Pattern of Breast Cancer Metastasis at the Radiotherapy Clinic, Ibadan - A Ten Year Review.

*T.N. Elumelu, *A.A. Adenipekun, *A.A. Abdus-salam, **A.D. Bojude

*Department of Radiotherapy, College of Medicine, University of Ibadan.
**Department of Radiotherapy, University College Hospital, Ibadan.
tessynek@yahoo.com

ABSRACT: Introduction: - Breast cancer is the commonest cancer among Nigerian women. In Nigeria and indeed Africa and most underdeveloped countries, majority of patients with breast cancer present to the Hospital late with advanced disease. At this stage, the cancer involves the axillary nodes, it may be attached to the underlying muscles and distant metastases are almost certainly present. The primary treatment intent therefore is palliative. **Objective:** The aim of this study is to determine the pattern of metastasis of breast cancer among patients treated at Radiotherapy Department, University College Hospital, Ibadan. **Methodology:** Five hundred and eighteen patients with histological diagnosis of breast cancer seen between 2000 and 2009 were studied. **Results:** There 5 were Males and 513 Females. The mean age was 48.15 years and 63.5% were between the ages of 30 and 50 years. Fifty eight percent of the women were premenopausal while 42% were postmenopausal. The percentage of patients that presented with stages 1, 11, 111 & 1V diseases were 6.2%, 24.7%, 38.8% and 30.3% respectively. The overall incidence of metastasis to distant organs were lung 25.7%, bone 24.1%, liver 7.7%, brain 5.8%, contra lateral breast 0.6% and kidney 0.2%. **Conclusion:** Based on the data obtained from this study, breast cancer mostly occurred among young women. Compared to earlier studies in Nigeria, breast cancer patients still present late with advanced stage disease with distant metastasis. Baseline bone scan, chest X-ray and abdominopelvic ultrasound scan are recommended for breast cancer patients before commencing treatment to enhance early detection of metastasis. Efforts should be increased towards early detection and treatment.

1. Introduction

Men and women have breasts; but they are better developed in women. The breasts are accessory to reproduction in women and rudimentary and functionless in men [1]. Breast cancer was regarded in early studies as the second commonest cancer among Nigerian women after carcinoma of the uterine cervix (1960-1980)[2]. However in 1992, Campbell et al, revealed that breast cancer was the commonest malignancy accounting for 23% of 5000 cancer cases reviewed at the radiotherapy centre, Ibadan and that a large proportion of these patients presented to the orthodox doctor with an advanced and metastatic diseases in stages 111 and 1V [3].

The incidence of breast cancer in Nigeria is on the increase from 13.8-15.3 per 100,000 in 1992 to 33.6 per 100,000 in 2000 in a report from Ibadan [4]. The peculiar characteristics of breast cancer among blacks are increasingly being appreciated by researchers worldwide. Blacks often have aggressive unpredictable disease, some patients come with relatively early stage disease and die of widespread metastasis within six months to one year, while others present with advanced disease and yet survive longer [5]. The current treatment of breast cancer includes surgery, chemotherapy, radiotherapy, hormonal therapy and targeted therapy using monoclonal antibodies like,

Bevacuzumab and Trastuzumab as well as palliative and supportive care in advanced cases. The aim of this study is to determine the pattern of metastasis in patients with breast cancer, A similar study was carried out by K K Ketiku in Lagos, between 1971 and 1981, 28 years ago, when breast cancer was the second commonest cancer after carcinoma of the cervix and at a time when diagnostic equipments like, whole body radioisotope scan, computer tomographic scan, magnetic resonance imaging were not available, as well as potent cytotoxic drugs like Epirubicin, Taxanes, Capecitabine, Gemcitabine and targeting agents like Herceptin and Avastin. A revisit is important so as to assess whether there is a change in the pattern of disease spread among these patients.

2. Material and Method

This is a retrospective study. All available radiotherapy case files with treatment and follow-up records of breast cancer cases attended to between 2000 and 2009 were retrieved and analysed. Data obtained included biodata, level of education, employment status, menopausal status, parity of the patient: (classified as nulliparous - no child birth, multiparity - 2-4 childbirth and grandmultiparity - >5 childbirth). The duration of the illness before presentation, and the distance the

patient had to travel from his/her home town to Ibadan in kilometres was also obtained. Pathological features like site of the disease (left, right or both breast), the stage at presentation using Manchester staging, the commonest staging system used by the surgeons referring patients for Radiotherapy, the lymph node status, the histological cell type, the histological grade of the disease, either well differentiated (grade 1) moderately differentiated (grade 2) or poorly differentiated (grade 3). The site(s) of metastasis at presentation were determined from records of clinical examination and radiological examination during pre-treatment evaluation. The treatment the patient received for example, conservative or radical surgery, the chemotherapy regime and number of cycles received, the site and the dose of radiotherapy treatment. Two year follow-up records for Manchester stage I to III cases were also extracted. The outcome of treatment was determined over two years of follow up in terms of absence or presence of locoregional recurrence and distant metastasis and the disease free interval in terms of locoregional recurrence free interval (LRFI) or distant metastasis free interval (DMFI) after oncology treatment as most patients are rarely seen beyond two years. The end point of observation or follow up was distant metastasis. Follow-up record of patients with Manchester stage 1V disease at presentation was not a concern to this study; instead the pattern of metastasis at this stage was documented. The above information was extracted from the records using a data extraction form. Only 518 cases met the inclusion criteria of case files with complete relevant information for the study. Case files with incomplete data were excluded.

The data obtained was analysed using the Statistical Package for Social Sciences version 15.0 (SPSS version 15.0). Data analysed was presented using percentages, tables and charts. **Ethical considerations:** Ethical clearance to conduct the study was sought from the Joint Ethical Review Committee of the University of Ibadan/University College Hospital, Ibadan.

3. RESULTS

Five hundred and eighteen (518) case files and treatment cards of breast cancer patients between 2000 and 2009 at the Radiotherapy clinic, University College Hospital, Ibadan were reviewed. Figure 1 shows the age distribution of the patients. Three hundred and twenty eight patients 328(63.5%) were between the age of 30 and 50 years, the age group with the highest frequency was 40-50 years (5th decade) and the mean age was 48.15 years.

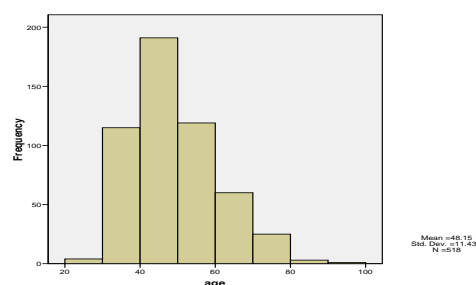**Figure 1 – Age distribution among the 518 breast cancer patients.**

Table 1 – Patients Characteristics.

Sex	
Male	5(1.0%)
Female	513(99.0%)
Menopausal status	
Premenopausal	303(58.5%)
Postmenopausal	210(40.5%)
Not documented	5(1.0%)
Parity	
Nulliparity	38(7.3%)
Multiparity	232(44.8%)
Grandmultiparity	243(46.9%)
Not documented	5(1.0%)
Education	
Primary	29(5.6%)
Secondary	110(21.2%)
Tertiary	103(19.9%)
None	81(15.6%)
Employment	
Employed	230(44.4%)
Not employed	288(55.6%)
Site of cancer	
Right	228(44.0%)
Left	253(48.8%)
Bilateral	37(7.2%)

Table 1 shows the patients characteristics the sex, menopausal status, parity and site of cancer of patients reviewed. There were 513 Females and 5 Men, 303 (58.5%) were premenopausal while 210 (40.5%) were postmenopausal. Thirty eight (7.3%) were nulliparous, 232 (44.8%) were multiparous and 243 (46.9%) were grandmultiparous. Twenty nine (5.6%) had primary school education, 110 (21.2%) had secondary school education, 103 (19.9%) had tertiary education where as 81 (15.6%) had no formal education. Corporate or self-employment was observed in 230 (44.4%) while 288 (55.6%) were not employed (House wives, Students, Retired, etc). Two hundred and twenty eight (44.0%) had disease on the right side, 253(48.8%) had disease on the left side while 37(7.2%) had bilateral breast disease.

Table 2 - Stage at presentation

Stage	Frequency	Percent	Valid Percent	Cumulative Percent
1	32	6.2	6.2	6.2

11	128	24.7	24.7	30.9
111	201	38.8	38.8	69.7
1V	157	30.3	30.3	100.0
Total	518	100.0	100.0	

Table 2 show the stage of the disease at presentation. The proportion of patients that presented with stages 1, 11, 111 and 1V diseases were 32(6.25%), 128(24.7%), 201(38.8%) and 157(30.3%) respectively. The minimum distance a patient has to travel to access radiotherapy facility was 0Km, the maximum distance was 1500Km and the average distance was 311Km. The minimum duration of illness before commencing treatment was one month, the maximum duration was 150 months where as the average duration of illness before commencing treatment was 11.4 months.

Table 3 – Histological subtypes

Histology	Developed Metastasis	Without Metastasis
Type Total No. (%)	No. (%)	No. (%)
Invasive ductal carcinoma 411(79.3%)	244(59.4%) 26(56.5%)	167(40.6%) 20(43.5%)
Invasive lobular carcinoma 46(8.9%)	13(86.7%) 10(100.0%)	13.3%) 0(0.0%)
Anaplastic carcinoma 15(2.9%)	9(100.0%)	0.0%) 2(40.0%)
Inflammatory breast carcinoma 10(1.9%)	3(60.0%)	4(80.0%) 2(50.0%)
Breast sarcoma 9(1.7%)	1(20.0%)	2(66.7%) 3(100.0%)
Malignant phylloides tumour 5(1.0%)	2(50.0%)	3(42.9%) 205
Mucinous carcinoma 5(1.0%)	1(33.3%)	
Medullary carcinoma 4(0.8%)	0(0.0%)	
Metaplastic carcinoma 3(0.6%)	4(57.1%) 313	
Colloid carcinoma 3(0.6%)		
Unspecified 7(1.4%)		
Total 518		

Figure 2 shows pie chart of grade of histology while Table 3 shows the distribution of histological subtypes. Invasive ductal carcinoma 411(79.3%) and invasive lobular carcinoma 46(8.9%) were the commonest subtypes diagnosed in the patients. All the patients with inflammatory carcinoma and sarcoma developed metastasis while 86.7% with anaplastic, 59.4% with invasive ductal and 56.5% with invasive lobular histological types developed metastasis.
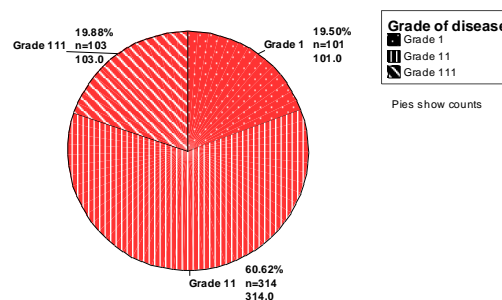

Figure 2 - **Grade of histology**

Table 4 – Grade of Histology

Grade	Total No. (%)	Developed Metastasis	Without Metastasis
Grade 1	101(19.5%)	35(34.7%)	66(65.3%)
Grade 11	314(60.6%)	193(61.5%)	
Grade 111	103(19.9%)	85(82.5%)	121(38.5%)
Total	518	313	18(17.5%) 205

Table 4 shows grade of histology, the proportion of patients with grades 1, 11 and 111 were 101(19.5%), 314(60.6%) and 103(19.9%) respectively. Table 4 also shows the distribution of metastasis by grade of differentiation. Thirty five patients with grade 1(34.7%) developed metastasis where as 193(61.5%) and 85(82.5%) of patients with grade 11 and 111 diseases developed metastasis respectively.

Table 5 – Frequency of metastasis to different sites at the time of presentation manchester stage 1V disease.

Site of metastasis	No. %
Lymphnodes	
Ipsilateralaxillary	89(17.2%)
Contralateralaxillary	40(7.7%)
Bilateralaxillary	10(1.9%)
Ipsilateralsupraclavicular	35(6.8%)
Contralateralsupraclavicular	15(9.6%)
Bilateralsupraclavicular	8(2.9%)
Lung	80(15.4%)
Bone	83(16.0%)
Liver	22(4.2%)
Brain	12(2.3%)
Kidney	1(0.2%)
Total	157(100%)

The frequency and pattern of metastasis in patients with stage 1V disease at the time of presentation are presented in Table 5. The number of patients presenting with stage 1V disease were 157. Multiple lymph node groups and multiple distant organ sites involvement were, however,

noted among the 157 patients studied above. Ipsilateral axillary lymph nodes was observed in 89(17.2%) patients, 40(7.7%) in contralateral axillary nodes, 10(1.9%) in bilateral axillary, 35(6.8%) in ipsilateral supraclavicular, 15(9.6%) in contralateral supraclavicular and 8(2.9%) in bilateral supraclavicular lymph node. Metastasis in lung was observed in 80(15.4%) patients, bone 83(16.0%), liver 22(4.2%), brain 12(2.3%) and kidney 1(0.2%).

Table 6 – Outcome of treatment in patients without distant metastasis at presentation (Manchester stage 1, 11 &111) post triple therapy * at 2 years from follow up Record.

Stage	Total	Disease Free	Locoregional Recurrence	Distant Metastasis
1	32(6.2%)	27(84.4%)	3(9.4%)	2(6.2%)
11	128(24.7%)	88(68.8%)	16(12.5%)	24(18.7%)
111	201(38.8%)	90.0(44.8%)	58.0(28.9%)	53(26.4%)

* Triple therapy = Surgery, Chemotherapy and Radiotherapy.

Table 6 shows the outcome of treatment in patients with stages 1, 11& 111 breast cancers from follow-up record after adjuvant chemoradiation therapy. Due to frequent default from follow up after treatment patients were observed for the development of locoregional recurrence and or distant metastasis within 2 years of follow up after treatment. Distant or locoregional metastasis was recorded in 156 out of 301 patients with stages 1, 11 &111 breast cancer. Over 95% of the patients completed radiotherapy dose of 40-50Gy to the breast or chest wall and 6 cycles of combination chemotherapy with either Adriamycin and Cyclophosphamide(AC), Cyclophosphamide, Adriamycin and 5 Flourouracil(CAF), Cyclophosphamide, Methotrexate and 5 Flourouracil(CMF), Epirubicin and Cyclophosphamide(EC), Cyclophosphamide, Epirubicin and 5Flourouracil(CEF), Adriamycin, Cyclophosphamide and Paclitaxel (AC+Paclitaxel), Paclitaxel and Epirubicin(ET), Docetaxel and Epirubicin(ET), Epirubicin and Cisplatin(EP), Docetaxel and Cisplatin(TP), Gemcitabine and Cisplatin(GP) etc. The 2 years disease free survival for stages 1, 11, & 111 were 84.4%, 68.8%, and 44.8% respectively.

Locoregional recurrence post chemoradiotherapy increased from 3(9.4%) in patients with stage 1 disease to 16(12.5%) in stage 11 and 58(28.9%) in patients with stage 111 breast cancer. Distant metastasis also increased from 2(6.2%) in patients with stage 1 to 24(18.7%) in

stage 11 and 53(26.4%) in stage 111 disease. The mean disease free interval post adjuvant chemoradiotherapy was 20.6 months, 11.6 months and 8.9 months for stages 1, 11 & 111 respectively, and 8.3% of locoregional recurrence or distant metastasis occurred within 6 months of follow up however, about two third 75.1% occurred between 6-12 months, while 9.4% and 7.2% occurred between 13-18 months and 10-24 months respectively.

Table 7 - Pattern and frequency of metastasis to different sites within two years of follow up for stages 1, 11 & 111 patients.

Site of Metastasis	Total No. (%)
Chest wall	58(15.0%)
Lymph nodes	
Contralateral axillary	23(4.4%)
Bilateral axillary	11(2.1%)
Ipsilateral supraclavicular	10(1.9%)
Contralateral supraclavicular	5(1.0%)
Bilateral supraclavicular	3(0.6%)
Contralateral breast	3(0.6%)
Lung	53(10.2%)
Bone	42(8.1%)
Liver	18(3.5%)
Brain	18(3.5%)

Table 8 – Pattern of metastasis between patients with (stages 1, 11 & 111) after triple therapycompared to patients with stage 1V disease (metastasis at presentation)

Site of Metastasis	Stage 1V	Stages 1, 11 & 111
Contralateral axillary	7.7%	4.4%
Bilateral axillary	1.9%	2.1%
Ipsilateral supraclavicular	6.8%	1.9%
Contralateralsupraclavicular	9.6%	1.0%
Bilateral supraclavicular	2.9%	0.6%
contralateral breast	___	0.6%
Lung	15.4%	10.2%
Bone	16.0%	8.1%
Liver	4.2%	3.5%
Brain	2.3%	3.5%
Kidney	0.2%	____

Overall, there was reduction (shown in table 8 above) in the pattern of metastasis when the proportions of metastasis in patients with stage 1V disease at presentation are compared with that of patients with (stages 1, 11 &111) treated with adjuvant chemoradiation post-surgery and who were distant metastasis free at presentation. There was, however, increase in proportion of metastasis in few sites notably in bilateral axillary and brain. Therefore, the pattern put together for stages (1, 11, 111 and 1V) were 12.1% to contralateral axillary

nodes, 4.0% to bilateral axillary nodes, 8.7% to ipsilateral supraclavicular nodes, 10.6% to contralateral supraclavicular nodes, and 3.5% to bilateral supraclavicular nodes while to the lung 25.7%, bone 24.1%, liver 7.7%, brain 5.8%, contralateral breast 0.6% and kidney 0.2%.

4. DISCUSSION

The results of this retrospective study between the year 2000 and 2009, shows that the mean age of the patients was 48.15 years and 63.5% of these patients are between the age of 30 and 50 years. This means that most of the patients are young, premenopausal and perimenopausal. Breast cancer at this age range is noted to be more aggressive, associated with higher mortality, shorter disease free survival and more likely to recur after treatment locoregionally or at distant sites than in older women [6]. Ohaeri et al [7] reported a mean age of 48 years in a series of breast cancer patients that is similar with that of our patients. Breast cancer is a disease of older women in developed countries which is contrary to the finding in developing countries[8]. The proportion of our patients that was premenopausal was 58.5%, while 40.5% were postmenopausal, this is in sharp contrast with the developed countries where premenopausal patients accounted for less than one-third of the patients. Adebamowo et al reported a much higher incidence of 80% of premenopausal women in Nigeria breast cancer patients[9]. The percentage of patients that was nulliparous was 7.3%, 40.5% were multiparous while 46.9% were grandmultiparous. These would have been the reverse since the higher the number of full term pregnancies, the greater the protection from breast cancer and that there is a reduction in risk of breast cancer by 7% for each birth after the first, in the absence of breast feeding, also women who breast feed reduces their risk compared to those who do not [10]. Nulliparity is also associated with 30% increase risk compared with parous women. Majority of our patients (68.8%) presented at an advanced stage. There was, however no change in the stage at presentation compared to earlier studies in this environment. The factors responsible for late presentation with advanced disease include low socioeconomic level as most of the patients in this study 55.5% were not employed (corporate or self employment). Fear of mastectomy is another major problem deterring early presentation of women with breast cancer [11]. Tumour biology of breast cancer seen in Nigeria and African Americans which tend to be more aggressive than in cases of breast cancer seen in Caucasians are of paramount importance [12]. This study also showed that the patients have to travel an average distance of 311 Km, range (0-1500Km) in order to have access to radiotherapy facility. This means that patients come from all over Nigeria, with a population of over 140 million.

World Health Organization (WHO) recommendation of radiotherapy facility to a population was 1: 250,000 persons [13]. These mean that there would be long waiting time and poor treatment outcome. The average duration of breast cancer symptoms before presenting for surgery and adjuvant treatment in our study was 11.4 months, all these may also lead to late presentation. Okobia et al reported a similar duration of illness before commencing treatment [14]. The histological subtype and grade of differentiation of breast cancer have a considerable influence on the development of metastasis and survival [15]. In this study invasive ductal and invasive lobular carcinoma were the commonest histology and accounts for more than half of the patients with metastatic disease. However, more than eighty five percent of patients with anaplastic carcinoma, inflammatory breast cancer and breast sarcoma presented with advanced disease with early metastasis [16].

The presence of high proportion of locoregional disease in these patients is an indication that they have advance stage disease [17]. Distant metastases in this study were most commonly to bone, lung, liver and brain. They were detected using chest X-ray, abdominopelvic ultrasound scan, skeletal X-ray, technetium T^{99} bone scan, computer tomographic scan (CT scan) and magnetic resonance imaging (MRI). Lung metastasis was the commonest visceral metastasis in this study accounting for 25.7% of cases. Adesunkanmi et al, from Ile Ife, reported a slightly lower incidence of 20.3% [18]. The disparity could be due to the fact that they receive referral from a small locality and the smaller sample size (212 patients). Glynne-Jones R et al [19], reported a lower incidence of 9.1% among Caucasians with breast cancer, the lower figures in Caucasians could be due to early presentation and less aggressiveness of their disease. Bone metastasis in this study, was 24.1%, K K Ketiku, from Lagos, reported an incidence of 19.6% [20]. Cox et al, reported an incidence of 18.1% among Caucasians[21]. These lower rates could be explained by the recent availability of bone scan diagnosis in our centre compared with the result from Lagos since patients in both studies present late. The rates were slightly higher among Caucasians, though lower than our results because bony metastasis is the commonest site of distant metastasis of breast cancer in the Caucasians [22]. Bone scan detects subclinical as well as symptomatic bony metastases. In this centre the frequently used modalities for detection of bone metastasis are skeletal X-ray and bone scan. Radiotherapy could be given to patients with bony metastasis to relieve pain, avert imminent fracture and to control tumour growth [23].

Liver metastasis accounted for 7.7% of distant metastasis in this study, a near similar incidence of 6.0% was reported by Panatanaphan et al [24], from

Baltimore, a lower incidence of 3.3% was reported by Shariari et al from Tehran [25], the lower value could be due to the fact that most of their patients presented with stage 11 and grade 11 disease compared to most of our patients who had stages 111 and 1V disease. The variations with these two groups of patients with our study could be due to racial difference in the tumour biology.

Brain metastasis accounted for 5.8% in this study, a similar value of 6.3% was reported by JNA Clegg-Lamptey et al, from Ghana [26]. Diagnosis of brain metastasis requires brain CT scan, MRI or PET scan, most of our patients by the time they develop brain metastasis might not afford CT scan or MRI and the fact that it occurs in a terminally ill patients who basically need palliative care, therefore, cost and benefit must be weighed.

From the result of this study, breast cancer mostly occurred among young women between the ages of 30 and 50 years. Most 58.5% are premenopausal and 69.1% presented with advanced stage disease. Compared with earlier studies in Nigeria, breast cancer patients still present late with advanced stage disease with distant metastasis. Overall, the commonest site of distant metastasis was to the lung followed by bone, liver, brain, contralateral breast and kidney. Therefore, baseline bone scan, chest X-ray and abdominopelvic ultrasound scan are recommended for breast cancer patients before commencing treatment to enhance early detection of metastasis. More efforts should be put into public awareness on breast cancer, health education and improving socioeconomic status of the patients at risk and the provision of more facilities for early detection and treatment.

Corresponding Author:
Dr Elumelu T.N
Department of Radiotherapy,
University College Hospital, Ibadan.
PMB 5116 Ibadan
Oyo State.
Nigeria.
Tel +234838090118
Fax +234-2-2413545
E-mail: tessynek@yahoo.com

References
1. Moore KL and Dally AF, Anatomy of the breast. Clinically oriented anatomy. Lippincott Williams & Wilkins, 5th Edition. 2006; p105
2. Abioye AA. The Ibadan cancer registry 1960-1980. In ''Cancer in Africa'' Proceedings of a workshop of the West African College of Physicians, held in Monrovia, Liberia 1981.Ed DA Olatunbosun. PP 1-3 Caxton press (West Africa) Ibadan.
3. Ntekim A, Abdullahi Adamu, Momoh I, Adenipekun A, Elumelu TN. and Campbell O B. Docetaxel chemotherapy in the management of advanced and metastatic breast cancer in Nigerians. A pilot study. West African Journal of Radiology. April 2001 Vol 8No.1 P25-28.
4. Adebamowo CA and Ajayi OO . Breast cancer in Nigeria. West Afr J Med. 2000; 19:179–191
5. Tavassoli FA. Epidemiology of Breast Cancer. In Pathology of The Breast, Fataneh A. Tavassoli, 2nd Edition. McGraw Hill Publishers. New York ,1999. p28.
6. Ntekim A, Nufu F T and Campbell O B. Breast cancer in young women in Ibadan, Nigeria. African Health sciences 2009; 9(4): 242-246.
7. Ohaeri J.U, Campbell O.B, IlesanmiA and Ohaeri B.M. The opinion of care givers of some women with breast and cervical cancer on aspects of the disease. West African Journal of Medicine 1999; 18:1.
8. Adelusola K, Fadiran OA, Adesunkanmi ARK, Odesanmi WO. Breast cancer in Nigerian women. Niger Med Pract 1996; 31: 17–29.
9. Adebamowo CA, Adekunle OO. Case control study of the epidemiological risk factors of breast cancer in Nigeria. Br J Surg 1999; 86:665–8.
10. Adebamowo CA, Ajayi OO. Breast cancer in Nigeria. West Afr J Med 2000; 19(3): 179–91.
11. Ajekigbe AT Fear of mastectom: the most common factor responsible for late presentation of carcinoma of the breast in Nigerei. Clin Oncol (R coll Radiol) 1991; 3;78-80
12. Ikpatt OF, Kuopio T, Collan Y. Proliferation in African breast cancer: biology and prognostication in Nigerian breast cancer material. Mod Pathol 2002;15(8):783–9.
13. da Lilly-Tariah OB, Somefun AO, Adeyemo WL. Current evidence on the burden of head and neck cancer in Nigeria. *Head and Neck Oncol*. 2009;1:14.
14. Anyanwu SN. Breast cancer in eastern Nigeria: a ten year review. West Afr J Med 2000;19:120–5.
15. RodrigoArriagada, Lars-Erik Rutqvist, Hemming Johansson, Andrew Kramer and Sam Rotstien. Predicting distant dissemination in patients with early breast

cancer. Acta Oncologica, 2008; 47:1113-1121.

16. Ikpatt OF, Kuopio T, Ndoma-Egba R, Collan Y. Breast cancer in Nigeria and Finland: epidemiological, clinical and histological comparison. Anticancer Res 2002;22:3005–12.

17. Ikpatt OFR, Ndoma –Egba R and Collan Y. Influence of Age and prognosis of Breast cancer cancer in Nigeria. East African Journal of Medicine. 2002;Vol 79: No12.

18. A.R.K. Adesunkanmia, O.O. Lawala, K.A. Adelusolab and M.A. Durosimi. The severity, outcome and challenges of breast cancer in Nigeria. The Breast (2006) 15, 399–409.

19. Glynne-Jones R, Young T, Ahmed A, Ell PJ, Berry RJ. (1991). How far investigations for occult metastasis in breast cancer aid the clinitian. Clin Oncol 3:65-72.

20. Ketiku K K The pattern of metastasis in Nigeria breast cancer patients. Clinical oncology.1986;37:563-565.

21. Cox MR, Gilliland R, Odlingsmee GW and Spence RA. An evaluation of radionuclide bone scanning and liver Ultrasonography for staging breast cancer.1992.Aust. N Z J 62:550-555.

22. Christoph Schneider , Mathias K. Fehr, Rolf A. Steiner, Daniela Hagen, Urs Haller and Daniel Fink. Frequency and distribution pattern of distant metastases in breast cancer patients at the time of primary presentation Arch Gynecol Obstet (2003) 269:9–12 DOI 10.1007/s00404-002-0445-x

23. Nuran Senel Bese, Krystyna Kiel, Brahim El-Khalil El-Gueddari, Oladapo Babatunde Campbell, Baffour Awuah, and Bhadrasain Vikram. Radiotherapy for Breast Cancer in Countries with Limited Resources: Program Implementation and Evidence-Based Recommendations. *The Breast Journal, Volume 12 Suppl. 1, 2006. S96–S102*

24. Patanaphan Inita, Omar M. Salazar and Rapael Risco. Breast Cancer: Metastatic Patterns and Their Prognosis. Southern Medical journal. Vol 81. No. 9, September 1988. P1109-1112.

25. Shahriari Ahmadi A, Ghavamzadeh A, Amiri A, Farnia V,Samadzadeh S and Malekniazi A. Clinical, Biological and Pathological characteristics of Breast cancer. Patients at the Taleghani University Hospital in Kermanshah, Iran. IJHOBMT Vol.2, No.6;2005/7.

26. JNA Clegg-Lamptey and W M Hodasi. A study of breast cancer in Korle Bu Teaching Hospital: Assessing the impact of health education. Ghana medical Journal; June 2007. Vol. 41;No. 2

7/10/2011