East African Scholars Multidisciplinary Bulletin
Abbreviated Key Title: East African Scholars Multidiscip Bull
ISSN 2617-4413 (Print) | ISSN 2617-717X (Online)
Published By East African Scholars Publisher, Kenya

Volume-4 | Issue-9 | Oct-2021 | DOI: 10.36349/easjmb.2021.v04i09.002

OPEN ACCESS

Original Research Article

Pattern of Overexpression of HER-2 Biomarker in Breast Cancers in South East Nigeria

Arinzechukwu MBBS, MWACP, FMCPath professor of pathology[1*], Uzoigwe Joseph MBBS, FMCPATH[1], Babatunde Omotowo MBBS, FMCP[2], Nwokoro Onyekachi MBBS, FMCPATH[1], Nnamani SUNDAY MBBS[1], Sule Emmanuel[4], Enemuo Vincent C MBBS, FWCS[3], Nzegwu Victor. Ifeanyichukwu MBBS in view[5], Nzegwu christie Okhen. BSc OD[6], Nwoye Ogochukwu MBBS, MWACP.[1], Aniume Onyekachi MBBS, MWACP[1], Edeh Anthony MBBS. FRCS[7], Ozumba Benjamin MBBS FRCOG, FACObs and Gyn[8], Oruamade ISIOMA MBBS[1], Okwulehi Vincent. MBBS, FWCS[1], Nwidenyi Isaiah MBBS[1]

[1]Department of Morbid Anatomy, University of Nigeria
[2]Department of Community Medicine, University of Nigeria
[3]Department of Surgery University of Nigeria
[4]Department of Surgery, Ambrose Alli University Ekpoma, Edo State 5University of Otago Dunedin New Zealand
[6]Grace PATHOLOGY Consults Enugu
[7]Department of Surgery Enugu State University of Science and Technology 8Department of Obstetrics and Gynecology, University of Nigeria

Article History
Received: 07.08.2021
Accepted: 11.09.2021
Published: 30.10.2021

Journal homepage:
https://www.easpublisher.com

Quick Response Code

Abstract: ***Purpose:*** To determine the prevalence of Her-2 overexpression in breast cancer and its features. Second highlight what is new and applicable in our setting. ***Material and methods:*** Data of all immunohistochemically typed blocks for breast cancer was pulled and only those negative for Estrogen receptor (ER), progesterone receptor (PgR) and Her 2 neu receptor (HER-2) amplification positive were used. ***Results:*** A total of 417 patients with Invasive Ductal Carcinoma of the breast participated, because we have an unscreened population with poor mammography screening penetrance, most cases came in as invasive ductal carcinoma. Majority were females 98.3%. More than half of respondents 60.2% were between 31 and 50 years old (Table 1). The mean age was 44.6 ± 6.4 years. Ten were HER-2 type making up 2.4% (table 2). All of them were females (Table 3). Majority 7 (70%) were found in the 41-50 years age group (Table 4). Six (6) had stage 3 disease while 4 (40%) had clinically detectable metastases mostly to the lungs with two also having central nervous system involvement in addition. Trastuzumab was recommended but only 3 (30%) could afford it and are still alive 2 years post treatment with a two having stage 2 disease and one with stage 3 disease, while the rest 6 had paclitaxel neoadjuvant chemotherapy without trastuzumab and half has passed away within 24 months leaving only 3 with terminal disease and central nervous system metastases. ***Conclusion:*** Most presented late at stage 3 or 4 as premenopausal, and survival was poor at 59% of stage 3. Trastuzumab was extremely beneficial where it was affordable.

Keywords: Breast Cancer, (HER-2), Estrogen receptor (ER), tumors.

INTRODUCTION

The HER2-array subtype of breast cancer refers to the larger group of hormone receptor–negative (low expression of Estrogen Receptor and related genes by array) tumors identified by complete immunostaining for HER2 overexpression or FISH for excess gene copy number [1]. Most tumors that are clinically HER2-positive will fall within the HER2-array subtype. However, other tumors that are HER2 positive by immunohistochemistry or FISH will also overexpress hormone receptors, and most of these tumors fall within the luminal subtypes rather than the HER2-array subtype [2-4]. In this section, we are referring only to the HER2-array subtype, which does not express hormone receptors. The HER2-array tumors are also characterized by overexpression of other genes in the ERBB2 amplicon such as GRB7 [5]. Like basal-like tumors, the HER2-array subtype tumors have a high proportion, 40% to 80%, of TP53 mutations, and are significantly more likely to be grade 3 than luminal a tumors [1, 6].

***Corresponding Author:** Martin Arinzechukwu Nzegwu

Applying immunohistochemical methods for the assessment of sections of breast tumours, using antibodies to the Her-2/neu protein, allows investigation of tumours for overexpression of the protein, and relating protein expression to tumour prognosis [7]. Her-2/neu overexpression is amplified in 20–25% of primary breast cancers and has been associated with poor prognosis [8]. The association between Her-2/neu amplification and poor prognosis was first determined in 1987 by Slamon and co-workers [8]. Amplification of Her-2/neu gene was shown to strongly correlate with time of relapse and overall survival. Her-2/neu status is also important for selecting those with metastasis for therapy with trastuzumab (Herceptin) [9].

The use of both internal and external quality control ensured reproducibility and reliability in the procedure.

MATERIALS AND METHODS

Four hundred seventeen cases of breast cancer seen over a period of 3 years from January 2014 to December 2016 were routinely tested for estrogen and progesterone positivity as well as Her-2 positivity.

The scoring was according to the 2013 ASCO/CAP recommendation for Her-2/neu scoring [10]. The Staining Pattern Score for Her-2/neu Staining Assessment are as below:
No membrane staining is observed = 0 negative Faint, partial staining of the membrane in any proportion of the cancer cells = 1 + Negative. Weak to moderate complete staining of the membrane, greater than 10% of cancer cells = 2 + Equivocal. Strong, complete staining of the membrane greater than 10% of cancer cells = 3 + Positive with (normal epithelial elements and external controls). FISH was used to confirm the positive cases.

Recruited Patients gave their consent to use their tissue blocks for this study. An approval was first secured from the relevant to meet the ethical guidelines to enable the study to be carried out. Results of these samples were and slides were collated and subsequently analyzed.

The sample size population was 500 patients was obtained but due to improper age documentations, 83 were dropped. Inclusive criteria are.

1. Established breast cancer diagnosis whose diagnosis has been verified by at least two pathologist.
2. Consent from patients to use their tissue blocks for the study as well as proper documentation of patient's details including age.
3. Those who were typed had their tissue blocks obtained using rabbit monoclonal antibodies.

All monoclonal Antibodies used were procured as predilute ready to use and stored at a cold chain of 2–8°C until they were used for typing.

Her-2-neu receptor description

Her-2 receptor also known as (c-ERB-2) is a member of the epidermal growth factor (EGFR) family. It is a cell membrane surface bound tyrosine kinase and is normally involved in signal transduction pathways leading to cell growth and differentiation. Her-2/neu is a mouse monoclonal antibody derived from cell culture supernatant that is concentrated, dialysed, filter sterilized, and diluted in buffer pH 7.5, containing BSA and sodium azide as preservative. Storage is at 2–8°C. [11]. Quality controlled procedural steps involved in this typing includes.

1. Microtomy to produce 2–4 μm thick sections.
2. Heating at 64° for 2 h.
3. Heat epitope retrieval using citrate in a Bios SB pressure cooker at 100°C for 25 min.
4. Peroxidase blocker application for 5 min.
5. Application of primary Antibody 30 min.
6. Secondary Biotylated link 10 min.
7. Application of HRP label 10 min.
8. Application of DAB substrate chromogen 5 min.
9. Application of Hematoxylin counter staining 11 min.11–15

RESULTS

A total of 417 patients with Invasive Ductal Carcinoma of the breast participated, because we have an unscreened population with poor mammography screening penetrance, most cases came in as invasive ductal carcinoma. Majority were females 98.3%. More than half of respondents 60.2% were between 31 and 50 years old (Table 1). The mean age was 44.6 ± 6.4 years.

Ten were HER-2 type making up 2.4% (table 2). All of them were females (Table 3). Majority 7 (70%) were found in the 41-50 years age group (Table 4). Six (6) had stage 3 disease while 4 (40%) had clinically detectable metastases mostly to the lungs with two also having central nervous system involvement in addition. Trastuzumab was recommended but only 3 (30%) could afford it and are still alive 2 years post treatment with a two having stage 2 disease and one with stage 3 disease, while the rest 6 had paclitaxel neoadjuvant chemotherapy without trastuzumab and half has passed away within 24 months leaving only 3 with terminal disease and central nervous system metastases.

Table 1: Socio-demographic characteristics of the patients

Variables	Categories	Frequency	Percentage
Sex	Male	7	1.7
	Female	410	98.3
Age (Years)	20-30	30	7.2
	31-40	133	31.9
	41-50	118	28.3
	51-60	87	20.9
	61-70	39	9.4
	>70	10	2.3

TABLE 2 molecular types of breast cancer.

Molecular Subtype	Frequency	Percentage
Her-2 type	10	2.4
Lumina B Her-2 type	20	4.8
Lumina B	238	57.1
Tripple Neg	149	35.7

Table 3: Molecular Subtype and Sex Relationship

Variables	Categories	Frequency	Percentage	X^2	P
Her-2 type	Female	10	2.4	17.323	0.793
	Male	0	0		
Lumina B Her-2 type	Female	20	4.9		
	Male	0	0		
Lumina B	Female	237	57.8		
	Male	1	14.3		
Triple Neg	Female	143	34.9		
	Male	6	85.7		

TABLE 4 showing age group of her-2 type

Age of Patient in Years	Her-2 Type N	Percent
21-30	0	0
31-40	2	20
41-50	7	70
51-60	1	10

DISCUSSION

Her-2 neu overexpression was found in a mere 2.4% and has never been reported in our immediate environment previously. Ukah *et al*., has reported a prevalence rate of 11.4% in an area quite close to our environment [12]. Other studies showed her-2 positivity in other parts of Nigeria to be 30.8% in Lagos [13]. Reports from other parts of Nigeria have shown values of 22.0%, 10.6%, 20.8% from Maiduguri (North-eastern Nigeria) [14], Nnewi (South-eastern Nigeria) 15 and Benin (Mid-western Nigeria) [16] respectively. We clearly had the lowest percentage most probably because we verified each report with a fluorescent in-situ hybridization method. Elsewhere in Accra Seshie *et al*., reported 25.5 her-2 positivity in a retrospective study done in Korle Bu Teaching Hospital Ghana [17]. The median age of presentation was the 41-50 years age group. The study by Sanni *et al*., found a mean age of presentation of 52+13 years13. However, there is no association of the HER2-array subtype with either age or race [12] and no association with known risk factors [18]. Human epidermal growth factor type 2 over-expressed breast cancer subtype was seen in 10.6% of cases, with a mean age of 45.8±11.7 years compared to the mean age of 46.3±12.3 years for all breast cancers [15].

All were females and the all had grade 111 tumours in keeping with its aggressiveness. Treatment with trastuzumab made a significant difference as all who were treated with trastuzumab survived 24 months after unlike those who did not receive tarstuzumab with 50% mortality over 24 months.

The case has been made again for a good health insurance policy which will help screen our population to help discover these cases earlier. Availability of trastuzumab is clearly an indispensable addition to neoadjuvant chemotherapy which clearly helped our remission rate.

CONCLUSION

Her-2/neu is a vital biomarker in the evaluation of breast cancer in our environment. The treatment with trastuzumab did make a significant difference in their survival. We have by this study established a baseline data for her 2 subtype of breast cancer going forward.

REFRENCES

1. Brenton, J. D., Carey, L. A., Ahmed, A. A., & Caldas, C. (2005). Molecular classification and molecular forecasting of breast cancer: ready for clinical application?. *Journal of clinical oncology*, *23*(29), 7350-7360.
2. Sørlie, T., Perou, C. M., Tibshirani, R., Aas, T., Geisler, S., Johnsen, H., ... & Børresen-Dale, A. L. (2001). Gene expression patterns of breast carcinomas distinguish tumor subclasses with clinical implications. *Proceedings of the National Academy of Sciences*, *98*(19), 10869-10874.
3. Sotiriou, C., Neo, S. Y., McShane, L. M., Korn, E. L., Long, P. M., Jazaeri, A., ... & Liu, E. T. (2003). Breast cancer classification and prognosis based on gene expression profiles from a population-based study. *Proceedings of the National Academy of Sciences*, *100*(18), 10393-10398.
4. Nzegwu, M., Uzoigwe, J., Omotowo, B., Ugochukwu, A., Ozumba, B., Sule, E., ... & Ukekwe, F. I. (2021). Predictive and prognostic relevance of immunohistochemical testing of estrogen and progesterone receptors in breast cancer in South East Nigeria: A review of 417 cases. *Rare Tumors*, *13*, 20363613211006338.
5. Perou, C. M., Sørlie, T., Eisen, M. B., Van De Rijn, M., Jeffrey, S. S., Rees, C. A., ... & Botstein, D. (2000). Molecular portraits of human breast tumours. *nature*, *406*(6797), 747-752.
6. Carey, L. A., Perou, C. M., Dressler, L. G., Livasy, C. A., Geradts, J., Cowan, D., ... & Millikan, R. C. (2004). Race and the poor prognosis basal breast tumor (BBT) phenotype in the population-based Carolina Breast Cancer Study (CBCS). *Journal of Clinical Oncology*, *22*(14_suppl), 9510-9510.
7. Rasheed, N. W., & Aziz, R. S. HER-2/neu overexpression in breast cancer. *J Fac Med*, 52(3), 290-294
8. Slamon, D. J., Clark, G. M., Wong, S. G., Levin, W. J., Ullrich, A., & McGuire, W. L. (1987). Human breast cancer: correlation of relapse and survival with amplification of the HER-2/neu oncogene. *science*, *235*(4785), 177-182.
9. Jacobs, T. W., Gown, A. M., Yaziji, H., Barnes, M. J., & Schnitt, S. J. (2000). HER-2/neu protein expression in breast cancer evaluated by immunohistochemistry: a study of interlaboratory agreement. *American journal of clinical pathology*, *113*(2), 251-258.
10. Wolff, A. C., Hammond, M. E. H., Hicks, D. G., Dowsett, M., McShane, L. M., Allison, K. H., ... & Hayes, D. F. (2014). Recommendations for human epidermal growth factor receptor 2 testing in breast cancer: American Society of Clinical Oncology/College of American Pathologists clinical practice guideline update. *Archives of Pathology and Laboratory Medicine*, *138*(2), 241-256.
11. Bio SB. www.biosb.com (accessed 12 January 2015).
12. Ukah, C. O., Emegoakor, C., Anyiam, D. C. D., Onyiaorah, I. V., Onwukamuche, M. E., Egwuonwu, O. A., ... & Anyanwu, S. N. C. (2017). The immunohistochemical profile of breast cancer in indigenous women of Southeast Nigeria. *Annals of Medical and Health Sciences Research*, *7*(7), 83-87
13. Sanni, D. A., Popoola, A. O., Ibrahim, N. A., Omodele, F. O., Emiogun, F. E., Oludara, M. A., & Obafunwa, J. O. (2019). Her-2/neu overexpression in breast cancers in patients of West African extraction seen in Lagos state University Teaching hospital, Nigeria. *European Journal of Surgical Oncology*, *45*(11), 2022-2025.
14. Imam, B. A., Okechi, O. O., Abdullahi, K., Abubakar, U., Musa, A. B., Okorie, N., ... & Umar, A. (2017). Immunohistochemical pattern of breast cancer in Maiduguri, Borno state. *Journal of Cancer and Tumor International*, 1-10.
15. Ukah, C. O., Emegoakor, C., Anyiam, D. C. D., Onyiaorah, I. V., Onwukamuche, M. E., Egwuonwu, O. A., ... & Anyanwu, S. N. C. (2017). The immunohistochemical profile of breast cancer in indigenous women of Southeast Nigeria. *Annals of Medical and Health Sciences Research*, *7*(7), 83-87
16. Ugiagbe, E. E., Olu-Eddo, A. N., & Obaseki, D. E. (2011). Immunohistochemical detection of Her-2/neu overexpression in breast carcinoma in Nigerians: A 5-year retrospective study. *Nigerian journal of clinical practice*, *14*(3), 332-337.
17. Seshie, B., Adu-Aryee, N. A., Dedey, F., Calys-Tagoe, B., & Clegg-Lamptey, J. N. (2015). A retrospective analysis of breast cancer subtype based on ER/PR and HER2 status in Ghanaian patients at the Korle Bu Teaching Hospital, Ghana. *BMC clinical pathology*, *15*(1), 1-8.
18. Carey, L. A., Perou, C. M., Dressler, L. G., Livasy, C. A., Geradts, J., Cowan, D., ... & Millikan, R. C. (2004). Race and the poor prognosis basal breast tumor (BBT) phenotype in the population-based Carolina Breast Cancer Study (CBCS). *Journal of Clinical Oncology*, *22*(14_suppl), 9510-9510.

Cite This Article: Nzegwu Martin Arinzechukwu *et al* (2021). Pattern of Overexpression of HER-2 Biomarker in Breast Cancers in South East Nigeria. *East African Scholars Multidiscip Bull*, *4*(9), 103-106.