic (age, ethnicity, marital status, family history, education level and occupation), disease characteristics (presenting symptom, duration of breast lump

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Corresponding Author: Mao Li Cheng, Department of Surgery, Hospital Segamat, KM 6, Jalan Genuang, 85000 Segamat, Johor Email: maoli\_84@hotmail.com

Category	Frequency (%)	Mean (SD)
	n = 52	
Age (Year)		53.9 (10.2)
≤ <b>40</b>	3 (5.8)	
41 – 50	17 (32.7)	
51 – 60	21 (40.4)	
≥61	11 (21.2)	
Ethnicity		
Malay	39 (75.0)	
Chinese	6 (11.5)	
Indian	6 (11.5)	
Other	1 (1.9)	
Family history of breast cancer		
Yes	10 (19.2)	
No	42 (80.8)	
Marital status		
Married	43 (82.7)	
Not Married	9 (17.3)	
Widow	5 (9.6)	
Single	4 (7.7)	
Educational level		
No formal education	14 (26.9)	
Formal education		
Primary school	28 (53.8)	
Secondary school	6 (11.5)	
Tertiary education	4 (7.7)	
Occupation		
Housewife	33 (63.5)	
Non Professional	14 (26.9)	
Professional	5 (9.6)	
	5 (510)	1

Table I: Socio-demographic Characteristics of Breast Cancer in Segamat Hospital

Table III: Histopathology Characteristics of Breast Cancer	' in
Segamat Hospital	

Category	Frequency (%)
Tumor pathology	
Invasive breast carcinoma	
Invasive ductal carcinoma	49 (94.2)
Invasive lobular carcinoma	3 (5.8)
Carcinoma in-situ	0 (0.0)
Estrogen receptor status	
Yes	26 (50.0)
No	21 (40.4)
Not Available	5 (9.6)
Progesterone receptor status	
Yes	34 (65.4)
No	13 (25.0)
Not Available	5 (9.6)
HER – 2 receptor status	
Yes	8 (15.4)
No	18 (34.6)
Not Available	26 (50.0)
Bloom-Richardson Grading	
Grade 1	7 (13.5)
Grade 2	24 (46.2)
Grade 3	13 (25.0)
Not Available	8 (15.4)

and tumour size), and histopathological characteristics (tumour pathology, tumour grading, oestrogen receptor status, progesterone receptor status and HER-2 receptor status) was collected and analysed.

Table II: Symptom Characteristics of Breast Cancer in Segamat Hospital

Category	Frequency	Median		
	(%)	(Range)		
Presenting symptom				
Breast lump	39 (75.0)			
Symptoms other than breast lump	13 (25.0)			
Systemic symptoms	4 (7.7)			
Breast pain	3 (5.8)			
Incidental Finding	3 (5.8)			
Chest Swelling	2 (3.8)			
Axillary Swelling	1 (1.9)			
Duration of breast lump (months)		4.0 (0.3,60.0)		
≤ 3 months	16 (41.0)			
>3 months	23 (59.0)			
Site of breast cancer				
Right breast	27 (51.9)			
Left breast	24 (46.2)			
Bilateral breast	1 (1.9)			
Tumour size (mm)		42.5 (8.0,150.0)		



Fig. 1: Stage of Breast Cancer at Presentation in Segamat Hospital.

Staging of the disease was in accordance to the American Joint Committee on Cancer (AJCC) Cancer Staging Manual, 7th edition.<sup>7</sup> The late stage is defined as breast cancer at either stage III or IV of the disease.

These secondary data were analysed using SPSS Statistics Desktop, V20.0.0 for Windows. Descriptive statistics were used for the analysis of the independent variables. Logistic regression were used to analyse the associations between socio-demographic, disease and histopathological characteristics, and stage of breast cancer.

The research had received approval from National Medical Research Register (NMRR-14-288-20209), and Malaysian Ethical Research Committee (MREC (3) KKM/NIHSEC/P14-419). Confidentiality of all the subjects' personal details were maintained.

# RESULTS

The total number of women diagnosed with breast cancer during the study period was 54. However, only 52 women's data was analysed. The other two women who defaulted after

n (%)         n (%)         Ratio         Odd Ratio $s50$ 8 (38.1)         12 (38.7)         -         1.00         - $s50$ 13 (62.0)         19 (61.3)         0.964         0.97         0.31,3.04           Ethnicity         27 (87.1)         0.019         5.06         1.30, 19.72         0.026         8.32         1.29, 53.72           Non-Malays         9 (42.9)         4 (12.9)         0.169         0.37         0.091, 1.52         1.00         -           Family history of breast cancer         Yes         6 (28.6)         4 (12.9)         0.169         0.37         0.09, 1.52         1.00         -           Marital status         15 (71.4)         27 (87.1)         -         1.00         -         1.00         -           Married         15 (71.4)         28 (90.3)         -         1.00         -         -         1.00         -           Formal education         7 (33.3)         7 (22.6)         0.393         0.58         0.17, 2.01         -         -         -         -         -         -         -         -         -         -         -         -         -         -         -         -         -	Category	Early	Late	p value <sup>a</sup>	Crude Odd	95% CI	p value ⁵	Adjusted	95% CI
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Ethnicity         Image         Image <thimage< th="">         Image         Image</thimage<>	>50	13 (62.0)	19 (61.3)	0.964	0.97	0.31,3.04			
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Family history of breast cancer Yes 6 (28.6) 4 (12.9) 0.169 0.37 0.09, 1.52 No 15 (71.4) 27 (87.1) - 1.00 Marital status Married 15 (71.4) 28 (90.3) - 1.00 No transried 6 (28.6) 3 (9.7) 0.090 0.27 0.06, 1.23 Educational level No formal education 7 (33.3) 7 (22.6) 0.393 0.58 0.17, 2.01 Formal education 14 (66.6) 24 (77.4) - 1.00 Cocupation 14 (66.6) 24 (77.4) - 1.00 Housewife 11 (51.4) 22 (71.0) 0.770 1.33 0.19, 9.19 Non-professional 8 (38.1) 6 (19.4) 0.513 0.50 0.63, 4.00 - Professional 2 (9.5) 3 (9.7) - 1.00 Presenting symptom Breast lump 19 (90.5) 20 (64.5) - 1.00 Duration of breast lump 2 (2.5) 11 (35.5) 0.047 5.23 1.02, 26.73 1.00 Symptoms other than 2 (9.5) 11 (35.5) 0.047 5.23 1.02, 26.73 1.00 Symptoms other than 2 (9.5) 16 (80.0) 0.009 6.86 1.63, 28.90 0.015 7.02 1.46, 33.81 Invasive ductal carcinoma 1 (4.8) 2 (65.) 0.798 1.38 0.12, 16.26 Oestrogen receptor status 7 (36.8) 15 (57.7) 0.716 1.24 0.39, 3.94 No 10 (47.6) 11 (42.3) - 1.00 Progesterone receptor status 7 (36.8) 13 (61.9) 21 (80.8) 0.157 2.59 0.70, 9.61 No 8 (38.1) 5 (19.2) - 1.00 Progesterone receptor status 7 (36.8) 15 (19.2) - 1.00 Progesterone receptor status 7 (36.8) 10 (12.2) - 1.00 Progesterone receptor status 7 (36.8) 0.157 2.59 0.24, 6.63 No 10 (71.4) 8 (66.6) - 1.00 Progesterone receptor status 7 (36.8) 0.157 2.59 0.24, 6.63 No 10 (71.4) 8 (66.6) - 1.00 Progesterone receptor status 7 (36.8) 0.157 2.59 0.24, 6.63 No 10 (71.4) 8 (66.6) - 1.00 Progesterone receptor status 7 (36.8) 0.157 2.59 0.24, 6.63 No 10 (71.4) 8 (66.6) - 1.00 Progesterone receptor status 7 (10.0) Progesterone receptor status 7 (	Non-Malays	9 (42.9)	4 (12.9)	-	1.00	-	-	1.00	-
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$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	Duration of breast lump								
>3 months       7 (36.8)       16 (80.0)       0.009       6.86       1.63, 28.90       0.015       7.02       1.46, 33.81         Tumour pathology       Invasive ductal carcinoma       20 (95.2)       29 (93.5)       -       1.00       -	≤ 3 months	12 (63.2)	4 (20.0)	-	1.00	-	-	1.00	-
Tumour pathology Invasive ductal carcinoma Invasive lobular carcinoma Oestrogen receptor status Yes       20 (95.2)       29 (93.5)       -       1.00       -         Oestrogen receptor status Yes       11 (4.8)       2 (6.5)       0.798       1.38       0.12, 16.26         Oestrogen receptor status Yes       11 (52.4)       15 (57.7)       0.716       1.24       0.39, 3.94         No       10 (47.6)       11 (42.3)       -       1.00       -         Progesterone receptor status Yes       13 (61.9)       21 (80.8)       0.157       2.59       0.70, 9.61         No       8 (38.1)       5 (19.2)       -       1.00       -         HER-2 receptor status Yes       4 (28.6)       4 (33.3)       0.793       1.25       0.24, 6.63         No       10 (71.4)       8 (66.6)       -       1.00       -         Bloom-Richardson Grading Grade 1       4 (20.0)       3 (12.5)       -       1.00       -         Grade 2       11 (55.0)       13 (54.2)       0.600       1.58       0.29, 8.61       -         Grade 2       5 (25.0)       8 (33.3)       0.427       2.13       0.33 13.81       -	>3 months	7 (36.8)	16 (80.0)	0.009	6.86	1.63, 28.90	0.015	7.02	1.46, 33.81
Invasive ducial carcinoma       20 (95.2)       29 (93.5)       -       1.00       -         Invasive lobular carcinoma       1 (4.8)       2 (6.5)       0.798       1.38       0.12, 16.26         Oestrogen receptor status       -       10 (47.6)       11 (52.4)       15 (57.7)       0.716       1.24       0.39, 3.94         No       10 (47.6)       11 (42.3)       -       1.00       -         Progesterone receptor status       -       1.00       -         Yes       13 (61.9)       21 (80.8)       0.157       2.59       0.70, 9.61         No       8 (38.1)       5 (19.2)       -       1.00       -         HER-2 receptor status       -       -       1.00       -         Yes       4 (28.6)       4 (33.3)       0.793       1.25       0.24, 6.63         No       10 (71.4)       8 (66.6)       -       1.00       -         Bloom-Richardson Grading       -       -       1.00       -         Grade 1       4 (20.0)       3 (12.5)       -       1.00       -         Grade 2       11 (55.0)       13 (54.2)       0.600       1.58       0.29, 8.61         Grade 3       5 (25.0)       8 (33	Tumour pathology								
Invasive lobular carcinoma       1 (4.8)       2 (6.5)       0.798       1.38       0.12, 16.26         Oestrogen receptor status       11 (52.4)       15 (57.7)       0.716       1.24       0.39, 3.94         No       10 (47.6)       11 (42.3)       -       1.00       -         Progesterone receptor status       -       1.00       -         Yes       13 (61.9)       21 (80.8)       0.157       2.59       0.70, 9.61         No       8 (38.1)       5 (19.2)       -       1.00       -         HER-2 receptor status       -       -       1.00       -         Yes       4 (28.6)       4 (33.3)       0.793       1.25       0.24, 6.63         No       10 (71.4)       8 (66.6)       -       1.00       -         Bloom-Richardson Grading       -       -       1.00       -         Grade 1       4 (20.0)       3 (12.5)       -       1.00       -         Grade 2       11 (55.0)       13 (54.2)       0.600       1.58       0.29, 8.61         Grade 3       5 (25.0)       8 (33.3)       0.427       2.13       0.33. 13.81	Invasive ductal carcinoma	20 (95.2)	29 (93.5)	-	1.00	-			
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Grade 1       4 (20.0)       3 (12.5)       -       1.00       -         Grade 2       11 (55.0)       13 (54.2)       0.600       1.58       0.29, 8.61         Grade 3       5 (25.0)       8 (33.3)       0.427       2.13       0.33, 13.81	Bloom-Richardson Grading								
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Grade 3 5 (25.0) 8 (33.3) 0.427 2.13 0.33 13.81	Grade 2	11 (55.0)	13 (54.2)	0.600	1.58	0.29, 8.61			
	Grade 3	5 (25.0)	8 (33.3)	0.427	2.13	0.33, 13.81			

<sup>a</sup> Univariable logistic regression<sup>b</sup> Only factors associated with late stage presentation in multivariate logistic regression model

initial tissue diagnosis (4%) were excluded as staging was not done. Among the 52 women, 31 (59.6%) were diagnosed as late stage (stage III or IV) (Figure. 1). The most common age group of the women diagnosed with breast cancer was 51 to 60 years (40.4%) and the mean age was 53.9-year-old (Standard Deviation (SD)=10.2). The youngest and oldest women were 31- and 82-year-old respectively. Out of the 52 women, 39 were Malay, six were Chinese, six were Indian and one was Orang Asli (Table I). Only ten of these women had family history of breast cancer and four of them presented at late stage. Among the 43 married women, 28 presented at late stage and among the 33 housewives, 22 presented at late stage. (Table IV). Most of the women had at least primary school education, 28 of whom attended primary school, six attended secondary school and four obtained tertiary education (Table I).

Breast lump was the main presenting symptom, with 39 out of the 52 women had breast lump. The remaining 13 presented with symptoms other than breast lump such as systemic symptoms (anaemia or jaundice), breast pain, incidental finding while admitted for other reason, chest swelling and axillary swelling. For the women who presented with breast lump, 23 were at late stage. The median duration from initial detection of breast lump until seeking medical consultation was 4.0 months (range 0.3, 60.0months) and the median of tumour size on presentation was 42.5mm (range, 8.0, 150.0mm) (Table II).

A total of 49 women were diagnosed with invasive ductal carcinoma and three had invasive lobular carcinoma. There were no women diagnosed with carcinoma in-situ. Furthermore, out of 47 women, 26 were ER positive and 34 were PR positive. HER-2 positive were detected in eight out 26 women. Among the 44 women, 24 were Grade 2 carcinoma (Table III).

In univariable logistics regression analysis, factors found to be statistically significant with late stage of breast cancer were Malay ethnicity (p=0.019), presenting symptoms other than breast lump (p=0.047), and duration of breast lump more than 3 months (p=0.009) (Table IV). In the multivariate logistic regression analysis, elevated risks for late stage at presentation were observed in women of Malay ethnicity (OR=8.32; 95% CI: 1.29-53.72) and women having breast lump more than 3 months (OR=7.02; 95% CI: 1.46-33.81) (Table IV).

# DISCUSSION

We found that majority of Malaysian women in Segamat Hospital were diagnosed with breast cancer at late stage: stage III (17.3%) and stage IV (42.3%) (Figure 1). The stage of breast cancer at presentation in Segamat Hospital is more advanced in comparison to the other reports in major hospitals within Malaysia. A cross-sectional study in three referral medical centres in the East Coast of Malaysia and two public hospitals in Kuala Lumpur demonstrated late stage at presentation to be 44.8% Stage III and 11.3% Stage IV.<sup>3</sup> Another prospective study done in Queen Elizabeth Hospital, Kota Kinabalu, Sabah, showed 36.6% Stage III and 15.6% Stage IV.<sup>5</sup>

In Segamat Hospital, breast cancer occurs more commonly in older women, aged between 51 and 60 years, compared to those diagnosed in major hospitals, where the peak prevalence is 40- to 49-year-old age group.<sup>3</sup> This study also demonstrated educational level was not a contributing factor for women to seek medical treatment early. Nearly half of the women diagnosed at late stage were women with formal educational. In contrast, studies conducted locally in Sabah,<sup>5</sup> and internationally in Sweden,<sup>8</sup> and South India,<sup>9</sup> demonstrated educational level influences the presenting stage of disease. The earlier stage at diagnosis was reported in women with formal education. The commonest occupation was housewife, which was similar distribution as seen in another study done in Malaysia.4 Our study supported that women's occupation is not associated with the stage of breast cancer at presentation.9

From our study, we discovered three factors significantly influencing late stage of breast cancer at presentation to be of Malay ethnicity, presenting symptoms other than breast lump, and duration of breast lump for more than 3 months. Malay women (27 out of the 52 women) tend to present late compared to non-Malays (four out of the 52 women). The same situation had been observed in the major hospitals.<sup>3</sup> Although breast lump was the commonest reason in seeking medical consultation, 13 of the women diagnosed with breast cancer presented with a variety of other symptoms. This pattern of presentation is similar to those living in the cities.<sup>4,5</sup> In Segamat Hospital, among those who presented with symptoms other than breast lump, 11 of them were diagnosed at late stage. Among women with breast lump more than 3 months duration, 16 presented at late stage. Similar delayed presentation more than 3 months were reported in other Malaysian cities.4 Delayed presentation beyond 3 months is associated with reduced 5-year survival by 7% to 12%.10

The late stage of breast cancer at presentation in Segamat Hospital is likely attributed to different sociocultural beliefs, strong belief in complementary and alternative medicine, and lack of awareness. The help-seeking behaviour among Malaysian women especially the Malay had been reported to be influenced by the complex interaction of sociocultural beliefs, complementary and alternative medicine and their awareness of the disease.<sup>11,12</sup>

Women's role as wife or daughter is submissive in the suburban and rural society especially among the Malays. For these women, losing a breast may be equivalent to losing the role as a wife or losing a chance to get married. Thus, these women developed denial as a protective mechanism against such threats. These women would seek complementary and alternative medicine such as shaman, prayer or spiritual healing after diagnosed with breast cancer,<sup>13,14</sup> hoping they will be cured without surgery. They would only seek treatment in the hospital after alternative treatment has failed. Lack of awareness in the society also contributes towards the situation. Pink October Month is a dedicated month where talks, seminars and screening programs are organised to promote breast cancer awareness. Unfortunately, most of these campaigns are focused in the urban areas.

The situation may be worsened by difficulty in accessing healthcare services. The majority of breast cancer women in Segamat district are elderly, who are dependent on the family members to gain access to health facilities and have to travel significant distances. The duration from referral to actual consultation at surgical clinic might be one to two months according to the availability of clinic time. Given the difficulty to access the breast clinic, many women choose to ignore their symptoms in the early stage.

This is the first research on breast cancer conducted in a district hospital with limited-resources (i.e., a hospital without mammogram and pathologist) in Malaysia that serves the suburban and rural areas. This study also helps to provide information on breast cancer in Johor state. However, the use of secondary data in this study may not represent the actual target population in Segamat district. This may be because some women may either seek treatment in other districts, private hospitals, or do not seek treatment at all. Further multicentre studies are required to evaluate the epidemiological distributions and to identify the underlying reasons associated with late stage of breast cancer at presentation in district hospitals. Future directions in research should focus on sociocultural, complementary and alternative medicine, access to healthcare services and survival rate.

More effective measures should be arranged towards earlier detection of breast cancer in district hospitals. It is undeniable that complementary and alternative medicine will continue to play a role in women with breast cancer. Therefore, it should be strictly regulated and monitored by the relevant authorities. Health education and breast awareness campaigns should be conducted frequently in suburban and rural areas. The primary healthcare service and non-governmental organisations, can play a pivotal role to raise awareness of breast cancer in suburban and rural areas. Finally, a more effective delivery of healthcare for women should be set up such as one-stop breast clinic<sup>15,16</sup> or adopting the United Kingdom's NHS Cancer Plan.<sup>17</sup>

# CONCLUSION

This study demonstrates that late stage of breast cancer at presentation is a major health concern in Segamat Hospital especially among the Malays. Poor understanding of disease and delay in presentation to healthcare services were shown to be associated with this situation. This may be attributed to different sociocultural beliefs, strong belief in complementary and alternative medicine, lack of awareness, and difficult accessibility to healthcare services. To increase the knowledge and awareness among the community, frequent breast cancer awareness campaigns should be organised. An easier access to breast clinics would also help in detecting breast cancer at earlier stage. Future studies evaluating the sociocultural beliefs, complementary and alternative medicine, awareness and accessibility of healthcare services are required before initiating other recommendations in detecting early stage of breast cancer in Malaysia.

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