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Patterns of breast cancer locoregional relapse, metastasis, and subtypes in Ghana

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Abstract

Background Significant advances have been made in targeted therapeutics and systemic therapy regimens for breast cancer (BC) treatment over the past decade. Tumour cells can however remain in the body, leading to locoregional relapse and/or metastasis. Subtypes of BC have distinct prognostic effects and have been linked to varying risks of early locoregional relapse and metastases, response to treatment, and overall survival. Most Low- and middle-income countries (LMICs) have no registries of BC locoregional relapse and metastasis.

Methods This study comprehensively reviewed, a 3-year retrospective single-centre data of female BC visiting the Komfo Anokye Teaching Hospital (KATH), Ghana to determine the prevalence of locoregional relapse and metastasis across our patient population. Prevalence of metastasis among the various BC subtypes was also determined.

Results Prevalence of BC locoregional relapse and metastasis were 3.4% and 47.6% respectively. For BC patients with documented locoregional relapse (***N***=36), 27.8% (CI=15.8 −44.0%) had relapse to the contralateral breast, 41.7% (CI=27.1 – 57.8%) had relapse to the ipsilateral breast, and 30.6% (CI=18.0 −46.9%) had relapse to regional lymph nodes. For BC patients with documented metastasis (***N***=503), 151 (30%) had multiple organs involvement, 141 (28%) had lung metastases, 80 (16%) had bone metastases, 45 (9%) had liver metastases, 16 (3%) had brain metastases and 70 (14%) had other metastases (ovary, uterus, spleen, peritoneum, or distant lymph nodes). Basal subtype was the most common subtype (***n***=82, 41%), followed by Luminal A (***n***=69, 34.5%), HER2+ (***n***=37, 18.5%) and Luminal B (***n***=12, 6%). Basal subtypes had the most metastasis (35%), with multiple metastasis being the most prevalent (13%).

Conclusion Close to half of the patients (46%) presented with metastatic BC. BC subtypes could influence the specific metastatic site. The most common BC subtype was the Basal subtype and had the most metastases (35%), with multiple metastasis being the most prevalent (13%). These findings should serve as a guide in the management of patients to enhance early prediction and detection of locoregional relapse and metastasis for improved overall treatment outcomes.

Keywords Breast cancer, Locoregional relapse, Metastasis, Subtypes, LMIC

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Background

Breast cancer (BC) is a disease in which malignant cells form in the tissues of the breast, and heterogeneity of the disease is characterized into distinct BC subtypes. These biological features are important in determining the systemic treatment regimen for a patient with BC. Specifically, depending on either the presence or absence of oestrogen receptor (ER), progesterone receptor (PR), and HER2 receptor [1]. While significant advances have been made in targeted therapeutics and systemic therapy regimens, tumour cells can remain in the body, leading to locoregional relapse and/or metastasis [2]. BC relapse refers to the re-emergence of BC after primary treatment and remission. This can occur months to several decades after primary treatment but most commonly occurs within the first two years after treatment [3, 4]. Variations in rates of relapse are influenced by several factors including genetic factors, BC stage and histology of the tumour and patient factors [5]. Relapse can be further categorized as locoregional, where the primary tumour has spread to nearby breast tissues and lymph nodes, or metastatic where tumour cells from the primary site travel to distant organs, such as the liver, brain, bones, or lungs [1]. Subtypes of BC have distinct prognostic effects and have been linked to varying risks of early relapse and metastases, response to treatment, and overall survival [6, 7]. BC locoregional relapse and metastasis tend to be more common in women with basal/triple negative BC (TNBC), which is the most aggressive subtype of BC.

lacking ER, PR, and HER2 positivity, compared to patients with ER/PR or HER2 positivity [8]. Low- and middle-income countries (LMIC) are facing an increasing burden of female BC where the limited availability of screening programs for early detection of BC and late reporting by women leads to higher rates of advanced or even metastatic BC diagnoses [9, 10]. Ghana, like most LMICs, has yet to have a national BC screening protocol and also has no population-based cancer registry [11]. The absence of a national BC screening protocol means there is no concerted effort across the country to detect the disease at the earliest stages where treatment is most effective. BC screening equipment like mammography machines are also unavailable at most hospitals across Ghana. Where screening equipment is available very few women can access them because of their location in urban areas only and due to the high cost [12]. The absence of a population-based BC registry in Ghana affects accurate national statistics on incidence and mortality which makes it difficult to influence policy decisions and compel key stakeholders to direct resources at reducing BC incidence and mortality in Ghana. The burden of communicable diseases like malaria, tuberculosis, and HIV/AIDS is also very high in African countries, as a result, very little funding is allocated to non-communicable diseases like BC [13]. In advanced economies, about 30% of early-stage BC patients develop disease relapse after treatment, which is metastatic in a vast majority of cases [5]. The prevalence of BC relapse among Ghanaian BC patients is however unknown, confounded by low rates of women with early-stage BC diagnoses and lack of follow-up into the oncological treatment outcomes of BC patients [10, 14, 15]. Additionally, there is an absence of institution-based registries of BC locoregional relapse and metastasis across the major referral centres for BC treatment in Ghana [11]. It is against this background that this study comprehensively reviewed, a 3-year retrospective single-centre data of female BC from 2019 to 2021 to determine and report the rates of locoregional relapse and metastasis across our patient population.

Methods

Study design/setting

This observational retrospective study was conducted from January to August 2022 at the Oncology directorate of the Komfo Anokye Teaching Hospital (KATH) in Kumasi, Ashanti Region of Ghana. KATH is a tertiary referral hospital located at Bantama in Kumasi. It is the second largest Hospital in Ghana, and it serves as the referral centre for most of the health facilities in the middle and northern part of Ghana with a bed capacity of 1200.

The hospital has 15 directorates which are made up of 13 clinical and two non-clinical directorates. The clinical directorates include Emergency Medicine, Surgery, Trauma and Orthopaedics, Medicine, Obstetrics and Gynaecology, Child Health and Family Medicine, Oncology, Eye, Laboratory services, Radiology, Oral health, Anaesthesia, Intensive Care, Ear, Eye, Nose, and Throat (EENT). The non-clinical directorates are Domestic and Technical services [16].

Retrospective data collection

The KATH cancer registry was reviewed for adult female patients who were registered from 2019 to 2021. Medical records of all adult female patients registered with BC as the primary diagnosis who had developed relapse (locoregional) after successful treatment and remission for at least one month and all BC were included in the review.

Additionally, all BC patients with documented metastasis were included in the review. Immunohistochemistry reports were also reviewed to determine BC subtypes. BC patients who were registered over the period under review with no treatment record were excluded from the review. BC patients who were registered over the period under review with treatment record who were lost to

follow-up, dead or referred out of KATH were excluded from the review.

Statistical analysis

A predesigned data-capturing tool was used to capture information on patients' year of registration into the KATH BC registry. Data on age, locoregional relapse, and metastasis as well as BC subtypes ($N=200$) were entered into Excel sheets and imported into R statistical software version 4.2.2. All statistical analyses and graphs were generated using the R software. For comparison of averages, a Kruskal-Wallis rank sum test was performed. When there were significant differences between groups being compared, identification of the pairs that showed significantly distinct distributions was achieved with the Dunn test. For comparing proportions, either a Chi-square test (when the lowest sample size was 5 or above) or a Fisher exact test (when the lowest sample size was below 5) was applied. For significant differences between more than two groups, the Bonferroni method was used. This method determined the significance between pairwise groups. A comparison of the averages of only two groups was carried out using the Wilcoxon rank sum test. The R package ggplot2 (version 3.4.0) was used for visual representation of the data. Significant difference was set at $p<0.05$.

Results

Prevalence of locoregional relapse and metastases among Ghanaian breast cancer patients

A total of 1057 adult female BC patients were registered into the KATH Oncology BC registry from 2019 to 2021, where 310 patients were registered in 2019, 286 patients in 2020, and 461 patients in 2021 (Table 1). The mean age of patients registered over the study period (2019–2021) was 53.9±13.33 years, with an age range between 22 and 92 years (Table 1).

Prevalence of locoregional relapse

The prevalence of locoregional relapse was 3.4% (CI=2.5 −4.7%) and the prevalence of metastasis was 47.6% (CI=44.6 −50.6%) (Table 1). There was no significant difference between the mean age at diagnosis of BC patients with metastasis (54.06 years) and those without metastases (53.79 years) (Fig. 1). For BC patients with documented locoregional relapse ($N=36$), 27.8% (CI=15.8 −44.0%) had relapse to the contralateral breast, 41.7% (CI=27.1 – 57.8%) had relapse to the ipsilateral breast, and 30.6% (CI=18.0 −46.9%) had relapse to regional lymph nodes (Table 2).

For BC patients with documented metastases ($N=503$), the distant metastatic site(s) was determined, 30% (CI=26 −34%) of patients with metastases had multiple organs involvement, followed by 28% (CI=24 −32%) with lung metastases, 16% (CI=13 −20%) with bone metastases, 9% (CI=7 −12%) with liver metastases, 3% (CI=2 −5%) with brain metastases and 14% (CI=11 −17%) with other metastases (ovary, uterus, spleen, peritoneum or distant lymph nodes) (Table 3). Overall, there was no significant difference between the age at diagnosis of patients with the different distant metastatic sites (p-value>0.05) (Fig. 2).

Prevalence of metastases among breast cancer subtypes

Data on BC subtypes were reviewed for 200 patients whose IHC reports were available (Table 4). Basal subtype was the most common subtype ($n=82$, 41%), followed by Luminal A ($n=69$, 34.5%), HER2+ ($n=37$, 18.5%) and Luminal B ($n=12$, 6%). There were overall significant differences in frequencies of BC subtypes (χ^2 p-value≤0.001) (Fig. 3). The pairwise comparison of BC subtypes showed that the frequency of the Basal subtype was significantly higher than Luminal B and HER2+ (p-value adjusted≤0.001 in both instances). However, there was no significant difference between the frequency of Basal and Luminal A subtypes (p-value adjusted>0.05). The frequencies of Luminal A and HER2+were also significantly higher than Luminal B (p-values adjusted≤0.001 in both instances).

Distribution of metastasis within molecular subtypes showed that 70 (35%) of the Basal, 43 (21.5%) of the Luminal A, 29 (14.5%) of the HER2+and 8 (4%) of the Luminal B subtypes had metastatic disease (Table 4). The metastatic sites across these subtypes included distant organs such as the lungs, bone, liver, multiple organ involvement as well as distant lymph nodes with one brain metastasis which was present in the basal subtype (Fig. 4). Metastasis within BC molecular subtypes showed a significant difference (χ^2 p-value≤0.001) (Table 5). The pairwise comparison showed that the Basal subtype had a significantly higher frequency of metastases than Luminal B (p-value adjusted≤0.001) and HER2+

Table 1 Classification of study population from 2019–2021

Variable/Year	2019 ($n=310$)	2020 ($n=286$)	2021 ($n=461$)	
Age distribution				
Age Mean (Range)	54.2 (27–92)	53.8 (25–90)	53.8 (22–91)	
Distribution of Locoregional relapse and Distant Metastasis				**Total**
Locoregional (n (%))	14 (4.1)	11 (3.8)	12 (2.6)	35 (3.4)
Metastasis (n (%))	143 (46.1)	156 (54.5)	204 (44.3)	503 (47.6)

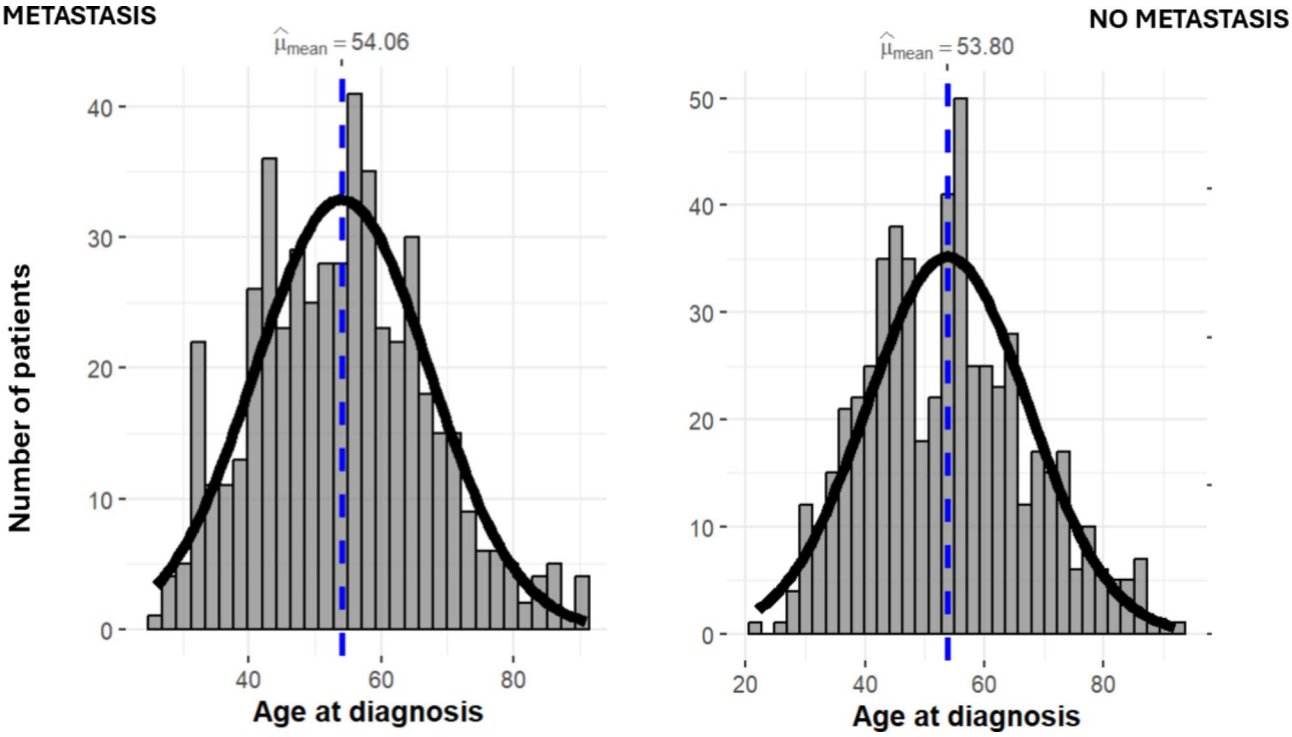

Fig. 1 Age distribution of patients with distant metastasis and those without distant metastasis: There was no significant difference between the mean age at diagnosis of BC patients with metastasis (54.06 years) and those without metastases (53.79 years)

Table 2 Distribution of locoregional relapse among breast cancer cohort

Variable (*n* (%))	2019 (*n* = 310)	2020 (*n* = 286)	2021 (*n* = 461)	2019–2021
Total Locoregional	13 (4.2)	11 (3.8)	12 (2.6)	36(3.4)
Contralateral breast	4(30.77)	4(36.36)	2(16.67)	10(27.78)
Ipsilateral breast	3 (23.08)	4(36.36)	5(41.67)	12(33.33)
Lymph nodes	6(46.15)	3(27.27)	5(41.67)	14(38.89)

For BC patients with documented locoregional relapse (*N* = 36), 27.8% (CI = 15.8 − 44.0%) had relapse to the contralateral breast, 41.7% (CI = 27.1 − 57.8%) had relapse to the ipsilateral breast, and 30.6% (CI = 18.0 − 46.9%) had relapse to regional lymph nodes

Table 3 Distribution of distant metastasis among breast cancer study population

Variable (*n* (%))	2019 (*n* = 310)	2020 (*n* = 286)	2021 (*n* = 461)	2019–2021
Total Metastasis	143 (28.43)	156 (31.01)	204 (40.56)	503(47.59)
Multiple	54 (37.76)	39 (25.00)	58 (28.43)	151(30.01)
Lung	37 (25.87)	49 (31.41)	55 (26.96)	141(28.03)
Bone	22 (15.38)	26 (16.67)	32 (15.69)	80(15.90)
Liver	17 (11.89)	10 (6.41)	18 (8.82)	45(8.95)
Brain	7 (4.90)	3 (1.92)	6 (2.94)	16(3.18)
Other	6 (4.20)	29 (18.59)	35 (17.16)	70(13.92)
None	167 (30.14)	130 (23.47)	257 (46.39)	554(52.41)

For BC patients with documented distant metastases (*N* = 503), the distant metastatic site(s) was determined, 30% (CI = 26 − 34%) of patients with metastases had multiple organs involvement, followed by 28% (CI = 24 − 32%) with lung metastases, 16% (CI = 13 − 20%) with bone metastases, 9% (CI = 7 − 12%) with liver metastases, 3% (CI = 2 − 5%) with brain metastases and 14% (CI = 11 − 17%) with other metastases (ovary, uterus, spleen, peritoneum or distant lymph nodes)

(p-value adjusted ≤ 0.001). However, there was no significant difference between metastasis within the Basal and Luminal A subtypes (p-value adjusted > 0.05). HER2 + and Luminal A also had significantly higher metastases than Luminal B (p-values adjusted ≤ 0.001 in both instances).

Review of stage at diagnosis of BC was also carried out for this subset of patients (*N* = 200) with 9 (4.5%) presenting as stage I, 38 (19%) presenting as stage II, 64 (32%) presenting as stage III and 89 (44.5%) presenting as stage IV.

Discussion

This study evaluated the prevalence of locoregional relapse and distant metastasis across the BC patient population from 2019 to 2021. Additionally, distant metastasis within molecular subtypes of BC was reviewed for a subset of the 2019 to 2021 patient population (*N* = 200). The prevalence of BC locoregional relapse and metastasis were 3.4% and 47.6% respectively. Review of BC stage at presentation for a subset of the study population (*N* = 200) revealed that two-thirds of the patients presented with advanced/metastatic (stage III-IV) disease.

The findings of this study show that about half of the studied population had metastatic disease (47.6%). The finding of 47.6% metastatic disease is consistent with the findings of Unger-Saldaña [17] who reported a 50%

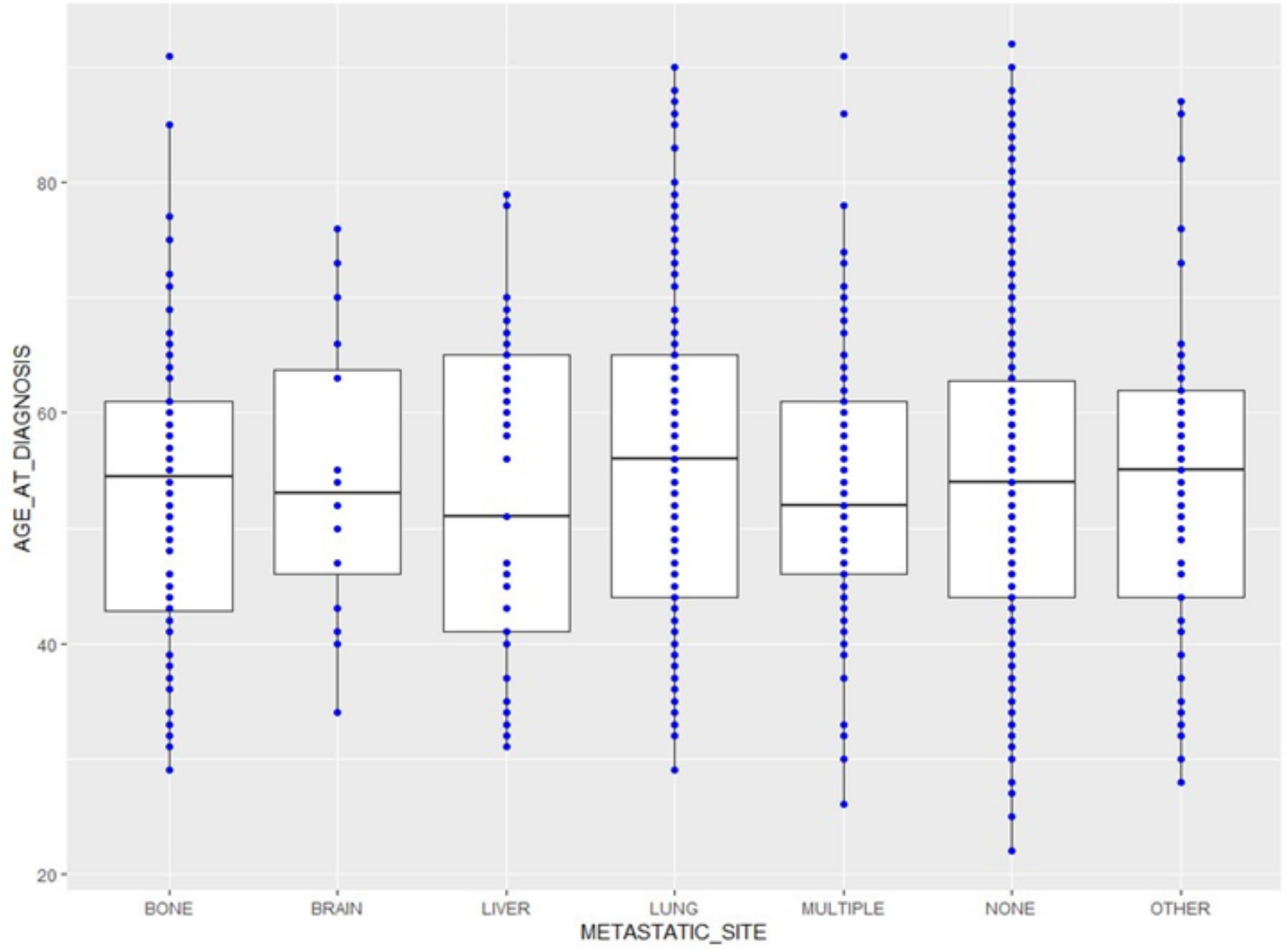

Fig. 2 Box plot showing age at diagnosis of breast cancer with different distant metastatic sites: Overall, there was no significant difference between the age at diagnosis of patients with the different distant metastatic sites (p-value > 0.05)

Table 4 Distribution of distant metastasis among molecular subtypes of breast cancer

Subtype	Bone (*n* = 27) *n* (%)	Brain (*n* = 1) *n* (%)	Liver (*n* = 7) *n* (%)	Lung (*n* = 38) n (%)	Multiple (*n* = 49) n (%)	None (*n* = 50) n (%)	Other (*n* = 28) n (%)
Luminal A	12 (6.0)	0 (0.0)	2 (1.0)	12 (6.0)	12 (6.0)	26(13.0)	5 (2.5)
Luminal B	2 (1.0)	0 (0.0)	0 (0.0)	1(0.5)	3 (1.5)	4 (2.0)	2 (1.0)
HER2+	4 (2.0)	0 (0.0)	2 (1.0)	4 (2.0)	8 (4.0)	8 (4.0)	11(5.5)
Basal	9 (4.5)	1(0.5)	3 (1.5)	21(10.5)	26(13.0)	12 (6.0)	10(5.0)

Distribution of distant metastasis within molecular subtypes showed that 70 (35%) of the Basal, 43 (21.5%) of the Luminal A, 29 (14.5%) of the HER2 + and 8 (4%) of the Luminal B subtypes had distant metastatic disease

prevalence of metastatic BC from patients in LMIC, and Adisa et al., [9] who also reported 52.5% of metastatic BC from Nigeria. Additionally, Dia et al., [18] reported a 49% prevalence of metastatic BC from Cote d'Ivoire. However, a low prevalence (6–9%) of metastatic BC has been reported in developed countries such as the United States [19] and the Netherlands [20]. The disparities in the prevalence of metastatic BC could be attributed to a myriad of factors including limited access to BC education, screening technology, care, and sometimes sociocultural practices in LMIC compared to the advanced countries [14, 21]. These contribute to more people in LMICs like Ghana reporting to hospitals late with advanced/metastatic BC. Fewer women from sub-Saharan Africa including Ghana are diagnosed with early-stage BC coupled with delays in commencement of treatment, disruptions in treatment and higher mortality which prevent completion of primary treatment and complete remission in most cases [9, 14]. There is a lack of data on follow-up

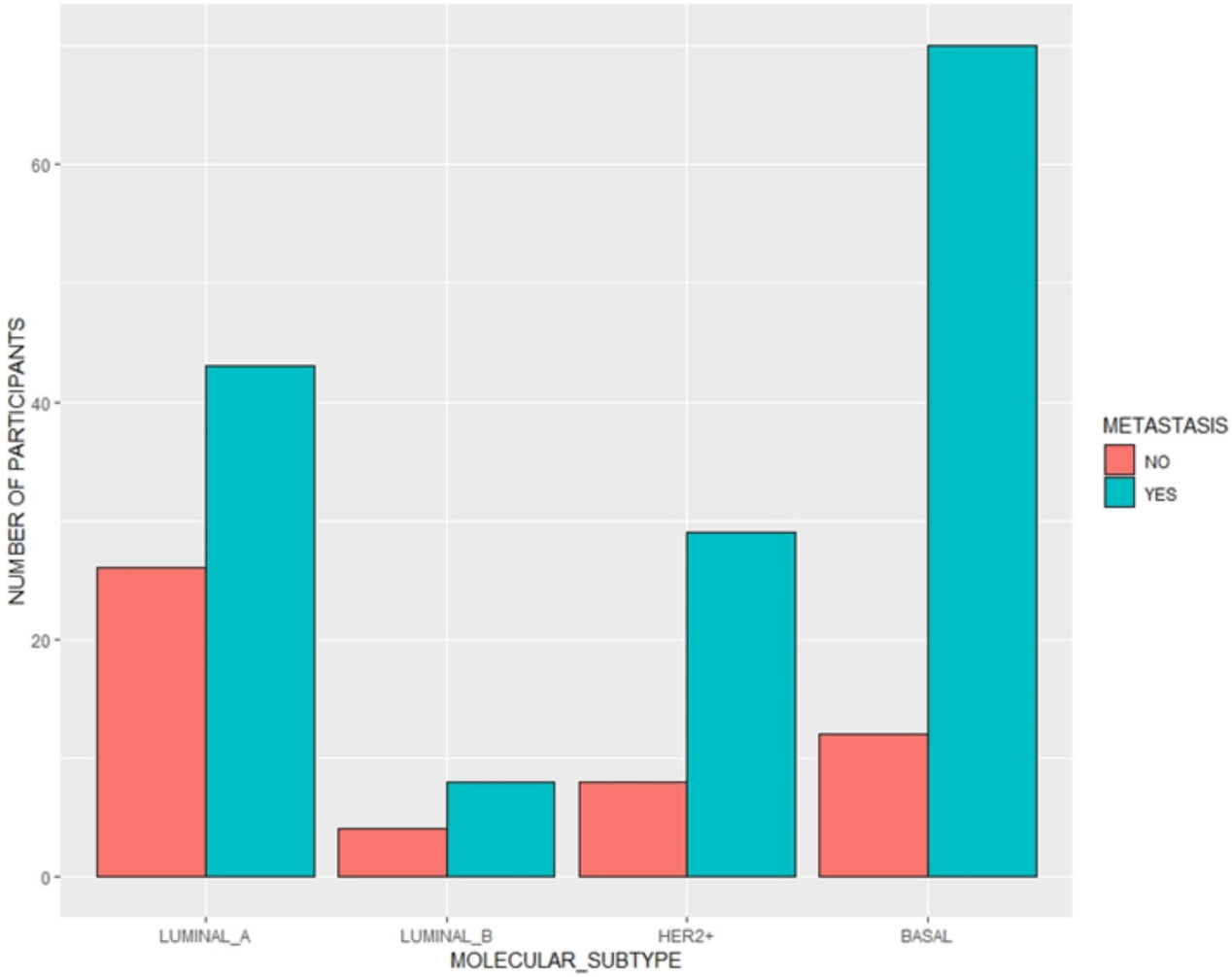

Fig. 3 Frequency of molecular subtypes of BC and the distribution of distant metastases among the various molecular subtypes: Review of molecular subtypes showed that the Basal subtype was the most common subtype ($n=82$, 41%), followed by Luminal A ($n=69$, 34.5%), HER2+ ($n=37$, 18.5%) and Luminal B ($n=12$, 6%). Distribution of distant metastasis within molecular subtypes showed that 70 (35%) of the Basal, 43 (21.5%) of the Luminal A, 29 (14.5%) of the HER2 + and 8 (4%) of the Luminal B subtypes had distant metastatic disease

after primary treatment across the major BC treatment centres in Ghana [21].

This study found a 3.4% prevalence of locoregional relapse. Studies on prevalence of locoregional relapse after primary treatment in Africa are lacking [21, 22] with some available studies focussing on incidence of relapse and others focussing on relapse after a particular treatment regimen [23–25]. Muddather and colleagues [24] reported a 6.5% incidence of BC relapse after primary treatment among Sudanese BC patients. A systematic review by Oppong et al., observed a 5–12% prevalence of locoregional relapse after BC radiotherapy from six studies conducted in Africa [25]. Another study by Ayettey Ani et al., among Ghanaian BC patients who received radiotherapy, observed an 8.0% prevalence of locoregional relapse after 4 years follow-up [26].

A review by Wang et al., [6] using the Surveillance, Epidemiology, End Result (SEER) database of the National Cancer Institute in the United States of America, observed 33.07% multiple metastases. A study among South African BC patients observed 35.4% metastases to multiple sites [22] and a study among Nigerian BC patients observed more than two-thirds of participants with multiple metastases [9]. These findings are consistent with the findings of this study (30% multiple metastases). We further observed higher lung metastasis (28%) compared to bone (16%), liver (9%), brain (3%), and other (ovary, uterus, spleen, peritoneum or distant lymph nodes) (14%) metastases which is also consistent with the findings of Phakathi and co-workers [22] from South Africa. The lung metastases reported in this study are also consistent with 21–32% reported by Medeiros & Allan [27]. However, it is higher than the 10.94% reported

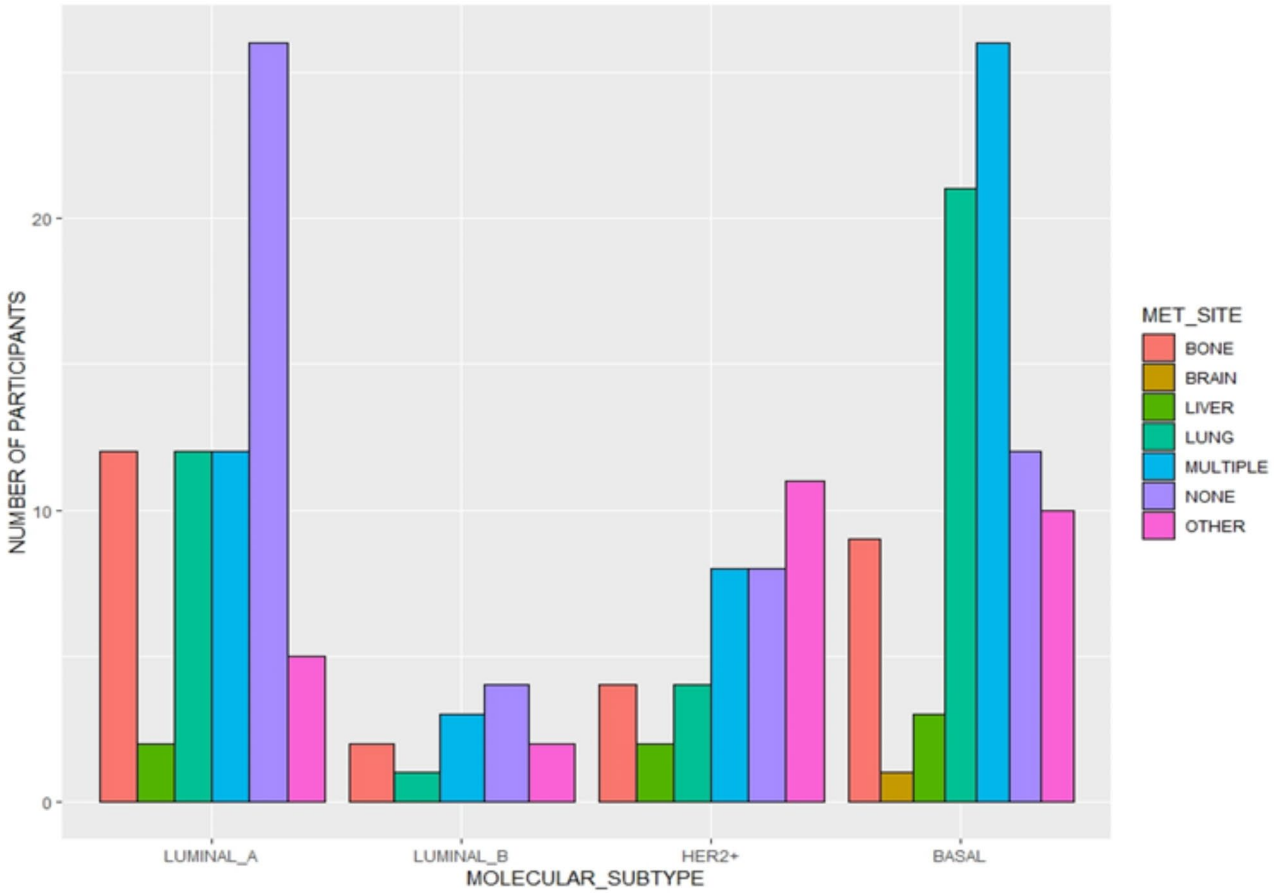

Fig. 4 Distribution of distant metastatic sites among the various subtypes: The Basal subtypes had the most metastases (35%) with multiple metastasis being the most prevalent (13%) followed by Luminal A (21.5%) with bone metastases being most prevalent (6%)

Table 5 Pairwise comparison of distant metastasis among molecular subtypes of breast cancer

Subtype	Luminal B	HER2+	Luminal A
Luminal A	1.4×10^{-9}	1.1×10^{-2}	-
HER2+	2.1×10^{-3}	-	-
Basal	3.1×10^{-12}	$2.2\times10-4$	1

Pairwise comparison of distant metastases between molecular subtypes of BC using χ^2 and post-hoc analysis using Bonferroni correction, showed that the metastasis of the Basal subtype was significantly higher than Luminal B and HER2+ (p-value adjusted ≤ 0.001 in both instances). However, there was no significant difference between the metastasis of Basal and Luminal A subtypes (p-value adjusted > 0.05). The metastasis of Luminal A and HER2+were also significantly higher than Luminal B (p-values adjusted ≤ 0.001 in both instances)

by Wang et al., [6], and lower than the 50.7% reported by Adisa et al. [9]. The bone, liver, and brain metastasis reported in this study are lower than that reported by Medeiros & Allan [27] who attributed 30–60% to bone, 15–32% to liver, and 4–10% to brain metastases and also lower than the findings of Adisa et al., [9] who observed 34% bone, 62.6% liver metastases and 11% brain metastases.

Our study did not find a significant association between age at diagnosis and specific distant metastatic sites even though some studies have established an association between age at diagnosis and specific distant metastasis [28]. According to Chen et al., [29] age at diagnosis plays a crucial role in BC metastasis since age-related factors like hormonal changes, chronic inflammation, and immunity may be important in the development of distant metastasis. They observed that older age was associated with lung metastases.

Factors that determine the specific organotropism of BC are complex and include BC stem cells (BCSC) [30], age at diagnosis, and BC subtypes [29, 31]. The oestrogen receptor status and HER2 expression of BC tumours have been linked with an increased risk of metastasis to specific organs [2, 32]. Even though very few research has looked at the molecular subtypes and risk of specific distant metastasis, brain metastasis has been associated with basal and HER2+subtypes [33] while Luminal tumours have generally been associated with bone metastasis and better prognosis than the basal and HER2+subtypes [31].

In evaluating metastases and subtypes from two hundred (200) of the BC records reviewed, we identified the Basal subtype as having the most metastases (35%) across

all sites with multiple (13%) and lung (10.5%) metastases being the most common among this subtype. This was followed by Luminal A (21.5%) which had more bone metastases (6%) than all the other subtypes. Moreover, HER2+ (14.5%) had more metastases to other sites (5.5%) such as distant lymph nodes, ovary, uterus, spleen, and peritoneum than the other subtypes. Luminal B which had the least metastasis (4%) could be a result of fewer BC patients sampled, presenting with luminal B. The findings in this study are consistent with other studies that have also reported an association between BC subtypes and specific distant metastasis [32, 34, 35]. A study by Soni et al., [34] observed that the Luminal subtype was significantly associated with bone metastasis. The finding of Basal subtypes with the most metastatic sites was also consistent with the findings of Makuch-Kocha et al., [36]. Savci-Heijink et al., [35] also observed that BC subtypes were associated with specific distant metastasis with more visceral metastases (81%) being observed in the basal subtype. However, Xiao et al., [33] identified the Luminal A subtype as having the most metastasis across all sites instead of the Basal subtype as identified in this study. Xiao et al., [33] used the SEER database, which was made up of mainly Whites, African Americans, Hispanics, and Asians while our cohort comprised only Africans. These disparities could be attributed to study population differences.

Aside from the molecular underpinnings of BC locoregional relapse and metastases, the disparities in locoregional relapse and metastases between the advanced economies and LMIC could be attributed to a myriad of factors. Fear has been identified as a major obstacle preventing women from seeking help early for BC. Fear of a positive BC diagnosis, divorce as a result of mastectomy, and stigmatization often deter women from going for clinical breast examinations [14, 37, 38]. Additionally, cultural and religious beliefs are part of the hurdles to early diagnosis and treatment of BC that make management in LMIC difficult [14]. A survey by Gyedu et al., [39] on BC perception among different religious groups in Ghana identified some women as unlikely participants in clinical breast examination and mammography. This is because exposing the breasts to be seen by someone apart from one's spouse is considered sinful. These factors deter early treatment-seeking behaviour, further aggravating BC locoregional relapse and metastasis in the Ghanaian population.

The early prediction of BC locoregional relapse and metastasis is important as it can help identify patients at risk of relapse so that appropriate adjuvant therapy can be instituted to improve survival. Prediction depends on the patient's age, tumour size, tumour grade, axillary lymph node involvement, molecular profiling of the tumour, identification of molecular signalling pathways, and genomic profiling for the identification of gene signatures that can predict BC metastasis [7]. Advanced technologies such as the identification of molecular signalling pathways and genomic profiling are not available even in the major referral hospitals in Ghana and in most LMICs [21]. It is therefore imperative that the many bottlenecks that currently delay the traditional investigations for BC diagnosis such as delays in receiving histopathology reports, missing reports, inappropriate biopsy specimens that require a repeat of biopsy for histopathology and cost of IHC which result in patients being put on blind BC therapies are urgently addressed. Additionally, Imaging technologies play a major role in metastasis diagnosis in Ghana and most LMIC [21]. However, most BC patients cannot afford the cost of these technologies so delay undertaking these investigations or do not do them at all when they are required [10]. In many LMICs, there is very little support in the health budget for BC management. In Ghana, the Ghana National Health Insurance Scheme (NHIS) offers some support for BC treatment, but this is inadequate as it covers mainly consultation fees and selected drugs like Arimidex, Vitamin C, Calcium, and Herceptin [40]. Thus, to improve early detection, treatment outcomes and quality of life of BC patients; expanding health support to include the cost of IHC and imaging technologies, will go a long way to prevent relapse and metastasis. Investing in advanced technologies that can predict locoregional relapse and metastasis is also paramount. These measures if instituted can improve the management of BC locoregional relapse and metastasis and enhance the overall survival of women living with such conditions since they represent the most severe form of BC.

This study is limited by the fact that BC subtypes and pathological features were carried out for 200 registered BC patients because, Immunohistochemistry data were only available for 200 out of the 1057 registered BC patients. Moreover, records of biopsy report were not available for all 1057 BC patients. Being able to review biopsy reports for more than 200 patients registered over the period under review would have allowed for further comparison of tumour characteristics between the various stages, prediction of treatment outcomes and discussion of appropriate management options for each stage reviewed. Also, this study did not distinguish between de novo metastasis and metastatic relapse because records reviewed did not provide information on the period when metastasis occurred.

Conclusions

Prevalence of BC locoregional relapse and metastasis accounted for 3.4% and 47.6% respectively. Basal subtypes had the most metastases (35%) with multiple metastasis being the most prevalent (13%). BC subtypes

could influence the specific metastatic site and should be a guide in the management of patients to enhance early prediction and detection of locoregional relapse and metastasis for improved overall treatment outcomes.

Abbreviations

BC	Breast cancer
LMIC	Low- and middle-income countries (LMICs)
TNBC	Triple negative breast cancer
KATH	Komfo Anokye Teaching Hospital
IHC	Immunohistochemistry

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Author contributions
GAB, LAF, CO: Conceived the research idea; LAF, CO, MBD: supervised the research; GAB, RM, BS, EOS, IK, LN, MBD: data collection and stratification of data; GAB, RM, MBA, EA, MBD: data analysis; GAB, LAF, RM, IK, CO, MBD: drafting of manuscript; GAB, RM, IK, LN, MBD, LAF, CO: review of manuscript: All authors read and approved the manuscript.

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Data availability
The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
The study was approved by the Institutional Review Board of KATH with the approval referenced KATH IRB/AP/147/21. Due to retrospective nature of the study, the Komfo Anokye Teaching Hospital Review Board waived the need for informed consent.

Consent for publication
Not Applicable.

Competing interests
The authors declare no competing interests.

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