

## The Pathological Stage at Diagnosis of Breast Cancer in Ghanaian Women: A Retrospective Study at the Korle-Bu Teaching Hospital Accra (2001 to 2014)

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### Authors' contributions

This work was carried out in collaboration between all authors. Authors EMD and SEQ conceptualized the idea. Author EMD collected, entered, analysed and drafted the manuscript. Authors EMD and YT read through the manuscript, edited and approve it for publication.

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### ABSTRACT

**Background:** Published data on breast cancer (BC) in Ghanaian women have not look at the relationships between pathological stage at diagnosis and the other clinico-pathological features. The aim of this study was to describe the relationships between the stage at diagnosis of BC in Ghanaian women and the effects on the other tumours variables.

**Material and Methods:** We reviewed and pathologically staged (I – IV) 1,317 BCs in our institution. Data were collected on the clinico-pathological features of females diagnosed with BC, entered and analysed using SPSS version 23 (Chicago).

**Results:** A total of 1,317 (30.4%) out of 4,336 BCs were pathologically staged using the TNM method and 57.4% were of high stage. The mean ages at diagnosis of BC for TNM stages I – IV were: 50.6, 53.3, 51.0 and 52.2 years respectively. The proportions of women aged less than 40

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years for stages I – IV were; 15.6%, 16.0%, 18.3% and 18.8%. Women in all the stages presented after 3 months (late) of noticing the swelling. Skin involvement and high histological grades were commoner in stage IV. The frequency of positive tumour margins and the mean number of positive lymph nodes increases with increasing stage at diagnosis.

**Conclusion:** Women in this study were found to have high pathological stages of BC at diagnosis. The proportions of women less than 40 years old were higher in stages III - IV. Skin involvement, number of positive lymph nodes and positive tumour margins were found to increase with increasing pathological stage at diagnosis.

*Keywords: Breast cancer; Ghanaian women; pathological stage; diagnosis; late presentation.*

## 1. INTRODUCTION

The tumour-node-metastasis (TNM) stage at diagnosis of breast cancer is widely recognized to be the most important prognostic factor in patients with breast cancer and essential in the determination of the appropriate treatment options for each tumour [1,2]. This system was first developed by Pierre Denoix in 1942 and represented an attempt to classify cancer based on the major morphological attributes of the tumours that were thought to influence disease prognosis: size of the primary tumour (T), presence and extent of regional lymph node involvement (N), and presence of distant metastases (M). This system has gone through several revisions [3,4]. Currently the most widely used system for staging breast cancer is the TNM system developed by the American Joint Committee on Cancer and Union for International Cancer Control [4]. The T, N and M data were combined to create stages (I, II, III and IV). The relative proportions of high stage breast cancer at diagnosis vary across the globe [5,6,7]. High TNM stage at diagnosis has been found by studies to be a predictor of poor prognosis and a low 5-year survival [1,2,8,9,10].

The stage of breast cancer determines the treatment option and the prognosis of tumours after treatment. Published data on breast cancer in Ghanaian women had not look at the relationship between the pathological stage at diagnosis and the other clinico-pathological features. The aim of this study was to describe the relationship between the stage at diagnosis of breast cancer in Ghanaian women and the other tumours variables.

## 2. MATERIALS AND METHODS

### 2.1 Study Site

Data for this study were from the Department of Pathology of the School of Biomedical Sciences;

University of Ghana Medical School. This is the largest Pathology Department in the country that 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.

### 2.2 Study Design

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

### 2.3 Data Collection

We retrospectively reviewed 1,317 women who had their breast cancer pathologically staged out of a total of 4 histologically confirmed breast cancers in our institution from 2001 to 2014. Data were collected on age at histological diagnosis, tumour size (cm), histological subtype, histological grade, lymph node status TNM stage and positive margins; defined as breast cancers cells within 2.0 mm of the resection margins. The histological subtypes of breast cancers in this study were classified according to World Health Organization (WHO) histology classifications of breast tumours. Histologic 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 6<sup>th</sup> 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).

### 2.4 Data Analyses

Data were entered into an SPSS software version 23 (Chicago). Frequency distributions

and descriptive statistics; age (mean and median), size of primary tumour and positive lymph nodes were determined for each TNM stage at diagnosis. Also frequency of positive tumour margins and histological subtype and histological grades were determined for the various stages. Results were presented in frequency tables.

### 3. RESULTS

A total of 4,336 breast cancers (BCs) were diagnosed in our institution during the period of study, of which 1,317 (30.4%) were pathologically staged using the TNM method (I – IV). Many (32.8%) of the women were in TNM stage III. Approximately, 57.4% were of high stage (stage III and IV combined) (Fig. 1).

The ages of the 1,317 women ranged from 14 – 98 years with a mean age of 52.0 years (SD  $\pm$ 12.6) and a median age of 52.0. The ages of women with TNM stage I BCs ranged from 29 – 82 years with a mean age of 50.6 years (SD  $\pm$  11.3). The great majority (84.4%) were 40 years and above (Table 1). For TNM stage II patients, their ages ranged from 23 – 85 years with mean of 53.3 years (SD $\pm$ 12.0), 84.0% being 40 years and above. The mean ages for stage III and IV patients were 51.0 years (SD $\pm$ 12.2) and 52.2 years (SD $\pm$  13.7) respectively. Approximately 81.7% and 81.2% of stage III and IV women were aged 40 years and above. Thus the proportions of women with BCs who were younger than 40 years increased with increasing TNM stage at diagnosis.

In all the stages, the commonest symptom of BC was a palpable lump in the breast. Skin involvement was the commonest additional symptom of BC. The great majority (87.6%) of the cases with skin involvement were in TNM stage IV (Table 2, Figs. 2 and 3).

The duration of BC at presentation for all the stages was commonly after 3 months (late) of noticing the swelling. This was more so with TNM stage IV cancers (Table 2). Mastectomy was the commonest surgical specimen in which stages I-III BCs were diagnosed. Stage IV BCs were commonly diagnosed in incisional biopsy due to the advanced clinical presentation (Table 2).

The commonest histological subtype of BC in all the stages was invasive ductal carcinoma not otherwise specified (IDC-NOS) (Table 3).

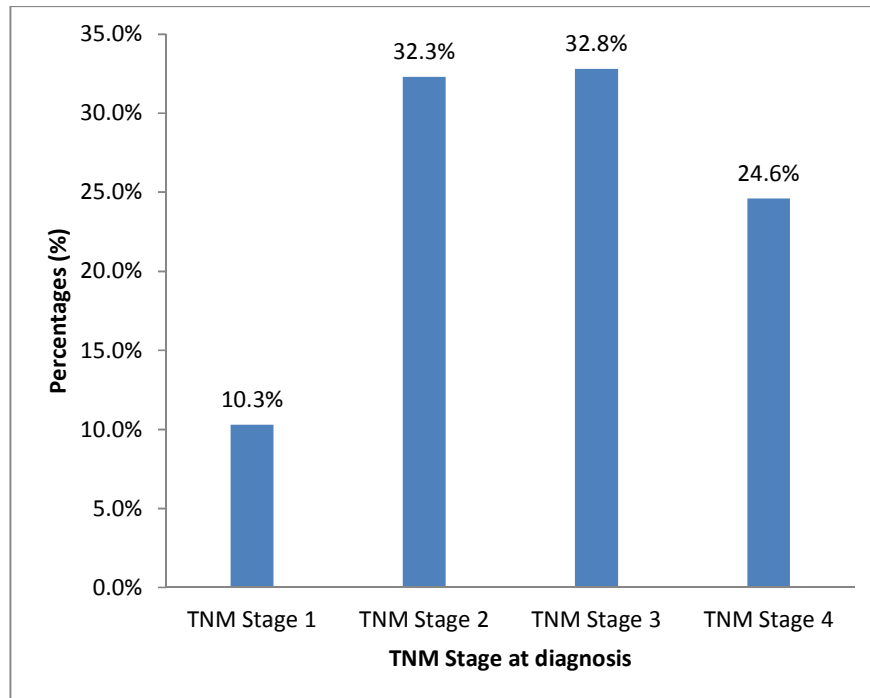
For the cases that had Bloom-Richardson grading done, the commonest grade for stage I-

III cancers was 2, but for stage IV cancers were commonly grade 3 (Table 4). The frequency of positive tumour margins was determined among mastectomy and excision specimens and this was generally found to increase with increasing pathological stage at diagnosis (Table 4). Similarly the mean number of positive lymph nodes increases with the stage at diagnosis (Table 4).

### 4. DISCUSSION

The pathological stage of breast cancer (BC) at histological diagnosis determines the treatment option and the prognosis [1,2]. The higher the stage at diagnosis, the shorter the 5 year survival rate [2]. In this current study, more than half of the women had higher pathological stages at diagnosis (stage III and IV combined). The pattern observed in this current study is in keeping with previous clinical and histopathological studies in Ghana [5,6]. The large proportions of breast cancer patients with high TNM stage at diagnosis in this current study however differs from Walters et al. [7] study which found fewer number of women to be diagnosed with high TNM stages of breast cancers in the countries where their study was conducted. For instance, they found that in Canada, 82.9% of the breast cancer patients were in stage I and II combined compared to 17.1% in stage III and IV combined. In UK, there were 87.4% with I and II combined compared to 12.6% within stage III and IV combined. Again it was found that in Sweden there were 91.8% in stage I and II combined while 8.2% were stage III and IV combined. Although we have no follow-up data on these women, which is partly due to the lack of national cancer registry in Ghana, the current findings seems to suggest that, the women in this study with high TNM stage BCs potentially had poor outcome of the disease and a low 5-year survival rate [1,2,8,9,10].

The mean ages of the women with BC in all the stages were around 50-years. This is closer to the mean ages of Ghanaian women diagnosed with BC in the most recent times, [6,11] but differs other studies also in Ghanaian women more than decades ago [12,13]. The mean age at which women were diagnosed with BC in this study was relative an advanced age (middle age) and thus a significant finding. This may suggest that the disease in the near future will be commoner in the elderly women. This is indeed supported by the 2014 report of the GDHS that recorded an increased in the life expectancy rate of Ghanaian women [14].



**Fig. 1. Pathological stages of primary malignant breast tumours (TNM stage)**



**Fig. 2. A 37 year old woman with left breast cancer associated with nipple retraction and ulceration**



**Fig. 3. A 48 year old woman with fungating (Mushroom) left breast cancer associated with satellite nodule and axillary lymph adenopathy**

Women with BC in this study commonly presented with large palpable lumps, similar to previous studies in Ghana [13,15] and beyond. [16,17].

One significant finding of the current study is that most of the women particularly those presenting with stage IV disease had skin involvement. Decades ago, a study on breast cancer in Ghanaian women found skin involvement as a key symptom at presentation [18]. Furthermore, most of the women with high combined TNM stage presented after 3 months (late) of noticing the lump. Data on the duration of breast cancer at presentation are generally limited in Ghana [13,18,19]. Literature from other parts of the world for the past 30 years had indicated that survival is worse among women with longer duration of symptoms [20-22]. Burgees et al. [23] who defined patient delay as 12 weeks of symptoms before first visit to the general practitioner (GP), found that 90% of their patients delayed (> or = 12 weeks) in seeing the GP and this is being supported by the current study. Other studies, however, have not shown that survival is affected by duration of symptoms [24,25] For instance, Dennis et al. [25] did not find any positive association between patient delay and survival ( $p = -0.053$ ). They found that most (23.2%) of the patients visited the GP at about 4 - 8 weeks of set of symptoms and

concluded that survival after the symptoms had appeared is not related to the duration of the symptomatic period but to establish pathologic criteria such as rate of growth, the tumor size, lymph node involvement, the number and location of lymph nodes involved, blood vessel invasion and the presence of systemic metastases.

There are few studies in Ghana that looked at the reasons for late presentation of BCs to health facilities [26,27]. For instance, Ohene et al. [26] study on the spectrum of complaints presented at a specialist breast clinic in Kumasi Ghana identified the painless nature of BC as the major reason for the late presentation. Again, Clegg-

Lampsey et al. [27] in their study on presentation of BC in Ghanaian women identified bad experience from previous medical consultation and ignorance from the women as the major reasons for the late presentation of breast cancer to health facilities. However, it may as well be that Ghanaian women are not conscious of self-breast examination and thus will only present to the clinician when the disease is obvious or advanced. Breast cancer awareness campaign and breast self-examination should be intensive at levels of education and social gatherings. This is because studies have shown that earlier detection and treatment offer the best chance of reducing the morbidity and mortality associated with the disease [23,28,29].

**Table 1. Age distribution of women who had TNM staging of their breast cancer**

Age groups (yrs)	Whole group (n/%)	Stage 1 (n/%)	Stage 2 (n/%)	Stage 3 (n/%)	Stage 4 (n/%)
≤19	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)
20 - 29	29 (2.2)	4 (3.0)	4 (0.9)	8 (1.9)	13 (4.0)
30 - 39	197 (15.0)	17 (12.6)	62 (14.6)	71 (16.4)	47 (14.5)
40 - 49	368 (27.9)	41 (30.4)	114 (26.8)	130 (30.1)	83 (25.6)
50 - 59	354 (26.9)	39 (28.9)	104 (24.4)	126 (29.2)	85 (26.2)
60 - 69	236 (17.9)	28 (20.7)	88 (20.7)	66 (15.3)	54 (16.7)
70 - 79	114 (8.7)	5 (3.70)	49 (11.5)	25 (5.8)	35 (10.8)
≥80	18 (1.4)	1 (0.7)	5 (1.2)	6 (1.4)	6 (1.9)
Total	1,317 (100.0)	135 (100.0)	426 (100.0)	432 (100.0)	324 (100.0)
Age ≤39	227 (17.2)	21 (15.6)	66 (15.5)	79 (18.3)	61 (18.8)
Age ≥40	1090 (82.8)	114 (84.4)	360 (84.0)	353 (81.7)	263 (81.2)
Mean age	52.0	50.6	53.3	51.0	52.1

**Table 2. Clinical features of breast and the TNM stage at diagnosis**

	Whole group (n/%)	Stage I (n/%)	Stage II (n/%)	Stage III (n/%)	Stage IV (n/%)
<b>Primary symptom</b>					
Breast lump	667	65	244	232	121
Nipple discharge	1		1		
<b>Additional symptom</b>					
Skin involvement	106 (67.5)	1 (33.3)	12 (35.3)	23 (57.5)	71 (88.7)
Chest wall invasion	5 (3.2)	0(0.0)	0 (0.0)	1 (2.5)	4(5.0)
Axiillary lymph adenopathy	23 (14.6)	0(0.0)	15 (44.1)	6 (15.0)	2 (2.5)
Nipple retraction	7 (4.5)	0(0.0)	3 (8.8)	4(10.0)	1 (1.3)
Nipple discharge	7 (4.5)	1(33.3)	1 (2.9)	5 (12.5)	0 (0.0)
Breast pain	5 (3.2)	0(0.0)	3 (8.8)	0 (0.0)	1 (1.3)
Weight loss	4 (2.5)	1(33.3)	0(0.0)	1 (2.5)	1 (1.3)
Total	157(100.0)	3(100.0)	34(100.0)	40(100.0)	80 (100.0)
<b>Duration of symptoms at presentation (months)</b>					
≤ 3	143 (22.9)	17 (25.4)	50 (26.0)	39 (20.9)	36 (20.6)
≥ 4	479 (77.1)	50 (74.6)	142 (74.0)	148 (79.1)	139 (79.4)
Total	622 (100.0)	67 (100.0)	192 (100.0)	187 (100.0)	175 (100.0)
<b>Type of surgical specimens</b>					
Mastectomy	947 (71.9)	81 (60.0)	339 (79.6)	390 (90.3)	137 (42.3)
Excision biopsy	189 (14.4)	54 (40.0)	86 (20.2)	39 (9.0)	10 (3.1)
Core needle biopsy	37 (2.9)	0 (0.0)	1 (0.2)	3 (0.7)	33 (10.2)
Incision biopsy	144 (10.9)	0 (0.0)	0 (0.0)	0 (0.0)	144 (44.4)
Total	1,317 (100.0)	135 (100.0)	426 (100.0)	432 (100.0)	324 (100.0)

**Table 3. The histological subtypes of breast cancer and the TNM stage at diagnosis**

<b>Histological subtypes</b>	<b>Whole group (n/%)</b>	<b>Stage I (n/%)</b>	<b>Stage II (n/%)</b>	<b>Stage III (n/%)</b>	<b>Stage IV (n/%)</b>
IDC-NOS	1,178 (89.5)	125 (92.6)	385 (91.3)	383 (88.7)	285 (88.0)
Lobular	33 (2.5)	4 (3.0)	10 (2.3)	12 (2.8)	7 (2.2)
Mucinous	26 (2.0)	0 (0.0)	8 (1.9)	13 (3.0)	5 (1.5)
Paget' disease	14 (1.1)	1 (0.7)	2 (0.5)	6 (1.4)	5 (1.5)
Medullary	11 (0.8)	1 (0.0)	6 (1.4)	2 (0.5)	2 (0.6)
Malig phyllodes tumour	2 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.3)
Cribriform	5 (0.4)	1 (0.7)	2 (0.5)	0 (0.0)	2 (0.6)
Neuroendocrine	4 (0.30)	0 (0.0)	2 (0.5)	2 (0.5)	(0.0)
Papillary	14 (1.1)	3 (2.2)	4 (0.9)	7 (1.6)	0 (0.0)
Metaplastic	7 (0.5)	0 (0.0)	3 (0.7)	1 (0.2)	3 (0.9)
Carcinosarcoma	4 (0.3)	0 (0.0)	0 (0.0)	2 (0.2)	2 (0.6)
Apocrine	4 (0.3)	0 (0.0)	3 (0.7)	1 (0.2)	0 (0.0)
Tubulo-lobular	2 (0.2)	0 (0.0)	0 (0.0)	1(0.2)	1 (0.3)
Squamous cell	6 (0.50)	0 (0.0)	1 (0.2)	0 (0.0)	5 (1.5)
Inflammatory	5 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	5 (1.5)
Secretory	2 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.3)
Total	1,317 (100.0)	135(100.0)	426(100.0)	432(100.0)	324(100.0)

**Table 4. The TNM stage of breast cancer at diagnosis the histological features**

	<b>Whole group (n/%)</b>	<b>Stage II (n/%)</b>	<b>Stage II (n/%)</b>	<b>Stage III (n/%)</b>	<b>Stage IV (n/%)</b>
<b>Histological grade</b>					
I	148 (13.3)	26 (22.4)	54 (14.8)	42(11.5)	26(9.6)
II	549 (49.2)	70 (60.3)	190 (52.1)	193 (53.0)	96 (35.4)
III	419 (37.5)	20 (17.3)	121 (33.1)	129 (35.5)	149 (55.0)
Total number graded	1,116 (100.0)	116 (100.0)	365 (100.0)	364 (100.0)	271 (100.0)
<b>Positive axillary lymph nodes</b>					
Range	1 - 42	1 - 12	1 - 23	1 - 28	1 - 42
1 - 3	304(43.2)	31 (49.2)	125 (51.0)	118 (39.9)	30 (30.0)
4 - 9	291 (41.4)	30 (47.6)	93 (38.0)	122 (41.2)	47 (47.0)
≥ 10	108 (15.4)	2 (3.2)	27 (11.0)	56 (18.9)	23 (23.0)
Total	703 (100.0)	63(100.0)	244(100.0)	296 (100.0)	100 (100.0)
Mean	5.3	4.3	4.7	5.6	6.6
<b>Positive tumour margin</b>					
Number of mastectomy and excision specimens	1,136	135	425	429	147
Proportions of positive margins	205 (18.1)	2(1.5)	42 (9.9)	82 (19.1)	44 (29.9)

Invasive ductal carcinoma not otherwise specified (IDC-NOS), was the commonest subtype of breast cancer in all the groups. This is similar to previous studies in Ghana, [30,31] and globally [32,33].

Breast cancers in this study were commonly of a high grade particularly those in stage IV. These findings are in accordance with studies in Ghana [15,31,34] and studies in other parts of the world the found higher grade at diagnosis to be associated with poor prognosis and a lower 5-year survival rate [35,36,37].

The status of the axillary lymph nodes is the most important single prognostic factor for breast cancer [38]. Nodal involvements by breast cancer in this study was found to be significantly increased with increasing TNM stage at diagnosis. It was further found that majority of the cases had 4 or more positive lymph nodes. Our findings could potentially suggest a poor prognosis of the disease in the affected women, because it has been shown that survival, speeds of recurrence and treatment failure all correlate with the number of positive nodes [39]. Disease free survival rate and overall survival diminish

with each additional positive axillary node [40]. It has been documented that about 70% of patients with nodal involvement will develop local and distant recurrence after mastectomy, and patients with 4 or more lymph node involvement have worse prognosis, compared with those having fewer nodal involvement [41,42].

The relative proportions of positive tumour margin among mastectomy and excision biopsy specimens in this current study (range from 1.5 – 29.9) had been found to increase with increasing TNM stage at diagnosis. This is closed to the prevalence rate of 4% to 31% in the published literature [43,44,45] but lower than a study in Ghana that found a rate as high as 44.0% among clinically diagnosis and excised benign breast lumps that were found by histological examination to be malignant and hence incompletely excised [46].

## 5. CONCLUSION

Women in this study were found to have high pathological stages of BC at histological diagnosis and that the proportions of women aged less than 40 years increases with increasing stage at diagnosis. Skin involvement, the histological stage, frequency of positive tumour margins and the mean number of positive lymph nodes all increase with increasing stage at diagnosis.

## 6. LIMITATIONS OF THE STUDY

1. This was a retrospective study and thus history and other tumours variable were not completely stated on the doctors request form.
2. The TNM staging was by the 6<sup>th</sup> of the American Joint Committee on Cancer (AJCC) staging manual, 2002, New York, and not current 7<sup>th</sup>.

## CONSENT

This was an autopsy study and permission was obtained from the deceased relatives.

## ETHICAL APPROVAL

It is not applicable.

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## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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