

## Clinicohistopathological evaluation of breast masses and profile of breast diseases in Eritrea: a case of poor concordance between clinical and histological diagnosis

Asmerom Tesfamariam<sup>1</sup>, Francisca Parilla<sup>1</sup>, Estifanos Paulos<sup>1</sup>, Mufunda J 1, Andemariam Gebremichael<sup>1</sup>

Institutional Affiliation of all the authors:

Orotta School of Medicine, PO Box 10549, Asmara, Eritrea

Correspondence to be sent to:

Asmerom Tesfamariam Orotta School of Medicine

PO Box 10549, Asmara, Eritrea Email: asmeromtesfa@yahoo.com

### Abstract

**Background:** Profile of breast disease varies with sex and age with predominance of cancers in older females. For patients presenting with breast masses, triple assessment using clinical, radiological and histological methods is desirable, with the latter considered to be the golden standard. Little information is available on the features of breast diseases in Eritrea.

**Objective of the study:** To investigate the profiles of breast diseases, and to determine the concordance between clinical and histological diagnoses so as to develop evidence based policies and cost effective management guidelines for the disease

**Methods:** This was a retrospective study of 89 patients presenting with clinical diagnosis of breast masses from 1st January 2006 to 31st December 2006. Biopsies taken from the patients were histologically examined and reported by one pathologist from the National Health Laboratory of the Ministry of Health, Asmara, Eritrea.

**Results:** The majority of cases were women (96.6%). The age at presentation ranged from 16 to 86 years. About half of the sample 43 (49.4%) had clinical diagnosis of breast cancer. The study found that, the concordance rates between clinical diagnosis and histological diagnosis were lower for carcinoma and benign lesions 46.5% and 80% respectively. Three quarters of the fibroadenomas were found in women younger than 36 years.

**Conclusion:** Benign breast lesions and carcinomas were common in females, with the former being more prevalent in women less than 36 years and the latter in women older than 50 years of age respectively, which is consistent with other reports. Because of relatively low concordance between clinical and histological diagnosis, findings from this report recommend that all patients with breast masses undergo biopsy and histological examination.

### Introduction

Breast lesions are a common heterogeneous group of disorders ranging from self limiting inflammatory lesions to life threatening invasive cancers 1. Globally, breast cancer is the commonest malignancy in women particularly during the menopausal period and ranks second commonest after cervical cancer in developing countries 2. Breast disorders are common in women because oestrogen cyclically stimulates breast development during their reproductive life, while in men the breast remains largely poorly developed providing formidable anti-neoplastic resistance 3, 4. Benign lesions are the predominant form of breast lesions in young women, presenting largely as functional fibrocystic mastopathy and fibroadenomas with varying degrees of hyperplastic proliferation<sup>5</sup>.

The diagnosis of breast lesions resides in the triple test comprising clinical, radiological and histological examinations with histological testing considered to be the golden standard 6. The WHO classification of breast cancer is routinely used as a reference for breast malignancies<sup>7</sup> whereas benign lesions are classified according to the proliferative changes 8. Samples obtained from either core biopsy or fine needle aspiration are used for histological evaluation with a wide range of specificity and sensitivity 8. Radiological assessment through mammography in good hands satisfies the Wilson's criteria for a screening test for breast masses 9. Developing countries have limited

human and technological resources and expertise necessary for investing and optimizing mammography as a routine test 10. Mammography is currently being offered routinely in resource rich countries, however, it demands both substantial financial and human resource expertise which may not be cost effective in a resource poor country where the magnitude and features of breast diseases are not known such as in Eritrea.

In spite of technological advancement coupled with screening, available treatment modalities ranging from surgical, chemotherapy and radiation or a combination of these modalities, the outcome of management of breast cancer has largely been disappointing 11. Patients who may appear to have early stages of breast cancer may already have micro-metastasis calling for adjuvant chemotherapy casting doubt on curative surgical treatment outcomes for this disease. In developing countries diagnosis of breast cancer has relied on clinical judgement with variable specificity and sensitivity not yet determined in Eritrea.

The objective of this study was to determine the profile of commonly encountered breast diseases and match clinical and histological diagnosis so as to formulate diagnostic policies and cost effective management guidelines of breast diseases.

### Materials and Methods

The study was a retrospective investigation

designed to document the profile of breast disorders from patients who had breast biopsy examination from 1st January to 31st December 2006.

Data was collected from the National Health Laboratory (NHL) department of pathology. Each patient's histological request and report was assessed and data on demographics (sex, age, and zonal distribution), laterality, histological diagnosis, and provisional clinical diagnosis, was collected. The biopsies were received from all zones of Eritrea. The samples were processed using standard procedures using the paraffin technique and stained by the routine haematoxylin eosin 12. All the biopsies were examined by one pathologist in the NHL pathology department.

### Data Analysis

The Bayesian Analysis Model was used to determine the Sensitivity, Specificity, and predictive value. The nine cases were excluded in determining the Sensitivity, Specificity, and predictive value as their clinical diagnosis was not defined.

### Results

There were 89 histological biopsies and this was the basis of our study. From the 89 patients one patient's histological result was not found and for nine of them their clinical diagnosis was not defined. Eighty nine breast samples were processed, examined, and reported in 2006. Demographic distribution (sex, age, and zone) and localization of the mass was summarized (Table 1). Almost all samples (96.6%) were obtained from female patients with only 3.4% from males. The age at diagnosis ranged from 16 to 86. 51.7% of the breast lesions and breast cancers occurred in women less than 35 years old. The breast lesion was localized on the right breast in 62.9% of cases and only 3.4% were on both breast. Fifty seven (64.1%) cases were from central zone and no case was from Southern Red Sea.

Sex	Characteristics	Frequency	Percent
	Female	86	96.6
Male	3	3.4	
Total	89	100.0	
Age category	16 – 25	29	32.6
	26 – 35	17	19.1
	36 – 45	11	12.4
	46 – 55	2	2.2
	56 -65	18	20.2
	> 65	12	13.5
	Total	89	100.0
Laterality	Left	30	33.7
	Right	56	62.9
	Both	3	3.4
	Total	89	100

Region	Central	57	64.1
	South	9	10.1
	Northern Red Sea	14	15.7
	Gash Barka	5	5.6
	Anseba	4	4.5
	Southern Red Sea	0	0
	Total	89	100

The common clinical diagnoses were carcinoma, fibroadenoma, benign mastopathy, and phyllodes tumour. Almost half of the cases (48.9%) were clinically diagnosed as carcinoma, one quarter as fibroadenoma and 10.2% were not clinically defined (Table 2).

Clinical diagnosis	Frequency	Percent
Carcinoma	43	48.9%
With no definitive clinical diagnosis	9	10.2%
Benign mastopathy	8	9.1%
Gynecomastia	1	1.1%
Phyllodes tumor	4	4.5%
Mastitis	2	2.3%
Fibroadenoma	21	23.9%

According to histological assessment, two thirds of the cases were diagnosed as benign breast lesions with the remainder being malignant. One third of the breast biopsies were fibroadenoma and another third was breast carcinoma (Table 3).

	Frequency		
	Male	Female	
Fibroadenoma	-	30	33.7
Cystic mastopathy	-	16	18.0
Proliferative mastopathy	-	3	3.4
Phyllodes benign tumor	-	2	2.2
Adenoma	-	3	3.4
Fat necrosis	-	2	2.2
Chronic mastitis	-	1	1.1
Gynecomastia	1	-	1.1
Intraductal papilloma	-	1	1.1
Mucinous carcinoma	-	1	1.1
Papillary carcinoma	-	1	1.1
Ductal carcinoma	2	25	30.3
Total	3	85	98.9
Missing	-	1	1.1
Total	3	86	100.0

\*Ductal carcinoma includes both ductal carcinoma in situ and invasive

A total of 59 cases out of 88 were benign breast diseases. The most common benign breast lesions according to histological examination in descending order with their frequency were fibroadenoma (50.8%), cystic mastopathy (27%), proliferative mastopathy (5.1%), adenoma (5.1%), fat necrosis (3.4%), phyllodes benign tumour (3.4%), chronic mastitis (1.7%), gynecomastia (1.7%), and intraductal papilloma (1.7%). Half of the benign lesions were fibroadenomas with three quarters found in women younger 36 years and only one case older than 65 years old. The cystic and proliferative mastopathy were predominant in women younger than 35 and older than 55 years old. The benign tumours including fibroadenoma, adenoma, phyllodes, and intraductal papilloma account 60% out of the total benign breast lesions.

A total of 29 cases were diagnosed as breast carcinomas with the majority 93.1 % of them being ductal carcinomas. The other two subtypes reported were papillary carcinoma and mucinous carcinoma. 20.6% of the cases with breast carcinoma were below 36 years age. The youngest case 22 years old. Two thirds of the cases were above 45 years of age.

poor concordance between clinical and histological diagnosis more for benign lesions.

The finding of similar proportions of cancers and benign lesions of breast diseases in this study was unique compared to other reports<sup>13</sup>. This observation is surprising especially give the high proportion of younger patients in our setting where the benign lesions are more frequent <sup>14</sup>. The study did not examine this finding and one can not establish the basis of this finding at this stage of our studies which is another scope for future investigations.

The distribution of cancers showed regional variation with higher rates in the predominantly urban highlands than in the lowlands which are mostly rural. One can speculate that the women from highlands have better access to health services making the higher rates a reflection of increased reporting rather than increased disease burden per se <sup>15</sup>. It is also likely that women in urban settings have better health seeking behaviours as has been reported in other studies comparing health seeking behaviour in rural and urban settings<sup>14</sup>. Another possible explanation could be the western like life style is more common in urban areas which increase the risk factor of breast cancer.

Degree of matching between histopathological and clinical diagnosis								
Histopathological diagnosis	Clinical diagnosis							Total
	Carcinoma	Clinical not defined	Benign mastopathy	Gyneco mastsia	Phyllodes benign tumor	mastitis	Fibro-adenoma	
Fibroade noma	17	1					12	30
Other benign breast disease	6	6	26	1	2	2	6	29
Carcinoma	20	2	2		2	2	3	29
Total	43	9	8	1	4	2	21	88

The clinical diagnosis was compared with histological diagnosis to determine the degree of matching or concordance. Twenty out of the 43 patients with clinically diagnosed as malignant were confirmed on histological examination giving a concordance of 46.5% and thirty six out of 45 clinically diagnosed as benign were confirmed by histological diagnosis giving a concordance rate of 80%. The study found that the sensitivity and specificity of clinical evaluation are 74% and 56% with positive and negative predictive 0.46 and 0.80 respectively.

### Discussion

The objective of the study was to determine the pattern of breast diseases and evaluation of breast masses in Eritrea so as to develop evidence based policies and guidelines for cost effective management. The main findings were that similar proportions of carcinoma and fibroadenoma were present. Carcinomas were common in women older than 50 years while fibroadenomas were prevalent in women younger than 36 years of age. There was

The triple test is the ideal approach to assessing women with breast lesions in resourceful countries. The test involves clinical, radiological and histological evaluation. In the best of hands the concordance of clinical and histological assessment is high <sup>15</sup>, but as we report in this study, the concordance rate was low especially for benign lesions. Core biopsy coupled with histological examination is the gold standard test for breast cancer diagnosis but it requires highly qualified pathologists who are not readily available in resource poor countries partly due to brain drain <sup>16</sup>. Although mammography is an effective screening test for breast cancer with relatively high specificity and sensitivity the technology and expertise are not always readily available in developing countries confounded by suboptimal patient follow up and relatively poor compliance <sup>17</sup>.

In our study, ductal carcinoma was the most prevalent form of breast cancer predominantly among women older than 45 years. This observation is consistent with reports from other studies <sup>18,19</sup>. Use of hormone replacement therapy (HRT) compounds the problem of carcinoma of the breast in postmenopausal

women especially in developed countries where that treatment is frequently used and may contribute to the higher prevalence of carcinoma of the breast than cervical cancer among women in those settings 20.

In our study, the concordance rates between clinical diagnosis and histological diagnosis were lower for carcinoma and benign lesions 46.5% and 80% respectively compared to reports from other studies which reported rates of nearly 80% for malignant lesions and more than 90% for benign lesions<sup>21-23</sup>. It is not clear why this finding is peculiar to our setting, certainly an area which needs to be examined and appropriate recommendations made to improve case management because diagnosis of breast cancer relies primarily on clinical judgement which is at best is non-conclusive. Plausible explanation for this could be the fear of "niddle and knife" and breast masses are complicated by traditional medications which farther complicate the diagnosis. Unnecessary excessive mastectomy could be done due to inaccurate diagnosis.

In conclusion, this study has found that breast masses presenting in younger women are mostly benign with up to one third of cases occurring below the age of 36 years while carcinomas occur in older age groups. Given the low concordance and low cost effectiveness of the radiological tests, the study recommends the conduct of the double test; clinical and histological assessment of all breast diseases in Eritrea.

## References

- Guray M, Sahin AA. Benign Breast Diseases: Classification, Diagnosis, and Management. *The Oncologist*. 2006; 11: 435- 49.
- Althuis MD, Dozier JM, Anderson WF, Devesa SS, Brinton LA. Global trends in breast cancer incidence and mortality 1973-1997. *Int J Epidemiol*. 2005; 34::405-12.
- Clemons M, Goss P. Estrogen and the Risk of Breast Cancer. *N Engl J Med* 2001; 344: 276-285.
- Kovacevic Z, Richardson DR. The metastasis suppressor, NdrG-1: a new ally in the fight against cancer. *Carcinogenesis*.2006; 27(12):2355-66.
- Hartmann LC, Sellers TA, Frost MH, et al. Benign breast disease and the risk of breast cancer. *N Engl J Med* 2005; 353: 229-237.
- Ahmed I, Nazir R, Chaudhary MY, Kundi S. Triple assessment of breast lump. *J Coll Physicians Surg Pak*. 2007; 17:535-8.
- Loughrey MB, Windrum P, Catherwood MA, Alexander HD, Markey GM, McManus DT, Morris TC. WHO reclassification of breast lymphomas. *J Clin Pathol*. 2004;57:1213-4.
- Michels JJ, Marnay J, Delozier T, Denoux Y, Chasle J. Proliferative activity in primary breast carcinomas is a salient prognostic factor. *Cancer*. 2004;100 :455-64.
- Yang JH, Lee WS, Kim SW, Woo SU, Kim JH, Nam SJ. Effect of core-needle biopsy vs fine-needle aspiration on pathologic measurement of tumor size in breast cancer. *Arch Surg*. 2005; 140: 1008-9.
- Anderson BO, Braun S, Lim S, Smith RA, Taplin S, Thomas DB; Global Summit Early Detection Panel. Early detection of breast cancer in countries with limited resources. *Breast J*. 2003;9 Suppl 2:S51-9.
- Braun S, Vogl FD, Naume B, Janni W, Osborne MP, et al. A pooled analysis of bone marrow micrometastasis in breast cancer. *N Engl J Med*. 2005 Aug 25;353:793-802.
- Groen RS, Oosterhuis AW, Boers JE. Pathologic examination of sentinel lymph nodes in breast cancer by a single haematoxylin-eosin slide versus serial sectioning and immunocytokeratin staining: clinical implications. *Breast Cancer Res Treat*. 2007;105:1-5.
- Neinstein LS<sup>13</sup>. Breast disease in adolescents and young women *Pediatr Clin North Am*. 1999;46: 607-29.
- Markopoulos C, Kouskos E, Mantas D, Kontzoglou K, Antonopoulou K, Revenas Z, Kyriakou V. Fibroadenomas of the breast: is there any association with breast cancer? *Eur J Gynaecol Oncol*. 2004; 25: 495-7.
- Chuma J, Gilson L, Molyneux C. Treatment-seeking behaviour, cost burdens and coping strategies among rural and urban households in Coastal Kenya: an equity analysis *Trop Med Int Health*. 2007; 12:673-86.
- Clemens MA, Pettersson G. New data on African health professionals abroad. *Hum Resour Health*. 2008 ;6(1):1 [Epub ahead of print]
- Adesunkanmi AR, Lawal OO, Adelusola KA, Durosimi MA. The severity, outcome and challenges of breast cancer in Nigeria. *Breast*. 2006;15:399-409.
- Guinebretièrè JM, Menet E, Tardivon A, Cherel P, Vanel D. Normal and pathological breast, the histological basis. *Eur J Radiol*. 2005;54: 6-14.
- Ekanem VJ, Aligbe JU. Histopathological types of breast cancer in Nigerian women: a 12-year review (1993-2004). *Afr J Reprod Health*. 2006; 10: 71-5.
- Collaborative Group on Hormonal Factors in Breast Cancer. Breast cancer and hormone replacement therapy: collaborative reanalysis of data from 51 epidemiological studies of 52 705 women with breast cancer and 108 411 women without breast cancer. *Lancet* 1997; 350:1047-59.
- Mansoor I, Zahrani I. Analysis of inconclusive breast FNA by triple test. *J Pak Med Assoc*. 2002;52: 25-9.
- De Gezelle H, Vanpeperstraete A, Defoort P, Serreyn R, Vandekerckhove D Comparison of breast tumours evaluated by ultrasound, mammography, and clinical investigation. 21. *Arch Gynecol*. 1981;230:219-23
- Herrada J, Iyer RB, Atkinson EN, Sneige N, Buzdar AU, Hortobagyi GN. Relative value of physical examination, mammography, and breast sonography in evaluating the size of the primary tumor and regional lymph node metastases in women receiving neoadjuvant chemotherapy for locally advanced breast carcinoma. *Clin Cancer Res*. 1997;3:1565-9
- Kolb TM, Lichy J, Newhouse JH. Comparison of the performance of screening mammography, physical examination, and breast US and evaluation of factors that influence them: an analysis of 27,825 patient evaluations. *Radiology* 2002; 225(1): 165-75.