Journal of Medical Sciences

ISSN 1682-4474

science alert

ANSInet
an open access publisher
http://ansinet.com

Research Paper

J. Med. Sci., 8 (4): 420-424
15th June, 2008

A Cross Sectional View of Estrogen Receptors in 32 Human Breast Cancer Tissues in Ghana

M.T. Agyei-Frempong, F.N. Ghartey,
S. Asante-Poku and B. Wiafe-Addai

The aim of this research was to determine the prevalence and proportion of estrogen-dependent, breast cancers in Ghana. Thirty two breast cancer tissues were obtained at random from patients seen at Komfo Anokye and Korle Bu Teaching Hospitals. Estrogen receptors were identified and quantitated using the cytosol-based dextran-coated charcoal assay. This was followed-up with a nationwide awareness and screening exercise from 1999 to 2002 to help improve awareness, encourage earlier detection and determine the prevalence of breast cancer in Ghana. Six out of 32 (18.75%, $p>0.05$) breast tumors were estrogen-dependent with receptor contents ranging from 12.75 to 101.31 (mean: 50.59±28.83) f mol mg^{-1} of cytosol protein. The mean tumor size was 12.58× 2.59 cm. Prevalence rate for breast cancer in Ghana ranged from 0.41-1.11% with a mean of 0.76±0.35% (at 95% confidence interval) among females aged 18 to 80 years. The mean age at diagnosis for breast cancer was 46.29 (±11.50) years/woman (confidence interval of ±22.54 years). Ghanaian women develop breast cancer some 10 to 15 years earlier than Caucasians and are less likely to respond to anti-estrogen therapy due to low proportion of estrogen receptor positive breast cancers.

Key words: Breast neoplasm, anti-estrogen therapy, prevalence, breast screening, menopause

JMS (ISSN 1682-4474) is an International, peer-reviewed scientific journal that publishes original article in experimental & clinical medicine and related disciplines such as molecular biology, biochemistry, genetics, biophysics, bio-and medical technology. JMS is issued eight times per year on paper and in electronic format.

For further information about this article or if you need reprints, please contact:

Margaret T. Agyei-Frempong,
Department of Molecular Medicine,
School of Medical Sciences (SMS),
College of Health Sciences (CHS),
Kwame Nkrumah University of Science and Technology (KNUST), Kumasi, Ghana

Tel: + 233 20 818 6136
Fax: +233 51 60 137

ANSInet
Asian Network for Scientific Information

Department of Molecular Medicine, School of Medical Sciences (SMS),
College of Health Sciences (CHS),
Kwame Nkrumah University of Science and Technology (KNUST), Kumasi, Ghana

INTRODUCTION

Breast cancer is the most common malignant neoplasm in women (Maaroufi *et al*., 2000). Breast cancer risk is related to the length of exposure of a woman to endogenous estrogens. Delayed onset of menses, early pregnancy and early menopause/oophorectomy lowers the incidence of breast cancer (Clavel-Chapelon and E3N-EPIC Group, 2002). Since breasts are estrogen dependent organs, they undergo changes throughout a woman's life. These changes are generally classified as physiological, aberrations of normal development and involution (ANDI) or malignant.

For reasons that are not fully understood the mammary epithelial cells behave in an aberrant manner. The cells of the breasts become disturbed and local control mechanisms fail to operate. This results in an increase in breast cell types, followed by derangement of both structure and function (Mommer *et al*., 1999).

Breast cancer types, which retain their estrogen dependency, are better managed by manipulations of endogenous estrogen levels. This can be achieved by using less toxic and less expensive hormonal therapy. However, in Ghana where breast cancer is the second most common malignant neoplasm in women, oncologists report a low response to anti-estrogen therapy. This is probably because the estrogen receptor status in breast cancers in Ghanaians has not been elucidated. Despite this, almost all cancer patients have to go through hormonal therapy which is a waste of patient's time and resources and also puts the patient at risk to some extent.

The objective of this study was to determine the proportion of estrogen dependent breast cancers and the prevalence of breast neoplasms, in Ghana.

MATERIALS AND METHODS

Estrogen receptor study

The study population: Specimens for estrogen receptor analysis were obtained at random from 32 breast cancer patients seen at Komfo Anokye and Korle Bu Teaching Hospitals (KATH and KTH) from January to October 1999. Patients' examination, specimen collection and subsequent submission of specimen for analysis were carried out by competent surgeons and analysis performed by research scientists at KATH and KTH with patients' consent in accordance with the Helsinki Declaration. Physical examination, with careful description of tumor size, weight, location, fixation, nodal status and contours were performed on each breast cancer patient by surgeons at KATH and KTH. In some cases mammograms were used to assess the extent and size of multiple tumors and invasions of skin and chest wall. Excision biopsy (with or without mastectomy) and axillary nodal removal was advised for all but the most advanced (T4 or N3) lesions.

Estrogen receptor assay: The cytosol-based dextran-coated charcoal assay (McGuire *et al*., 1978) was used to identify and quantitate the estrogen receptor in breast cancer. Cytosolic preparations from breast cancer tissue (histologically confirmed) were incubated with various concentrations of ^{3}H-estrogens (0.5-20.0 nM) at 4°C for 16 h. The free ligand was removed with dextran-coated charcoal suspension and ligand-receptor complex quantitated using Scatchard analysis.

Follow-up breast cancer awareness and screening programme: Women aged 18 to 80 years nationwide were included in this exercise. The screening and awareness team was made up of nurses, a biomedical scientist and administrator, under the supervision of a breast pathologist/general surgeon. The team visited women's groups at their churches, mosques, work places and market and screened them manually after creating awareness.

A total of 15,221 women nationwide were involved from 1999 to 2002.

Statistical analysis: Estrogen receptor values, the mean age at diagnosis, prevalence and confidence intervals were computed with Microsoft excel computer software.

RESULTS AND DISCUSSION

The quantitative determination of estrogen-receptors in breast cancer tissue samples is used to predict their response to anti-estrogen therapy (Maaroufi *et al*., 2000). Patients with ER-negative tumors have a higher recurrence rate within the first 20 months following mastectomy (Crowe *et al*., 1991). These patients have low response rates to hormonal manipulations when they develop metastatic cancer (less than 10%). Such patients are better managed with cytotoxic chemotherapy, possibly including adjuvant chemotherapy, even in the absence of tumor in the axillary lymph nodes (Fitzgibbons *et al*., 2000). Therefore, receptor data are helpful in deciding whether to employ hormonal therapy for metastatic disease and delaying the generally more toxic chemotherapeutic approach. Estrogen binding studies performed on 32 human breast cancers (one male and 31 female patients) identified six (18.75%) estrogen-dependent tumors which is not significant [$\chi^2 = 0.07018$, $p>0.05$] (Table 1). This is in conformity with the results obtained by Olopade (2005) and Ikpatt and Ndoma-Egba (2003), who reported that only 23 and 24%, respectively of

Table 1: Menopausal status versus estrogen receptor status of 31 female breast cancer patients

Menopausal status	Estrogen receptor positive (%)	Estrogen receptor negative (%)	Total (%)	p-value
Pre/peri	3 (50)	14 (56.00)	17 (54.84)	p>0.05
Post	3 (50)	11 (44.00)	14 (45.16)	
Total	6 (100)	25 (100.00)	31 (100.00)	

At 95% confidence level ($\chi^2 = 0.07018$, p>0.05)

Table 2: Mean estrogen-receptor contents (results of scatchard analysis) related to menopausal status of patients

Menopausal status	Mean±ER (fmol mg^{-1})
Pre/peri	72.12±26.94
Post	29.06±19.41
Total (pre/peri/post)	50.59±28.83

Range (ER) (fmoles mg^{-1} protein) = 12.75 (in a postmenopausal woman) to 101.31 (in a pre-menopausal woman), (ER) = Estrogen receptor concentration

African breast cancer tumors are estrogen-dependent as compared to 80% in Caucasians. The only male breast cancer specimen was estrogen receptor (ER) negative.

Breast cancer tumor weight and size are good proxy measures of late diagnosis and treatment. After analyzing cross-sectional data on breast cancer tumor weight and size, it became obvious that the majority of breast cancer patients in Ghana had bulky breast cancer tumors at presentation for treatment. The mean weight of these mastectomy/lumpectomy/biopsy specimens was 916.91 g. The smallest lumpectomy specimen weighed 18.00 g and the largest weighed 1780.00 g. More than three-quarters of the breast masses analyzed for estrogen-receptors had dimensions of 12.5×2.5 cm or more. The mean specimen size was 12.58×10.59 cm. The smallest specimen size was 2.0×1.3 cm and the largest was 23×16 cm. One study has reported a mean primary tumor diameter of 10 cm in 129 Nigerian women (Hassan *et al*., 1992). This feature may point to late presentation of breast cancer for treatment leading to low survival in Ghana. In fact, a number of retrospective studies have reported that African women present with stage 3 or 4 disease (Hassan *et al*., 1992; Amir *et al*., 1984, 1997; Muguti, 1993).

The estrogen-dependent (estrogen receptor positive) tumors had receptor contents ranging from 12.75 (in a post-menopausal woman) to 101.31 (in a pre-menopausal woman) femtomoles mg^{-1} (fmoles mg^{-1}) of cytosol protein (Table 2). The cut-off point for ER positive status was 10.0 f moles mg^{-1} protein. The lower limit for estrogen-dependency in most specialized laboratories worldwide corresponds to [ER] of 10.00 femtomoles mg^{-1} of cytosol protein. Prior to this study, which established [ER] in Ghana for the first time, many surgeons/oncologists in Ghana reported a low response rate to anti-estrogen therapy among their patients (unpublished data).

The mean age at diagnosis for breast cancer in this study was 46.29±11.50 years/woman; with a confidence interval of ±22.54 years. This is in concordance with the results in other African countries and confirms that African women may develop breast cancer at an earlier age (approximately 10-15 years earlier) as compared to Caucasians whose mean age at diagnoses is 60 years (Olopade, 2005; Adebamowo *et al*., 2003; Yawitch *et al*., 2000; Ihekwaba, 1992; Ikpatt *et al*., 2002). Out of the 31 breast cancer women, 54.84% were of pre/peri-menopausal status whiles 45.16% were of post-menopausal status (Table 1). This confirms the report of Chiedozi (1995), who has indicated that breast cancer in Nigeria is a disease of pre-menopausal and peri-menopausal females. Thus, breast cancer among Ghanaian women and for that matter black women may not necessarily be more common in post-menopausal women in contrast to that in the Caucasian women. The modal (peak) age at diagnosis for the pre/peri-menopausal women was 39 years while that for the post-menopausal women was 54 years.

Estrogen receptor positive versus menopausal status: Menopausal and estrogen receptor status were analyzed in all the 31 women studied. Three (50%) of the six estrogen receptor positive (ER+) breast cancers were observed, in post-menopausal women and three (50%) in pre/peri-menopausal women. (Table 1). The mean estrogen receptor concentration for the post-menopausal women was 29.06±19.41 fmoles mg^{-1} protein as compared to 72.12±26.94 fmoles mg^{-1} protein in pre/peri-menopausal women as a group (Table 2).

Estrogen receptor negative versus menopausal status: Fourteen (56.00%) out of twenty-five estrogen receptor negative (ER-) breast cancers were observed in pre/peri-menopausal women, whiles, eleven estrogen receptor negative (ER-) breast cancers (44%) were seen in post-menopausal women (Table 1).

Nationwide breast cancer awareness and screening programme: The earlier observations were confirmed in a larger follow-up awareness and screening programme involving 15,221 women from the period 1999 to 2002 (Table 3). The programme is still ongoing and has captured over 44,777 women nationwide till date.

In this study, the mean age at first menses (menarche) determined for 500 Ghanaian women selected at random from the total (15,221) countrywide was 14.91 years. By the age of 16 years, 88.91% of them had had their first menses.

Table 3: Data from follow-up breast cancer awareness and screening programme for the period 1999-2002

	Year						
Breast condition	1999	2000	2001	2002	Total No. of cases	SD	Mean
Breast cancer[a]	23	36	21	22	102		
Yearly prevalence[a] (%)	1.22	0.57	0.67	0.57		0.31	0.76
Benign breast mass[b]	147	199	48	104	498		
Yearly prevalence[b] (%)	7.81	3.16	1.52	2.68		2.77	3.79
ANDI/NAD	1,712	6,072	3,084	3,753	14,621		
Total	1,882	6,307	3,153	3879	15,221		

[a]95% confidence interval = 0.76 + 0.35, median = 0.62, [b]95% confidence interval = 3.79 + 3.10, median = 2.92, NAD = No abnormality detected

Polish girls, who started menstruating before the age 16 years had a risk for breast cancer, which was twice that for those whose menarche was later than 16 years (Osborne, 1998). This indicates that as far as menarche is concerned about 11% of the Ghanaian female population may have about twice as much risk for developing breast cancer than the others.

The mean age at menopause was estimated from the data in this study to be 47.77 years for Ghanaian women. More than 90% of them had menopause between the ages 40.75 and 54.79 years.

Approximately 44.29% of them had menopause between 40.75 years and 47.77 years. A few had menopause beyond 55 years (2.86%). Some researchers have reported doubling of the risk for women who continued menstruating beyond the age of 55 years compared with those whose natural menopause was before the age of 45 years (Osberne, 1998).

Prevalence rate for breast cancer ranged from 0.41-1.11% with a mean of 0.76±0.35% (95% confidence interval) among females aged 18 to 80 years in Ghana. The prevalence of benign breast lumps ranged from 0.69-6.89% with a mean of 3.79±3.10% (95% confidence interval) (Table 3).

For the first time, the prevalence of breast cancer and benign breast conditions have been established in Ghana, through data captured nationwide as presented in this study (Table 3). The low prevalence rate and the early age of onset of breast cancers in Ghanaian women as observed in this study have been confirmed by Olopade (2005), who has reported that breast cancer strikes fewer women in Africa, but, it hits earlier and harder.

Availability of such statistical estimates of prevalence rates is crucial and timely for fund managers and policy makers of our infant National Health Insurance scheme (NHIS), which covers treatment for benign and malignant breast conditions.

CONCLUSIONS

Ghanaian women diagnosed with breast cancer have been known to have a low response rate to anti-estrogen therapy. The reason for this has clearly been shown in this study; a low proportion of estrogen receptor positive breast cancers in Ghana (18.75%, $p>0.05$) and for that matter black African women has been demonstrated.

The low estrogen receptor status in Ghanaians could be attributed to the fact that they are late cancers that have lost their estrogen dependency through malignant transformation, since most cancer patients report late at the hospital.

Breast cancer among Ghanaian women may not necessarily be a disease that is more common in post-menopausal women. In this study the mean age at diagnosis for breast cancer (46.29±11.498) indicates that Ghanaian women develop breast cancer 10-15 years earlier than Caucasians (60 years).

Currently, public concern about breast cancer and its destructive consequences on women in their reproductive ages is rising in Ghana, but the awareness level is still low and as a result most victims or families of victims still suffer heavy losses due to low survival rates prevalent in Ghana, cumulating from late detection. It is therefore suggested that awareness programmes are stepped-up and the survival rate for breast cancer during the first five years after treatment is estimated.

ACKNOWLEDGMENTS

We wish to thank surgeons at KATH and KTH for providing fresh breast cancer tissue samples for the estrogen receptor study. We are grateful to the various Ladies associations of Social Security Bank, Ghana Commercial Bank, Tema oil Refinery and Unilever-Ghana for their financial support. We thank the Director of Noguchi Memorial Institute for Medical Research-Ghana for giving us access to their well equipped laboratories. We thank the Latter Day Saints Charities for financing the follow up awareness and screening and database program, which has covered over 44,777 women till date. We also wish to thank Mr. Samuel K. Yeboah of KNUST who helped to type this manuscript.

REFERENCES

Adebamowo, C.A., T.O. Ogundiran, A.A. Adenipekun, R.A. Oyesegun, O.B. Campbell and E.U. Akang *et al.*, 2003. Obesity and height in urban Nigerian women with breast cancer. Ann. Epidemiol., 13: 455-461.

Amir, H., J.N. Kitinya and D.M. Parkin, 1984. A comparative study of the carcinoma of the breast in an African population. East Afr. Med. J., 71: 215-218.

Amir, H., M.R. Azizi, C.K. Makwaya and S. Jessani, 1997. TNM classification and breast cancer in an African population: A descriptive study. Cent. Afr. J. Med., 43: 357-359.

Chiedozi, C., 1995. Morbidity, mortality and survival in the management of cT4 breast cancer in Nigeria. Ann. Saudi Med., 15: 227-230.

Clavel-Chapelon, F. and E3N-EPIC Group, 2002. Differential effects of reproductive factors on the risk of pre-and postmenopausal breast cancer. Results from a large cohort of French women. Br. J. Cancer, 86: 723-727.

Crowe, J.P.Jr., N.H. Gordon, C.A. Hubay, R.R. Shenk and R.M. Zollinger *et al*., 1991. Estrogen receptor determination and long term survival of patients with carcinoma of the breast. Surg. Gynecol. Obstet., 173: 273-278.

Fitzgibbons, P.L., D.L. Page, D. Weaver, A.D. Thor and D.C. Allred *et al*., 2000. Prognostic factors in breast cancer. College of American Pathologists Consensus Statement 1999. Arch. Pathol. Lab. Med., 124: 966-978.

Hassan, I., E.E. Onukak and O.A. Mabogunje, 1992. Breast cancer in Zaria, Nigeria. J. R. Coll. Surg. Edinb., 37: 159-161.

Ihekwaba, F.N., 1992. Breast cancer in Nigerian women. Br. J. Surg., 79: 771-775.

Ikpatt, O.F., T. Kuopio and Y. Collan, 2002. Proliferation in African breast cancer: Biology and prognostication in Nigerian breast cancer material. Mod. Pathol., 15: 783-789.

Ikpatt, O.F. and R. Ndoma-Egba, 2003. Estrogen and progesterone receptors in Nigerian breast cancer: Relationship to tumor histopathology and survival of patients. Central Afr. J. Med., 49: 122-126.

Maaroufi, Y., M. Lacroix, L. Lespagnard, F. Journé and D. Larsimont *et al*., 2000. Estrogen receptor of primary breast cancers: Evidence for intracellular proteolysis. Breast Cancer Res., 2: 444-454.

McGuire, W.L., K.B. Horwitz D.T. Zava, R.E. Garola and G.C. Chamness *et al*., 1978. Hormones in breast cancer: Update 1978. Metabology, 27: 487-501.

Mommer, E.C.M., P.S. Van Diest, A.M. Leonhart, C.J.L. MeiJer and J.P.A.M. Baak, 1999. Balance of cell proliferation and apoptosis in breast carcinogenesis. Breast Cancer Res. Treat, 58: 163-169.

Muguti, G.I., 1993. Experience with breast cancer in Zimbabwe. J. R. Coll. Surg. Edingb., 38: 75-78.

Olopade, F., 2005. Study reveals dramatic difference between breast cancers in US and Africa. 2005. University of Chicago Medical Center. http://www.bio-medicine.org/biology-news/Study-reveals-dramatic-difference-between-breast-cancers-in-US-and-Africa-583-1.

Osborne, C.K., 1998. Steroid hormone 11 receptors in management of breast cancer. Breast Cancer Res. Treatment, 51: 227-238.

Yawitch, T.M., E.I. Van Rensburg, M. Mertz and C.I. Falkson, 2000. Absence of commonly recurring BRCA 1 mutations in black South African women with breast cancers. S. Afr. Med. J., 90: 788-788.