Journal of Cancer Science & Therapy

Gemta et al., J Cancer Sci Ther 2019, 11:2
DOI: 10.4172/1948-5956.1000581

Research Article Open Access

Patterns of Breast Cancer Among Ethiopian Patients: Presentations and Histopathological Features

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Abstract

Background: Breast cancer is the most common malignancy in women and the leading cause of cancer deaths worldwide. In Ethiopia breast cancer is among the most prevalent cancer and occurs at young age. It usually presents at an advanced stage.

Objective: To describe the frequency, stages, histological patterns, staging and grading of breast cancers among Ethiopian women in three Hospital in Addis Ababa, Ethiopia.

Methods: A prospective study of 197 patients who presented to three hospital with breast cancer and underwent surgery from December 2013-December 2015. Tissue were fixed in 10% formalin solution and paraffin embedded. Hematoxylin and Eosin (H&E) stained slides were prepared in all cases and reviewed and classify according to the WHO.

Results: The mean ± SD age of the participants was 44.77 ± 13.6 and the median was 42 years. Most patients were aged less than 50 years (70.6%) at the time of diagnosis. 57.4% were pre-menopausal and 42.6% were postmenopausal. The duration of symptom before presentation ranged from 2 to 48 months with mean ± SD 18.11 ± 13.2 months. Invasive ductal carcinoma was the commonest (79.2%) histologic type of breast cancer. Of all patients, (46.2 %) of patients had grade 2, while (36.5%) of the cases were grade 3 or poorly differentiated tumors. Most patients (70%) presented with advanced stage (III and IV) and more than (90 %) tumor were >2 cm in size.

Conclusion: Our study shows breast cancer is a common disease that affects young Ethiopian women, and that there is a significant delay in presentation and advanced stage presentation is a major concern. It should be recognized that breast cancer is a disease with a serious public health implication.

Keywords: Breast cancer; Histology; Grade; Ethiopia; Delay in presentation

Introduction

Globally Breast cancer (BC) is a common form of cancer among women [1]. The disease mostly occurs in women, but men also develop the disease. The incidence rates vary greatly worldwide from 19.3 per 100,000 in Eastern Africa, to 89.7 per 100,000 in Western Europe [2]. Recent report showed, nearly 1.7 million new women diagnosed worldwide. It represents about 12% of all new cancer cases and 25% of all cancers in women [3].

Like other sub-Saharan countries, the incidence of cancer is rising in Ethiopia [4]. The exact burden of cancer in Ethiopia and many African countries remains poorly understood when compared to data of resourced settings. The exact national incidence rate in Ethiopia is not known because of lack of comprehensive data. Currently, Ethiopia has only one cancer treatment center at the Tikur Anbessa specialized Hospital (TASH) and only one institutional cancer registry in Addis Ababa city. Therefore, the estimate of cancer burden in the country is made on basis of extrapolations of data from these two sources. Recently Abate [5] reported retrospective data of over a period of sixteen years (1997-2012), more than 50 cancer types and a total of 16,622 new cases were registered in TASH. Out of this, 3460 (≈ 20.8%) were new cases of BC representing approximately 216 cases per annum. On the other hand, a study by the Addis Ababa City Cancer registry in 2014, has reported BC was the leading type (34 %) of all cancers diagnosed in that specific year among females [6].

BC is complex disease, comprising distinctive histological patterns. Breast cancer is usually asymptomatic in the early stages during which it is curable, this is the puzzle of breast cancer, and it is a heterogeneous disease with various impacts and different outcomes. Histologic classification is one of the most important diagnostic steps that had to be performed before any treatment [7]. Standard histopathological evaluation not only differentiates the *in situ* lesions from invasive ones but also determines the grade and type of disease [8]. This study intends to describe the frequency, stages, histological patterns, staging and grading of breast cancers affecting Ethiopian women at three Hospital in Addis Ababa, Ethiopia.

Methods

A prospective study of 197 patients who presented to three different hospital with a confirmed diagnosis of breast cancer and underwent surgery from December 2013-December 2015 was done. All specimens sent for histo-pathology (open incisional biopsies, mastectomies and wide excision biopsies with lymph nodes) were fixed in 10% formalin

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Received January 16, 2019; **Accepted** February 11, 2019; **Published** February 13, 2019

Citation: Gemta EA, Bekele A, Mekonen W, Seifu D, Bekurtsion Y, et al. (2019) Patterns of Breast Cancer Among Ethiopian Patients: Presentations and Histopathological Features. J Cancer Sci Ther 11: 038-042. doi: 10.4172/1948-5956.1000581

solution, processed with histokinette automated tissue processor, paraffin embedded and sectioned at 3-5 microns before staining with H and E. All slides were reviewed by the experienced pathologist in order to classify according to the WHO classification. The tumor grading was performed according to Elston-Ellis criteria by quantifying three major elements: nuclear morphology (nuclear pleomorphism), differentiation (tubule formation), and proliferation (mitotic frequency) according to the Nottingham grading system (NGS). The attending surgical resident or General practitioner was required to fill a form containing the patient's data such as age, sex, educational back- ground, occupation, symptoms, duration of symptoms, and findings on clinical examination. The study was approved by the ethical review committee of the department and the patients gave informed consent. Data obtained were analyzed using the Statistical Package for the Social Sciences version 20 statistical package (SPSS) Incorporated, Chicago, Illinois, USA, and value presented descriptively.

Results

Patient characteristic

A total of 197 female BC biopsies were collected from three different hospital in Addis Ababa (Saint Paul hospital, Betezata hospital and from Tikur Anbessa Hospital). As shown in Figure 1, the age of the patients ranged from 22 -76 years. (Mean ± SD: 44.77 ± 13.6; median: 42). 35/197 (17.8 %) were younger than 30 years.

Pattern of tumor at presentation

The duration before presentation ranged from 2 to 48 months with a mean ± SD of 18.11 ± 13.2 months. 52/197 (26.4%) presented to the health facilities after 2 years of onset of symptoms. Almost all 188/197 (95.4 %) had a palpable breast mass, among which 172/197 (87%) were found accidentally. Only 3/197 (1.5 %) of the cases were diagnosed as part of routine Physical examination. Right breast was involved in 106/197 (53.8%), patients, and the upper outer quadrant was involved in 154/197 (78.2%) patients (Table 1).

Histopathological features of BC

Invasive ductal carcinoma was the commonest histologic type of BC seen (79.2%), Table 2 followed by lobular carcinoma (8.1%) and cribriform (7.1%). It was observed that most of patients (46.2 %) had moderately differentiated tumour (G2 grade) while 36.5% of the cases were grade 3 or poorly differentiated tumors. Macroscopically,

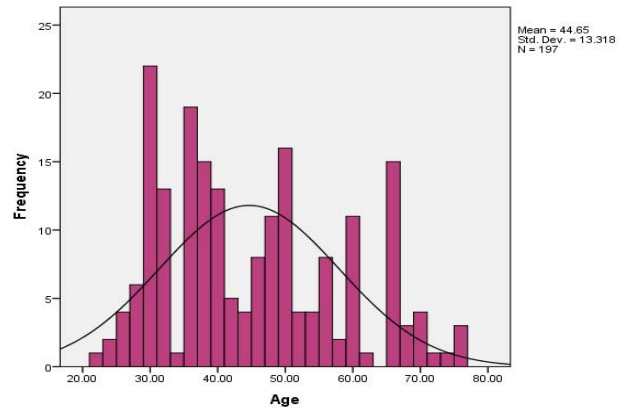

Figure 1: Age distribution at diagnosis of histologically verified BC patients.

Variables	N	%
Duration of symptom		
1-6 mth	35	17.8
7-12 mth	67	34
13-18 mth	21	10.7
19-24 mth	22	11.2
>24 mth	52	26.4
Lump		
Yes	188	95.4
No	9	4.6
How was the lamp found		
Self accidentally	172	87.3
Self as part of regular physical examination	22	11.2
Routine physical examination	3	1.5
Site		
Right Breast	106	53.8
Left Breast	91	46.2
Anatomical location		
Upper outer quadrant	154	78.2
Upper inner quadrant	14	7.1
Lower inner quadrant	17	8.6
Central	12	6.1

Table 1: Distribution of tumor presentation during diagnosis among study participants.

Variables	Frequency	Percentage
Histology		
Invasive ductal carcinoma	156	79.2
lobular carcinoma	16	8.1
Cribriform	14	7.1
Metaplastic	4	2
mixed carcinomas	7	3.6
Clinical tumor size		
T1	8	4.1
T2	93	47.2
T3	71	36
T4	25	12.7
Stage		
Stage I	6	3
Stage II	54	27.4
Stage III	113	57.4
Stage IV	24	12.2
Histological grade		
Grade I	34	17.3
Grade II	91	46.2
Grade III	72	36.5

Table 2: Characteristics, histopathological subtypes, tumor size, stage and histological grade of BC among study participants.

the tumour size at presentation ranged from 2 to 17 cm in diameter. Only 21/197 (10.7 %) patients had tumors less than size of 2 cm and the rest which accounts 180 (89.3%) patients had tumours above 2 cm in diameter. Lymph node involvement was seen in 62.4 % of the cases and the 37.6 % were absent. Table 3 illustrates significant association between tumor stage (p=0.01), tumor size (p<0.001) and histological grade (p =0.01). Most of patients presented with stage III disease (57.4%) followed by stage II (27.4%), stage IV accounts (12.2%) and only 3% of the study were presented with stage (I) (Figures 2 and 3).

Discussion

BC management has been a main challenge to clinicians in

Character	N (%)	Lymph node involvement		p-value
		Yes	No	
Stage, n (%)				
I	6 (3)	2 (1.6)	4 (5.4)	0.01*
II	54 (27.4)	27 (22)	27 (36.5)	
III	113 (57.4)	77 (62.6)	36 (48.6)	
IV	24 (12.2)	17 (13.8)	7 (9.5)	
Histology, n (%)				
Ductal	156 (79.2)	97 (78.9)	59 (79.7)	0.8
Lobular	16 (8.1)	10 (8.1)	6 (8.1)	
Others	25 (12.7)	16 (13)	9 (12.2)	
Size, n (%)				
0-2 cm	17 (8.6)	6 (4.7)	11 (15.7)	0.001*
2-5 cm	130 (66)	80 (63.0)	50 (71.4)	
>5 cm	50 (25.4)	41 (32.3)	9 (12.9)	
Grade, n (%)				
I	34 (17.3)	16 (12.6)	18 (25.7)	0.04*
II	91 (46.2)	61 (48.0)	30 (42.9)	
III	72 (36.5)	50 (39.4)	22 (31.4)	

Table 3: Distribution of tumor characteristics and node status among study participants.

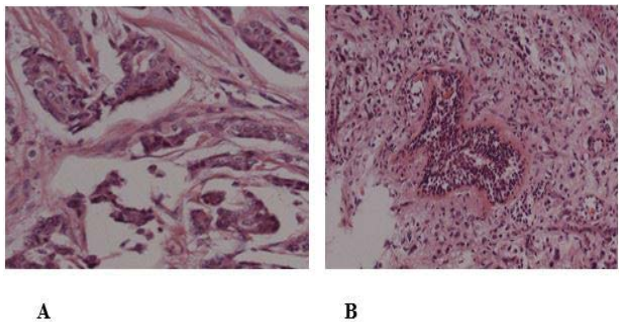

Figure 2: Photomicrograph of invasive ductal carcinoma ductal (A), Lobular (B), H and E stain (10x).

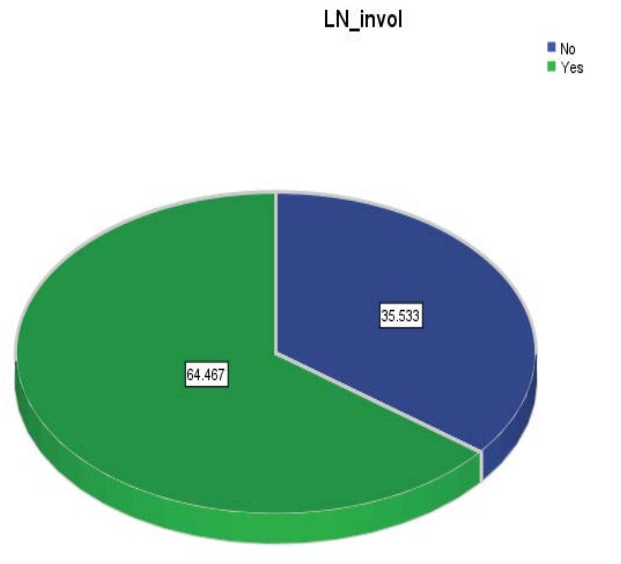

Figure 3: Lymph node involvement.

developing countries, primarily due to late presentation of patients to the hospital and shortage of advanced technology to investigate its wide range of pathologic aspects and clinical behavior [9]. BC development increases with age, beginning to rise at approximately age 30 years [10]. In this study (Figure 1), the median age of patients was 42 years. Women aged 30–39 years of old being the largest group of the study population 61/197 (33%). The median age in our data was comparable to previous studies by Kantelhardt et al. (43 years) in patients at Addis Ababa (AA) University Radio Therapy Center and another previous study in the same center that revealed a median age of 40 years [10]. Reports show a median age of 45-51 years in different African countries [11,12]. Our study reveals much lower than the median age reported in western countries where the median age at diagnosis was in the sixth decade of life. It has been reported that the occurrence of BC at young age is associated with a worst prognosis and but prognosis improves with age [12]. In African women, the diagnosis of BC is often made between 35 and 45 years of age. This is approximately 10–15 years earlier than peak incidence for western countries [13]. It used to be interpreted in context of the lower life expectancy in developing world (relative to life expectancy in developed health systems). As fewer developing women reach old age, this might be expected to skew the median age of BC diagnosis towards a younger age since many of those who might have developed BC at an older age will have died of other causes, including infectious diseases. The reasons for the early age at onset of BC among black women are poorly understood but could probably be connected to the aggressive nature of the disease that may be a reflection of African BC biology [13]. Currently in Africa, the population is younger than western countries, therefore the age structure may not entirely explain the younger BC ages in Africa. It was reported that, African American women tends to develop BC at younger ages than Caucasian women in US. Thus, there may be additional factors involved including genetics, environmental or interplay of the two. Subsequently African women develop unique BC subtype which could be important contributory factor to unusual age distribution noted in our study [14]. This factor further needs population based active registration of cases and baseline genetic studies to recognize the burden of cancer.

Late presentation in BC is defined as patient delay between first detection of the symptom and initial medical consultation. In our study 82.7% of patients with BC had a delay more than 6 months and the mean duration of presenting symptom was 18.11 ± 13. 2 months. This number is quite similar with data before a decade in Ethiopia [10], and other developing countries like Nigeria, Egypt, Ghana and Tanzania [9]. However gross difference seen in developed countries like Germany [15]. Late presentation at time of diagnosis are considered as high risk for relapse as well as overall survival. Early diagnosis and improved survival in western countries reported in several studies has been attributed to screening programs, where prognosis of BC has been well and a 10 year relative overall survival of 70% has been achieved [16]. We could not establish the reasons for the late presentation in our study but we agree with study by Dye [17] Ethiopian patients typically visited three health facilities before being referred to a specialized cancer center and also lack of national BC screening program, poor access to advanced health facilities including pathology service or combined effect of these could be factors for late presentation disease. The Breast Health Global Initiative summit in 2007 [18] recommended the promotion of breast self-awareness and clinical breast examination (CBE) at the basic level to encourage women to seek medical evaluation of breast problems. Imperative actions are needed for BC program in Ethiopia which includes, establishment of National cancer registries, comprehensive health education to build up awareness and development of centers for management BC.

In this study, the right breast was mostly affected with the upper outer quadrant mostly involved either separately or in combination with other parts of the breast (Table 1). This is in contrast to previous studies conducted in other centers where the left breast was reported to be the most commonly affected [19]. BC occurs more frequently in the left breast, which is typically slightly larger than the right. Few studies have directly investigated the effect of breast size as a risk factor for BC, those studies used a variety of designs and techniques, and the evidence is inconclusive and it is not known whether laterality has any prognostic significance in breast cancer [20]. The upper outer quadrant is also reported to be commonly involved in a West Africa study [19]. This may probably be due to the association of the upper outer quadrant with the axillary tail which is a channel for drainage of lymph to the axillary lymph nodes and may carry micro-metastasis more than the other quadrants of the breast.

Our study showed that the commonest sign/symptom was a breast mass similar to the report from Malawi [20], this agrees with current clinical practice which encourages excision of a breast lump for histological examination to rule out malignant lesions. Unfortunately Most of our patients (88%) had accidentally discovered the malignant breast masses this is due to the fact that routine breast self-examination is not a common practice. The authors believe lack of awareness and ignorance of the breast mass is partly attributable to late presentations reason for the late presentation.

Histological type of tumor is a known factor influencing prognosis and survival of patients with BC. Invasive ductal carcinoma was the commonest histological type of BC in our study, similarly most studies have shown invasive ductal carcinoma to be the most common histological type in breast carcinoma. Studies in Tanzania [12] reported invasive ductal carcinoma accounts for 90%. In Nigeria, 95% of patients had infiltrating ductal carcinoma [14]. Another similar results was seen in a large register- based study in Norway of BC patients where 81.4% of all cases were ductal carcinoma, 6.3% lobular and 5.5% other unspecified carcinomas [19]. Patients with ductal, solid lobular, mixed ductal and lobular carcinoma have been found to have a 10year survival below 50% [20]. Tubulo-lobular and mucinous type have usually an excellent prognosis with a 10years survival of >80% [17]. The findings of the current study implies that most of our patients have a risk to poor prognosis due to the dominating ductal carcinoma histological type. Ductal carcinoma starts in a milk duct of the breast, breaks through the wall of the duct, and grows into the fatty tissue of the breast. At this point, it may be able to spread (metastasize) to other parts of the body through the lymphatic system and bloodstream, due to this most of our patients have a risk to poor prognosis.

It has been suggested that tumor size is crucial for BC staging to determine the invasiveness of tumor, and it is one of the most important prognostic factors in BC as investigated in previous study [21]. In our study, majority of the tumors (91.1 %) had a diameter larger than 2 cm. In developing countries the presentation of large primary tumor is common, due to behavior of breast cancer presentation which is painless initially. In our work the mean tumor size was 6.3 cm which remains within the range of large tumor size. Comparable to a study done on surgical specimens from BC patients in Tanzania before a decade found the mean tumor size was 8 cm, none of the tumors were less than 2 cm. Tumor greater than 5 cm in diameter are at high risk of relapse of the disease [12] and in our study more than 25% of the tumors exceeded 5 cm in diameter which is indicating, quarter of patients are at high risk of relapse of disease. These findings are different when compared with the one done in Cuba and other western countries where tumor <2 cm was more prevalent (49.2%) than intermediate and larger tumor size [22]. The difference could be due to well established screening programs in Cuba and increased awareness. In our study we observed, tumors larger than 2 cm, (95.1%) of patients were presented with nodal involvement. In agreement with various studies [23-25], there is increased incidence of axillary lymph node involvement and the frequency of positive axillary nodes also increased with increasing size of the tumor. Larger tumour size could be used as an independent predictor of node positive disease in our study, in agreement with data from Eastern India [26]. Large tumour size at presentation may be explained by the aggressive behaviour of these tumours and also due to the lack of health education and breast screening programmes for BC in Ethiopia. Lack of the program may contribute to the late presentation of patients and the poor prognosis of the disease.

Conclusion

Breast carcinoma is a common cancer affecting comparatively young age group with high rate of invasive ductal carcinoma advanced stage, high grade and lymph node metastasis at the time of diagnosis. National screening program and early diagnosis of symptom disease relies on in primary health-care professionals and thus increased breast health awareness and recognition of symptoms is a key element of interventions at all resource levels. Delay in presentation and late stage presentation is a major concern. There is a need for health education on self-breast examination and early presentation to a health facility for better management.

Funding

This work was funded by Addis Ababa University, School of Graduate Studies and the thematic research group "clinico-epidemiological characterization of breast cancer in Ethiopia" for designing the study and sample collection.

Competing Interests

The authors declare that they have no competing interests.

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