

Patient age at diagnosis and the clinicopathological features of breast cancer in women: A comparative study at the Korle-Bu Teaching Hospital Accra

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RESEARCH

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ABSTRACT

Background

Breast cancer (BC) is diagnosed commonly in younger Ghanaian women compared to women in western countries.

Aims

The aim of this study was to compare the clinicopathological features of BC in young women (≤ 39 years) with older women (≥ 40 years) and draw conclusions.

Methods

This was a retrospective review (2001–2014).

Results

Approximately 19.6 per cent of the study population were women aged ≤ 39 years (Group A). Bilateral BCs were commoner in group A compared to B (women aged 40 years

or older), [(1.1 per cent vs. 0.6 per cent), ($p=0.002$)]. About 60.7 per cent of group A had skin involvement compared to 71.3 per cent for B, ($p=0.002$). About 75.7 per cent of group A women presented with breast lumps after 3 months of onset (late), compared to 70.1 per cent of group B women ($p=0.000$). The mean size of primary BC for A was 5.6 cm compared to 5.1 cm for B, ($p=0.004$). Positive tumour margins were found in 27.7 per cent of BCs in A and 24.2 per cent in B, ($p=0.003$). Grade 3 tumours were common in group A than B [(35.8 per cent vs. 31.0 per cent), $p=0.002$]. Approximately, 70.5 per cent group A women had positive nodes compared to 88.8 per cent of group B ($p=0.001$). Higher TNM stages were found in group A compared to B [(58.1 per cent vs. 51.1 per cent, $p=0.033$)].

Conclusion

The study found that 19.6 per cent of the women were age 39 years or younger. Features of advanced BC were common in younger women. Routine self-breast examination is recommended for all Ghanaian women to enhance early detection and management of neoplastic lesions.

Key Words

Ghanaian women, breast cancer, younger age, advanced disease

What this study adds:

1. What is known about this subject?

This study showed that a significant proportion of breast cancer is still diagnosed in younger Ghanaian women.

2. What new information is offered in this study?

Ghanaian women are still presenting with advanced stage of the disease.

3. What are the implications for research, policy, or practice?

Features of worse prognosis are found to be associated with younger age at diagnosis with breast cancer.

Background

Breast cancer (BC) is the leading cause of cancer related morbidity and mortality in Ghana, in keeping with global statistics.¹⁻³ Publications from 1956 to 2015 on breast cancer (BC) in Ghana found the disease to be relatively common in younger Ghanaian women, who usually present late with advanced stages of the disease with poor treatment outcomes.^{4,5} The aim of this institution-based retrospective study was to compare the clinico-pathological features of BC in young women (≤ 39 years old) with older women (≥ 40 years old).

Method

Study Site

Data were gathered from the Department of Pathology, School of Biomedical Sciences, University of Ghana Medical School. This is the largest Pathology Department in the country. It reports between 5,000 and 8,000 histology cases annually. This Department receives surgical specimens from Korle-Bu Teaching Hospital, (the largest referral hospital in Ghana) and other hospitals in Ghana.

Study design

This was a retrospective study covering the period 2001–2014.

Data collection and analysis

We retrospectively analysed data from 4,336 Ghanaian women with histologically confirmed breast cancers. The women were divided into two age groups: ≤ 39 years (group A) and ≥ 40 years (group B). The following data were reviewed: age at histological diagnosis, tumour size (cm), histological subtype, histological grade, lymph node status, TNM (Tumour, nodal involvement and distant metastasis) stage and positive margins; - defined as breast cancer cells found within 2.0mm of the resection margins. Data were entered into and analysed using SPSS software (version 23). The clinico-pathological characteristics and prognostic factors were compared between the two age groups using paired samples test. The histological subtypes of breast cancers in this study were classified according to World Health Organization (WHO) histology classification of breast tumours. Histological grading of female breast cancers in this study was performed according to the modification of Bloom-Richardson system by the Elston and Ellis. The TNM

staging (pathological) for female breast cancers in this study was the system recommended by the American Joint Committee on Cancer (AJCC), (AJCC 6th edition of the cancer staging manual, 2002, New York) which takes into account the size of the primary tumour (T), presence and extent of regional lymph node involvement (N), and whether or not the cancer has spread to other areas of the body (metastasis, M).

Results

A total of 4,336 cases of female breast cancers (BCs) were diagnosed. Of this number, 851 (19.6 per cent) were 39 years old or younger (Group A), while the majority 3,484 (80.4 per cent) were 40 years or older (Group B). The ages of Group A women ranged from 14–39 years, with a mean of 33.6 years (SD \pm 4.7), and a modal age group of 30–39 years (82.6 per cent). For women in Group B, the ages ranged from 40–107, with mean age of 55.0 years (SD \pm 11.0), and a modal age group of 40–49 years (37.1 per cent) (Table 1).

The commonest primary symptom of BC in both groups of women was a palpable lump. The other primary symptoms were Scaly skin and bloody nipple discharge (Table 2). Bilateral palpable breast cancers were found in 1.1 per cent of Group A women and 0.6 per cent in Group B ($p=0.002$). For women with additional symptoms, skin involvement by breast cancer was found in 60.7 per cent of Group A women compared to 71.3 per cent for Group B ($p=0.002$) (Table 2).

For cases with stated duration of BCs at presentation, it was found that the majority of women in both groups presented after three months (late presentation) to a health facility after noticing the lump [(75.7 per cent for Group A versus 70.1 per cent for Group B), $p<0.001$] (Table 2).

BC in Group A women was commonly diagnosed using core needle biopsy specimens (35.5 per cent), while for Group B women it was mastectomy specimens (35.9 per cent) (Table 3). The sizes of BCs ranged from 0.4cm–24.0cm for Group A women compared to 0.4cm–22.0cm for Group B. The mean size of primary tumour was 5.6cm (SD \pm 4.0) in Group A patients but was 5.1cm (SD \pm 3.4) for women in Group B ($p=0.004$). Many of the women in Group A (46.2 per cent) had lumps greater than 5.0cm (T3); however, for Group B patients, 45.2 per cent of the lumps were greater than 2.0cm but less than or equal to 5.0cm (T2) ($p=0.002$) (Table 3). Approximately 27.7 per cent of mastectomy and excision specimens (combined) from Group A women had positive tumour margins, compared to 24.2 per cent for Group B women ($p=0.003$) (Table 3).

Invasive ductal carcinoma not otherwise specified (IDC-NOS) was the commonest type of BC in both Group A (84.3 per cent) and B (87.2 per cent) patients. Breast lesions such as; DCIS, malignant phyllodes tumour, Paget's disease, neuroendocrine carcinoma and lymphomas were common in Group A, while mucinous, invasive lobular, medullary, papillary, metaplastic and apocrine carcinomas were common in Group B women (Table 4).

In both age groups, many of the BC cases were grade 2 by the Bloom-Richardson grading system [(42.4 per cent for Group A versus 48.2 per cent for Group B), $p=0.002$] (Table 5).

The commonest TNM stage of women in Group A was stage 3 (31.8 per cent), but it was stage 2 (31.3 per cent) for Group B women. In all, Group A women had a combined (stage 3 and 4) TNM stage of 58.1 per cent, compared to a combined (stage 3 and 4) TNM stage of 51.1 per cent for Group B women ($p=0.033$) (Table 5).

Of the cases from which lymph nodes were retrieved from the axillary tail, a total of 179 (70.5 per cent) out of 254 Group A women had positive nodes compared to 1,461 (89.1 per cent) out of 1,640 Group B patients ($p=0.001$). The number of positive lymph nodes retrieved from Group A women ranged from 1–23 with a mean of 4.9 (SD=4.0), but it was 1–42 positive lymph nodes were retrieved for Group B women, with a mean of 5.0 lymph nodes (SD±4.3). Women in both groups had approximately equal numbers of 4 or more positive lymph nodes (52.8 per cent vs. 53.6 per cent) (Table 5).

Discussion

In this retrospective descriptive study, it was noted that a significant proportion (19.6 per cent) of the women diagnosed with BC were younger than 40 years of age. This value is far greater than the 5.0 per cent found in Native American women⁶ and the 10.6 per cent in Brazilian women,⁷ but compares favourably with values such as 14.9 per cent in African American women.⁸ The current figure for this study is however lower than the 30–40 per cent found in other studies.^{9,10} Several studies globally have demonstrated that breast cancers in younger women have a more aggressive biology, correlating with poorer outcomes when compared with older women^{11,12} The implication for this age category of Ghanaian women in this study is that they may have worse prognosis. However, age alone will not explain the poor prognosis of breast cancer in these young Ghanaian women. Further studies on predisposition,

gene and environmental interaction in this age group may increase our understanding of the situation.

The great majority (80.4 per cent) of the women diagnosed with BCs were aged 40 years and above. Breast cancer is a disease that is commoner in the elderly.¹³ As the population ages, increasing proportion of women aged 40 years and above will be diagnosed with breast cancer.^{13,14} Ghanaian women are ageing and thus the proportion of the women 40 years and above is similarly increasing and hence the high percentage in this study. Our findings are in keeping with the global statistics^{13,14} and also with studies from Nigeria.^{15,16}

The common primary symptoms of BC in both groups of women were palpable lumps. This is to be expected, as there is neither a population-based breast cancer screening programme, nor a routine mammography screening programme as commonly pertains in the western societies. Most Ghanaian women are either screened voluntarily or will seek medical advice when an abnormality is found in the breast. Furthermore, Ghanaian women aged 39 years or younger are even less likely to participate in a voluntary screening programme, they are thus more likely to present with a self-discovered obvious abnormality. The presentation of BC in this study is similar to those reported by Kwong et al.¹⁷ on BCs among Chinese women younger than 40 years. The current study also found that bilateral BCs were more common in younger women as compared to those aged 40 years and above. This finding differs from the study of Nelly et al in Egypt who found that bilateral BCs were frequent in older women.¹⁸

Symptoms of advanced clinical stage of BC at presentation such as skin involvement, axillary lymphadenopathy, nipple discharge, breast pain, chest wall invasion and nipple retraction in this study were frequent in younger women compared to older women. Late and advanced clinical stage of BC presentation in younger women in this current study is in accord with previous studies in Ghana and across the globe.¹⁹⁻²²

Delayed presentation of women with breast cancer at health facilities has been found to be associated with poor prognosis.²³ Late presentation (after 3 months) of breast cancer in this study was common in both groups, but more so in the younger age group [(75.7 per cent vs. 70.1 per cent) $p=0.000$]. This differs from the study by Arndt et al.²⁴ in Germany that found that older women waited longer than younger women before presenting their symptoms to a physician.

Mastectomy was commonly performed as a treatment option for BC in the older women compared to the younger women ($p=0.002$). The reasons for these differences are not apparent, but may be attributed to the choice of the BC patient, age at diagnosis, psychological and cosmetic impact on body image after surgery. These suggestions are supported by studies comparing mastectomy as a treatment option for breast cancer between women younger than 40 years and older women.^{25,26}

Stratifying the size of the primary breast tumours in this current study, it was found that larger tumours, particularly those greater than 5.0cm were common in the younger age group compared to the older age group ($p=0.002$). These findings support results of other studies that found larger tumour to be commonly associated with young age at diagnosis of BC.^{27,28} This however differs from Elrasheid et al.²⁹ study in the Galway University Hospital, that found larger tumour size to be commoner in older women.

The current study found that younger women with BCs are more likely to have positive tumour margins after surgery (mastectomy and excisions) compared to the older women. This may be a reflection of the larger tumours found in the younger age group. However, the positive tumour margin rates found in both groups are within the range of values from 4.0 per cent to 44.1 per cent found in previous studies in Ghana and globally.^{30,31}

Invasive ductal carcinoma (IDC-NOS) was the commonest BC in both groups. This is in line with studies in West Africa that found IDC-NOS as the commonest invasive BC in women.³² DCIS, malignant phyllodes, neuroendocrine, lymphomas and sarcomas were commoner in the younger age group while invasive lobular, medullary, papillary, metaplastic and apocrine carcinomas were commoner in women aged 40 years and above. This in keeping with the findings of what Elrasheid et al.²⁹

Higher histological grade (grade 3) of breast cancer at diagnosis was common in younger women compared to the older women ($p=0.002$). This is in accordance with studies that found younger age at diagnosis of BC to be associated with higher histological grades of invasive BCs.^{33,34}

The current study found that more than 50.0 per cent of the study population had 4 or more nodal involvement by breast cancer. This may be a reflection of the large primary tumour sizes in both groups and thus support the findings of Carter et al.³⁵ who found larger tumour to be associated with increased risk of nodal involvement. Our findings

however differ from those of Bonnier et al.³⁶ that concluded that younger women diagnosed with BC are more likely to have higher positive lymph nodes compared to older women.

Higher TNM stages of invasive BCs (Stages 3 and 4 combined) were common in women aged 39 years or younger compared to those aged 40 years or more ($p=0.033$). This differs from studies that found higher combined TNM stages to be common in older women compared to the younger age group.^{18,29,37} Our current findings however support studies that found young women, particularly African American women, with ancestral origins from Africa presenting to health facilities with advanced stages of the disease.^{38,39} Part of the explanation given for young women having higher TNM stage at presentation has been suggested to be the increased potential for a delayed diagnosis.⁴⁰

Conclusion

This is the first study that compared the clinicopathological characteristics of breast cancer in Ghanaian women younger than 40 years of age and their older counterparts. The study found that about one-fifth of the study population were women younger than 40 years of age. This group of women presented late with signs and symptoms of advanced and more aggressive BCs compared to their older counterparts. Routine breast self-examination is recommended for all Ghanaian women to enable early detection and the appropriate management. Genetics studies are needed to further evaluate the biology of BC in younger Ghanaian women.

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CONFLICTS OF INTEREST

The authors declare that they have no competing interests.

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Table 1: Age distribution of Ghanaian women diagnosed with breast cancer

Age (years)	Frequency (n)	Percentage (%)
Women age ≤39 (Group A)		
≤19	14	1.6
20–29	134	15.7
30–39	653	82.6
Total	851	100
Women age ≥40 (Group B)		
40–49	1,292	37.1
50–59	1,092	31.3
60–69	670	19.2
70–79	334	9.6
≥80	96	2.8
Total	3,484	100

Table 2: Symptoms and duration at presentation of breast cancers

	Group A	Group B	P-value
Primary symptom (n/%)			
Palpable lumps in one breast	839 (98.6)	3,463 (98.8)	0.007
Palpable lumps in both breasts	9(1.1)	20(0.6)	0.002
Nipple discharge	3 (0.3)	16 (0.5)	0.003
Scaly skin rash	0 (0.0)	3 (0.1)	0.064
Total	851(100.0)	3,484 (100.0)	
Additional symptoms (n/%)			
Skin involvement	54 (60.7)	301(71.3)	0.002
Axillary lymphadenopathy	13 (14.6)	50 (11.8)	0.002
Nipple discharge	7 (7.7)	18 (4.3)	0.002
Breast pain	6 (6.7)	18 (4.3)	0.002
Nipple retraction	3 (3.4)	10 (2.4)	0.002
Attachment of lump to the chest wall	4 (4.5)	10 (2.4)	0.002
Breast abscess	0 (0.0)	2 (0.5)	0.002
Weight loss	2 (2.2)	2 (0.5)	0
Lymphedema	0 (0.0)	1(0.2)	0.002
Itchy nipple	0 (0.0)	1 (0.2)	0.002
Total	89 (100.0)	422 (100.0)	
Duration of symptoms (months) (n/%)			
≤3	84 (24.3)	412 (29.9)	0
>3	262 (75.7)	964 (70.1)	0
Total	346 (100.0)	1,376 (100.0)	

Table 3: Categories of surgical specimens and size of primary tumour

	Group A (≤39 years) n (%)	Group B (≥40 years) n (%)	P-values
Type of surgical specimen			
Mastectomy	255 (30.0)	1251 (35.9)	0.002
Core needle biopsy	302 (35.5)	1216 (34.9)	0.001
Excision	241 (28.3)	803 (23.1)	0.002
Incision	53 (6.2)	214 (6.1)	0.003
Total	851 (100.0)	3,484 (100.0)	
Size of primary tumour (cm)			
Mean	5.6	5.1	0.004
≤2.0	68 (14.2)	342 (17.4)	0.002
2<S≤5	181 (39.6)	886 (45.2)	0.002
>5	222 (46.2)	732 (37.4)	0.002
Total	481 (100.0)	1,960 (100.0)	
Positive tumour margins	133 (27.7)	474 (24.2)	0.003

Key: S = size of primary tumour

Table 4: Histological subtypes of breast cancers

Histological subtype	Group A women (≤39 years) n/per cent	Group B women (≥40 years) n/per cent	P-value
IDC – NOS	723 (84.3)	3058(87.2)	0.002
Lobular	17 (2.0)	105(3.0)	0.002
Mucinous	18(2.1)	77(2.2)	0.033
Medullary	3(0.4)	30(0.9)	0.002
Malignant Phylloides	25(2.9)	22(0.6)	0.002
DCIS	28(3.3)	67(1.9)	0.002
Cribriiform	1(0.1)	10(0.3)	0
Neuroendocrine	5(0.6)	3(0.1)	0.003
Papillary	6(0.7)	36(1.0)	0.003
Metaplastic	3(0.4)	16(0.5)	0.001
Sarcoma	9(1.1)	16(0.5)	0.002
Lymphoma	4(0.5)	0(0.0)	0.003
Apocrine	0(0.0)	13(0.4)	0.003
Tubulolobular	1(0.1)	6(0.2)	0.001
Squamous cell	3 (0.4)	13(0.4)	0
Inflammatory	4 (0.5)	3(0.1)	0.001
Others	2 (0.2)	8(0.2)	0
Total	851 (100.0)	3,484 (100.0)	

Table 5: Histological grade, TNM stage and nodal involvement

	Group A (≤39 years), n (per cent)	Group B (≥40 years), n (per cent)	P- value
Histological grade			
Grade 1	156 (21.9)	633 (20.8)	0.001
Grade 2	302 (42.3)	1,465 (48.2)	0.002
Grade 3	255 (35.8)	940 (31.0)	0.002
Total	713 (100.0)	3,038 (100.0)	0.002
TNM stage			
I	46 (14.1)	364 (17.5)	0.002
II	91 (27.8)	654 (31.4)	0.002
III	104 (31.8)	554 (26.6)	0.002
IV	86 (26.3)	513 (24.6)	0.002
Total	327 (100.0)	2,085 (100.0)	
I+II	137 (41.9)	1,019 (48.9)	0.002
III+IV	190 (58.1)	1,067 (51.1)	0.033
Nodal involvement			
Total number of positive lymph nodes	179 (70.5 per cent)	1,460 (89.1 per cent)	0.001
01-Mar	85 (47.5)	414 (46.40)	0.002
04-Sep	72 (40.2)	358 (40.2)	0
>10	22 (12.3)	120 (13.4)	0.002