

## BREAST MALIGNANCIES IN NORTHERN GHANA: A 7-YEAR HISTOPATHOLOGICAL REVIEW AT THE TAMALE TEACHING HOSPITAL (2013 – 2019)

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### Abstract

**Objectives:** The Clinicopathological features of female breast malignancies (BMs) diagnosed in northern Ghana have not been documented adequately. The objectives of this review were to describe the annual trend, the clinico-pathological features of female BMs in northern Ghana, and offer recommendations.

**Material and methods:** Clinical and biographical data of the patients were correlated with pathological data, such as tumour size, histological subtype, histological grade, TNM stage and the completeness of excision (Tumour margins). The data were analysed using SPSS software version 26.0 (Chicago). Fisher's exact test was used to compare tumour variables.

**Results:** There were 712 (61.0%) benign and 455 (39.0%) malignant lesions ( $P < 0.0001$ ). There was an annual rise in BMs over the review period. The mean age at diagnosis with invasive BMs was  $47.5 \pm 15.4$  years. Approximately, 35.0% were aged  $\leq 39$ -years,

compared to 65.0% aged  $\geq 40$ -years ( $p < 0.0001$ ). The commonest clinical presentation in both age groups was a painless palpable lump. Painful swelling (7.9% vs 4.6%) and skin involvement (27.2% vs 22.5%) were more common in women aged  $\leq 39$ -years. Increased prevalence of positive tumour margins ( $P = 0.0544$ ), high histological grade ( $P < 0.0001$ ) and TNM stages ( $P < 0.0001$ ) were common in women  $\leq 39$ -years. However, mean nodal involvement by tumour was more common in women' aged  $\geq 40$ -years ( $6.1 \pm 4.5$  vs  $8.4 \pm 5$ ).

**Conclusion:** There was a steady annual rise in breast malignancies over the study period. Breast malignancies commonly affect relatively younger women with advanced stages at presentation. There is the need to intensify breast self-examination and early reporting to health facilities for treatment.

**Key Words:** Breast malignancies, clinical features, histopathological features, Tamale Teaching hospital

### Introduction

Malignancies of the female breast are common causes of morbidity and mortality across the globe and therefore are of a great public health concern.<sup>1-2</sup>In Sub-Saharan Africa, malignancies of the female breast are the leading cause of deaths among women.<sup>3-5</sup>In Ghana, available published data reported breast malignancies as the commonest cause of cancer related morbidity and mortality in women.<sup>6-10</sup>

The reported incidence of breast malignancies vary globally, more so in Sub-Saharan Africa, where it is reported to be on the rise.<sup>2,11-14</sup>The increasing numbers of breast malignancies among women in Sub-Saharan Africa has been attributed to increased urbanization with the associated changes in life style, the use of hormonal birth control pills, improved health delivery services,

increased awareness of the disease, the practice of breast self-examination and early reporting with breast abnormalities to health facilities for treatment.<sup>15-20</sup>

Breast malignancy in the published literature from Africa, reported the disease to be common among younger women with advanced stages at presentation.<sup>21-24</sup>Similarly, published data on breast malignancies in Ghanaian women between 1956 and 2019, from the middle and southern belts of the Ghana found the disease to affect relatively younger women who presented late with large palpable masses, some with skin involvement.<sup>7-9,14,25,26</sup>Data on breast malignancies in northern Ghana are very scarce, but the disease is reported to be a major component of cancers in this part of the country.<sup>27</sup> For the past years, efforts have been made by the staff of the Department of Pathology of the School of Medicine, University for Development Studies (SOM, UDS), as well as nurses and doctors from the Tamale teaching hospital (TTH) to create awareness of the disease among the public and the need for early reporting of any breast abnormalities to health care facilities.

There is the need to know how these breast cancer awareness activities in northern Ghana have impacted on the disease pattern. The objectives of this retrospective study were to describe the annual trend and

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the clinicopathological features of female breast malignancies diagnosed in northern Ghana, and to offer recommendations. These findings could help to inform future planning, research and policy implementation in the catchment area.

## Materials and Methods

**Study Design:** This was a retrospective histopathological review, using data and material from 1<sup>st</sup> January 2013 to 31<sup>st</sup> December, 2019.

**Study Site:** The Department of Pathology, Tamale Teaching Hospital (TTH). This is the largest referral hospital serving the five regions in northern Ghana and beyond, particularly, neighbouring Burkina Faso, as reported in previous studies.<sup>33</sup>

**Data collection, entry and Analysis:** Histological request forms and the completed histopathological reports of all breast samples submitted to the department from 1<sup>st</sup> January, 2013 to 31<sup>st</sup> December, 2019, were retrieved. All cases of neoplastic breast lesions were selected (n=1,167). Malignant breast lesions (n = 455) were extracted. Finally, malignant tumours were further grouped into invasive (n = 431) and non-invasive (n = 24) lesions. The invasive breast lesions were used as the sample population (n = 431).

Data were collected on the age at presentation (grouped into  $\leq 39$ -years and  $\geq 40$ -years), relevant clinical history (symptoms, duration, laterality, type of operation) and type of surgical specimens. We also collected data on the histopathological characteristics of malignant breast lesions: size of primary tumour (only for excision biopsies and mastectomy specimens), histological diagnosis, histological grade (for invasive ductal carcinoma), lymph node involvement, the TNM stage and the status of the resection margins (forexcision and mastectomy specimens). Tumours with malignant tumour cells within 3.0mm of the excision margins were considered incompletely excised (positive tumour margins).

In this study, breast malignancies were classified according to World Health Organization (WHO) classification which is based on the tissue type. Histologic grading of female breast cancers in this study was performed according to the modification of Bloom-Richardson system by the Elston and Ellis.<sup>50</sup> The TNM staging (pathological) for 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) measured macroscopically and in some instances microscopically by the pathologist, 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).

The data was entered into a statistical database and analysed using SPSS software version 26.0 (Chicago). Fisher's exact test was used to compare tumour

variables. The results were presented in bar charts and frequency tables.

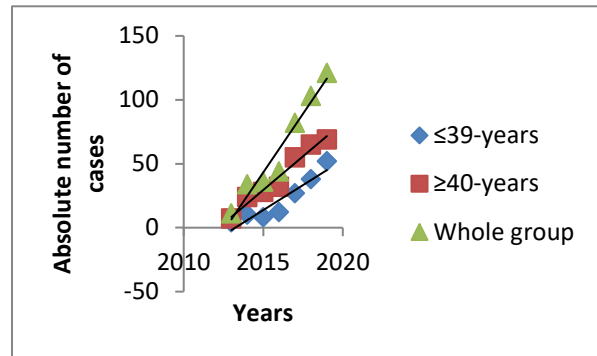
**Inclusion criteria:** All breast malignancies diagnosed during the period of review and were histologically confirmed by the pathologist.

**Exclusion criteria:** All cases of improperly stored (melted) paraffin embedded tissue blocks and those with incomplete records were excluded.

## Results

### *Annual trend in the number of breast cases diagnosed (2013 – 2019) in the department of pathology, TTH*

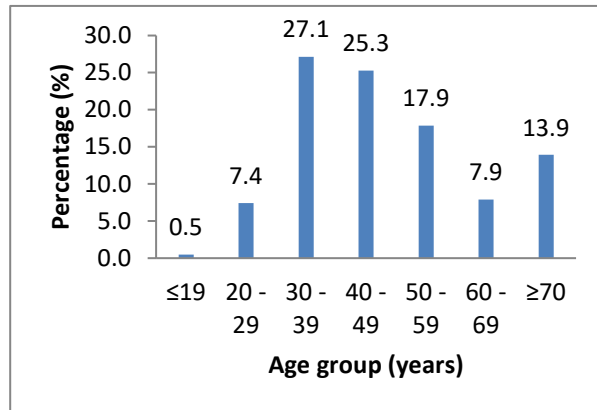
Of the 1,167 neoplastic breast lesions reviewed in our institution, 712 (61.0%) were benign, with 455 (39.0%) malignant forms. A total of 431 (94.7%) of the malignant breast lesions were invasive, with 24 (5.3%) non-invasive lesions ( $P < 0.0001$ ). There was a sharp rise in the trend of absolute numbers of invasive breast malignancies during the period of review, especially from 2016 to 2019 (Figure 1).



**Figure 1:** Yearly Trend in breast malignancies over the study period (Age)

### *Age characteristics of women diagnosed with invasive breast cancer*

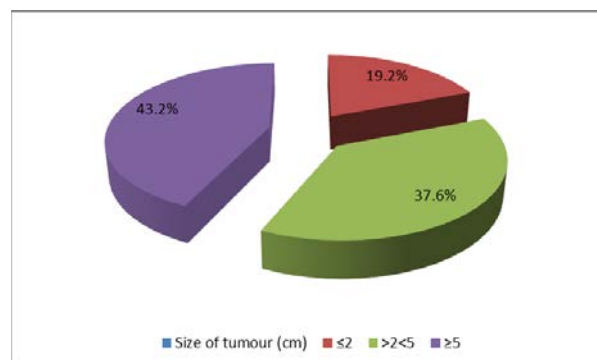
The ages of women diagnosed with invasive breast cancer ranged from 15 – 88 years, with a mean of  $47.5 \pm 15.4$ . The modal age group was 30 – 39 (27.1%) years. A total of 151 (35.0%) were aged  $\leq 39$ -years, compared to 280 (65.0%) who were aged  $\geq 40$ -years ( $p < 0.0001$ ). A significant number 60 (13.9%) were aged 70-years and above (figure 2). There was an annual rise in the total number of cases in the two age categories (Figure 1).



**Figure 2:** Age distribution of women diagnosed with breast malignancies (2013 – 2019)

### Clinical presentation of breast cancer among the study group

The commonest clinical presentation of malignant breast lesion in the women studied was a painless palpable breast lump 286 (66.4%). There were 99 (23.0%) with skin involvement and 25 (5.8%) with painful breast swellings. A little above half, 220 (51.0%) of the malignant breast lesions involved the left breast. A total of 334 (77.0%) women out of the 431 with invasive lesions had stated duration of illness at presentation, and this ranged from 1 – 60 months with a mean of  $11.3 \pm 9.3$ . The great majority (87.0%;  $P < 0.0001$ ) reported at least 3 months after noticing the lump. A total of 306 (71.0%) of the cases were diagnosed in small samples (trucut and incision biopsies), while 125 (29.0%) were in large samples (mastectomy and excision biopsies) (Table 1). The size of primary tumour diagnosed in large samples varied from 1 – 16 cm, with a mean of  $7.5 \pm 2.7$ . Many (43.2%) were larger than 5.0cm (Figure 3).



**Figure 3:** Size of primary tumour in large samples ( $N = 125$ )

### Histopathological features of invasive breast cancer

#### i. Histological subtypes of invasive breast cancer

The common histological subtypes of malignant breast lesions were: invasive ductal carcinoma (IDC-NOS) (84.3%), invasive papillary (2.8%), metaplastic (2.6%), medullary (2.1%), mucinous (1.9%) and lobular carcinomas respectively (1.2%) (Table 2).

#### ii. Lymph node involvement by tumour

A total of 42 (32.8%) of the large samples had lymph node metastasis, and the number of nodes involved ranged from 1 – 28 with a mean of  $7.5 \pm 5.2$ . Majority 33 (78.6%) of the samples had 4 or more positive lymph nodes ( $p < 0.0001$ ) (Table 2).

#### iii. Histological grades of invasive breast malignancies

A total of 361 (99.4%) of the cases diagnosed with IDC-NOS had Bloom-Richardson grading, with a mean grade of  $2.4 \pm 0.6$ . The great majority 342 (94.7%) were in grades II – III ( $P < 0.0001$ ) (Table 2).

#### iv. TNM Stage of invasive breast malignancies

A total of 207 (47.8%) breast lesions with dimensions macroscopically and in some instances microscopically determined, had TNM staging done, and many 101 (48.7%) were in stage IV, followed by stage III 43 (20.8%) (Table 2).

#### v. Positive tumour margins

Positive tumour margins were found in 44 (35.2%) of the large samples, many arising from local excision breast samples (54.5%) (Table 2).

### Relationship between age at diagnosis and tumour variables

The commonest clinical symptom at presentation in both age groups ages:  $\leq 39$ -years and  $\geq 40$ -years was a painless palpable lump. However, painful swelling (7.9% vs 4.6%) and skin involvement (27.2% vs 22.5%) were common among women aged  $\leq 39$ -years (Table 4). Values for the mean duration (months) at presentation and the mean size of primary tumour (cm) as measured macroscopically in large samples were slightly higher in women aged  $\geq 40$ -years (Table 4).

High histological grade and TNM stages were common in women aged  $\leq 39$ -years. Again, increased prevalence of positive tumour margins was commonly identified in women aged  $\leq 39$ -years. However, higher rate of lymph node involvement was found in women aged  $\geq 40$ -years (Table 4).

**Table 1:** Clinical presentation of invasive breast cancer among the study group

	Frequency (n)	Percentage (%)	P-Values
Symptom at presentation			0.0001
Painless lump	286	66.4	
Lump with skin involvement	99	23.0	
Nipple discharge	7	1.6	
Lump with nipple retraction	9	2.1	
Mass fixed to chest wall	5	1.2	
Painful swelling	25	5.8	
Total	431	100.0	
Laterality			0.3369
Left breast	205	47.6	
Right breast	220	51.0	
Bilateral	6	1.4	
Total	431	100.0	
Duration at presentation (months)			0.0001
≤3	44	13.0	
4.-6	116	35.0	
7.-12	96	29.0	
>12	78	23.0	
Total	334	100.0	
Type of surgical specimen			0.0001
Small biopsies	306	71.0	
<i>Trucut</i>	225	52.2	
<i>Incision</i>	81	18.8	
Large biopsies	125	29.0	
<i>Excision</i>	55	12.8	
<i>Mastectomy</i>	70	16.2	

**Table 2:** Histological subtypes of invasive breast cancer (n = 431)

Subtype	Frequency (n)	Percentage (%)
IDC-NOS	363	84.2
Lobular	5	1.2
Mucinous	8	1.9
Medullary	9	2.1
Invasive papillary	12	2.8
Neuroendocrine	3	0.7
Apocrine	1	0.2
Clear cell	1	0.2
Malignant Phylloides tumour	3	0.7
Spindle sarcoma	9	2.1
Metaplastic carcinoma	11	2.6
Tubular	2	0.5
Lymphoma	1	0.2
Paget's disease	1	0.2
Signet ring carcinoma	2	0.5
<b>Total</b>	<b>431</b>	<b>100.0</b>

**Table 3:** Histological grade, TNM stage and positive tumour margins of invasive breast malignancies

	Frequency (n)	Percentage (%)	P-values
Histological grade			0.0001
1	19	5.3	
2	177	49.0	
3	165	45.7	
<b>Total</b>	<b>361</b>	<b>100.0</b>	
Positive lymph nodes			0.0001
≤3	9	22.0	
≥4	32	78.0	
<b>Total</b>	<b>41</b>	<b>100.0</b>	
TNM stage			
I	10	8.0	
II	28	22.4	
III	32	25.6	
IV	55	44.0	
<b>Total</b>	<b>125</b>	<b>100.0</b>	
Positive tumour margins			
1. Excision biopsy			
Yes	30	54.5	
No	25	45.5	
2. Mastectomy			
Yes	14	17.5	
No	56	82.5	

**Table 4:** Age characteristics of some key prognostic factors

Variable	≤39-years (n/%)	≥40-years (n/%)	P-values
1. Clinical Presentation of breast malignancies			
a. Painless lump	92(60.9)	194(69.3)	<0.0001
b. Painful lump	12(7.9%)	13(4.6%)	1.0000
c. Lump with skin involvement	41(27.2%)	63(22.5%)	0.0035
d. Nipple involvement	6(4.0%)	10(3.5%)	0.2890
e. Mean duration at presentation (months)	10.9±9.2	11.5±9.4	
f. Mean of primary tumour (large specimens)	2.2±2.2	2.3±2.2	
2. Histological characteristics of breast malignancies			
a. Mean number of positive lymph nodes	6.1±4.5	8.4±5	
b. Positive tumour margins	17(11.3%)	27(9.6%)	0.0544
c. Histological grade of tumour at diagnosis			
I	11(9.1%)	8(3.4%)	0.5171
II	47(38.8%)	130(54.6%)	<0.0001
III	63(52.1%)	100(42.0%)	<0.0001
<b>Total</b>	<b>121(100.0)</b>	<b>238(100.0)</b>	
d. TNM stage at diagnosis			
I - II	20(27.4%)	43(32.3%)	<0.0001
III - IV	53(72.6%)	90(67.7%)	<0.0001
<b>Total</b>	<b>73(100.0)</b>	<b>133(100.0)</b>	

## Discussion

The incidence of malignancies of the female breast varies across the globe, more so in Sub-Saharan Africa, where it is reported to be on the rise.<sup>1,2,11-14</sup> The current study in Tamale, Ghana although a single institution-based study, found a rising annual trend in the absolute numbers of breast malignancies diagnosed in the histopathology department specifically the period 2016 to 2019. This trend is similar to that reported in a previous institution-based study conducted at the Korle-Bu teaching hospital in Accra Ghana using mastectomy specimens.<sup>14</sup> The reasons for the rising yearly trend of breast malignancies in the Tamale Metropolis are currently not clear, but may be similar to those reported in previous studies in Ghana and other developing countries.<sup>13-21</sup> For instance; rapid urbanization with the associated changes in life style, the use of hormonal birth control pills, improved health care delivery system, increased awareness of the disease, health education on the disease, increased practice of breast self-examination and early reporting of breast abnormalities to health facilities have been identified as factors contributing to the rising trends in breast cancer in Ghana and some developing countries.<sup>13-21</sup>

However, in the opinion of the authors, the important driving factors for the rising trend of breast malignancies in health facilities in Ghana and beyond are increased awareness of the disease, the increasing use of non-invasive methods of breast examination in health facilities, the practice of breast self-examination and early reporting. For instance, Der et al<sup>19</sup> in a study in Tamale Ghana titled “Assessing the knowledge and attitude of tertiary students on the risk factors of breast cancer in the Tamale Metropolis” found that the great majority of their respondents were aware of breast cancer and that more than half practice monthly breast self-examination. That study found that the main source of information on breast cancer was the electronic media.<sup>19</sup> Ouyang et al<sup>21</sup> in a study among women in China titled “The effect of breast cancer health education on the knowledge, attitudes, and practice: a community health centre catchment area” reported a significant increase in the practice of breast self-examination among the women following health education on the disease. Similarly, Kocaöz et al<sup>18</sup> in Turkey reported an increase in breast self-examination in women after public education regarding early detection and diagnosis of breast cancer.

The current study reported a mean age of women at diagnosis with breast malignancies to be 47.5±15.4 years and that many were within the age group of 30 – 39-years. The commonest clinical presentation of breast malignancies was a painless palpable lump. However, painful breast lump, skin involvement, and nipple destruction, all symptoms of clinically advanced disease, were common in women aged ≤39-years. The clinical presentation of breast malignancies in this study are similar to other published data from Africa<sup>22-24</sup> and Ghana (between 1956 and 2019), that found the disease

to affect relatively younger women who presented late with large palpable masses, some with skin involvement.<sup>7-10,14, 20,25-27</sup>

A significant finding in the Tamale study is the fact that 35.0% of the women were aged ≤39-years at the time of diagnosis with breast malignancies. This is higher than the 19.6% reported in Accra Ghana,<sup>10</sup> The expected outcome for these 35.0% women is not clear, but previous studies in Ghana<sup>10</sup> and across the world found young age at diagnosis with breast malignancies to be a poor prognostic indicator, because of the aggressive nature of the disease in this age group.<sup>28,29</sup>

The commonest histological subtype of invasive breast malignancy was invasive ductal carcinoma, not otherwise specified (IDC-NOS), in line with findings of previous publications in West Africa.<sup>8,10,30</sup>

High histological grades were reported in this study, but more significantly in women aged ≤ 39-years (P<0.0001). Our findings support studies in the past that associated high histological tumour grade with younger age at diagnosis.<sup>8,31,32</sup>

In this study breast malignancies were more commonly diagnosed in small samples (tru-cut and incision biopsies) 306 (71.0%), compared to mastectomy and excision biopsies 125 (29.0%) (P<0.0001). This is similar to what was reported in earlier institution-based studies in the department of pathology, Korle-Bu Teaching Hospital.<sup>8,10</sup> The mean primary tumour size measured in the large samples was 7.5±2.7; with approximately 43.2% being larger than 5.0cm, much larger than the sizes reported in other studies.<sup>8,33</sup>

Of the 125 large samples, only 42 (32.8%) had positive nodal involvement by tumour, with a mean of 7.5±5.2 positive nodes, and majority 33 (78.6%) of these cases had 4 or more positive lymph nodes (p<0.0001). Regarding age at diagnosis, women aged ≥40-years had mean positive nodes of 8.4±5.0, compared to 6.1±4.5 for women aged ≤39-years. The differences in the mean values may partly be explained by the fact that women aged ≥40-years had slightly larger size primary tumours and a longer duration (months) before presentation (11.5±9.4 vs 10.9±9.2), and this is in line with previous studies.<sup>34-37</sup> Studies globally, have stressed on the prognostic significance of positive lymph nodes, particularly those with four or more positive nodes, and their association with reduced disease free interval.<sup>38-40</sup> Our findings however differ from studies that found young at diagnosis with breast malignancy as a predictor of increased nodal involvement.<sup>41-43</sup>

Again, the current study reported higher TNM stages at diagnosis to be associated with younger women aged ≤ 39-years (P<0.0001). Our findings support similar studies conducted previously at the Korle-Bu Teaching Hospital in Accra Ghana.<sup>10,14</sup>

Positive tumour margins in excised breast mass has been reported to be associated with increased risk of local recurrence and systemic disease.<sup>44,45</sup> However, the rate varies globally based on the study types and

methods.<sup>14, 46</sup> In this current study conducted in the northern part of Ghana, the prevalence of positive tumour margins in large samples was 35.2%. This rate is much higher than what was reported in previous studies in Ghana.<sup>14,46</sup> For instance, Der et al.,<sup>46</sup> in Accra Ghana reported a rate of 21.1% in wide local excision specimens.

A further stratification of the prevalence rate of positive tumour margins based on the age at diagnosis, revealed that, women aged  $\leq 39$ -years had higher prevalence rate, compared to those aged  $\geq 40$ -years (11.3% vrs 9.6%). This may be due to the fact that in dealing with younger age group with breast malignancies, surgeons attempt to conserve as much breast tissue as possible and this may be a contributory factor for the incomplete excision. This age group is therefore subjects of poor treatment outcome as reported in other studies.<sup>47-49</sup>

**Conclusion:** There was a steady rise in the numbers of breast malignancies diagnosed in our institution over the period of review. Breast malignancies commonly affect relatively younger women, with advanced stages of disease at presentation. There is the need to increase awareness of the disease among women, especially the need for breast self-examination and early reporting of any breast abnormalities to health facilities for appropriate management.

### Recommendations:

1. The government of Ghana, the ministry of health and other organisations should support efforts in intensifying the awareness of the disease at all levels in our society.
2. Women should be encouraged to practice regular monthly breast self-examination, as this is the first and the most important step in the fight against breast cancer in Ghana.
3. Women should further be educated on the need to report early with detectable breast abnormality to a health facility for prompt diagnosis and treatment. Furthermore, family support is required for a good treatment outcome of the disease.

### Limitations:

1. The present data depended largely on the availability of surgeons and pathologists during the review period.
2. Cases reported in laboratories outside the catchment area were not part of the data used in this article.
3. Inadequate relevant clinical history, particularly the duration of symptom at presentation was a major limitation.
4. Being retrospective in nature, the data used here are associated with problems/issues inherent in retrospective studies globally.

**Conflict of Interest:** The authors have no conflict of interest to declare

**Ethical consideration/informed consent:** Permission to write and publish the data in this manuscript was granted by the head of department of pathology of the Tamale Teaching hospital.

**Author's contributions:** DEM conceptualized the manuscript, collected and analysed data, and wrote the manuscript. SM, SA provided the needed clinical information. DEM, SM and SA, read through the final manuscript and approved it for publication.

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