

Prospective Study

Assessment of breast cancer immunohistochemistry and tumor characteristics in Nigeria

Usman Malami Aliyu, Abdulrahman Auwal Musa

ORCID number: Usman Malami Aliyu 0000-0002-8939-6894; Abdulrahman Auwal Musa 0000-0001-5052-2585.

Author contributions: Aliyu UM drafted the methodology and discussion; Musa AA assisted with data analysis and interpretation of the result; Aliyu UM and Musa AA performed the writing and editing for the original manuscript.

Institutional review board

statement: This study was reviewed and approved by the Research Ethics Committee. The research topic is in line with the rule and regulation of the institution.

Conflict-of-interest statement: The authors of this manuscript have no conflicts of interest to disclose.

Data sharing statement: There are no additional data available.

Open-Access: This article is an open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution NonCommercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially,

Usman Malami Aliyu, Department of Radiotherapy and Oncology, Usmanu Danfodiyo University/Teaching Hospital, Sokoto 840212, Nigeria

Abdulrahman Auwal Musa, Department of Histopathology, Usmanu Danfodiyo University Teaching Hospital, Sokoto 840221, Nigeria

Corresponding author: Usman Malami Aliyu, MBBS, Senior Lecturer, Department of Radiotherapy and Oncology, Usmanu Danfodiyo University/Teaching Hospital, No. 1 Garba Nadama Road, Gawon Nama Area, Sokoto 840212, Nigeria. aamusa08033@gmail.com

Abstract

BACKGROUND

Female breast cancer is the leading type of cancer worldwide with an incidence of approximately 2.1 million in 2018. Hormone receptor status plays a vital role in its management.

AIM

To determine the molecular expression pattern of biomarkers in breast cancer and their correlation with tumor variables.

METHODS

This prospective study was designed to analyze expression patterns of estrogen receptor(ER), progesterone receptor (PR) and human epidermal growth factor receptor(HER2/neu) in breast cancer patients. The dataset has been taken from the Department of Radiotherapy and Oncology of Usmanu Danfodiyo University Teaching Hospital Sokoto, Nigeria from 1 January 2015 to 2 December 2019. The dataset had 259 records and 7 attributes. SPSS version 23.0 for statistical analysis was used. The data analyzed demographic and other clinicopathological characteristics as categorical variables. The mean and standard deviation were determined for the quantitative variable.

RESULTS

A total of 259 breast cancer cases were included in the study. The mean age was 48.3 ± 11.0 , with an age range of 26-80 years and a median age of 46 years. The morphological categories were invasive ductal carcinoma 258 (99.6%) and invasive lobular carcinoma 1 (0.4%). ER, positivity increased in 73 patients (50%) under the age of 50 years, as well as PR positivity increased in 34 patients (23.6%) under the age of 50 years. HER/2neupositivity decreased in 8 patients (5.6%)

and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Unsolicited manuscript

Specialty type: Oncology

Country/Territory of origin: Nigeria

Peer-review report's scientific quality classification

Grade A (Excellent): 0
Grade B (Very good): 0
Grade C (Good): C
Grade D (Fair): 0
Grade E (Poor): 0

Received: April 23, 2020

Peer-review started: April 23, 2020

First decision: June 15, 2020

Revised: September 16, 2020

Accepted: October 5, 2020

Article in press: October 5, 2020

Published online: November 24, 2020

P-Reviewer: Peng X

S-Editor: Wang DM

L-Editor: Filipodia

P-Editor: Wang LL



under the age of 50 years. Hormonal receptors were statistically significant with clinicopathological characteristics ($P < 0.05$).

CONCLUSION

Our study showed that ER, PR and HER2/neu expression had a strong correlation with age, tumor grade, tumor size and lymph node status. Hence, hormone receptor assessment is highly recommended because of its significance in clinical management and prognostication.

Key Words: Breast cancer; Hormonal receptors; Sokoto state; Tertiary Health Institution; Northwestern; Nigeria

©The Author(s) 2020. Published by Baishideng Publishing Group Inc. All rights reserved.

Core Tip: Breast cancer is the most common malignancy in Nigeria as it is in the whole world. Assessment of immunohistochemical profile and its tumor characteristic is paramount to the management of this disease entity. The paucity of literature on breast cancer biomarkers in sub-Saharan Africa (*e.g.*, Nigeria) has contributed to the increase in morbidity and mortality recorded in the region.

Citation: Aliyu UM, Musa AA. Assessment of breast cancer immunohistochemistry and tumor characteristics in Nigeria. *World J Clin Oncol* 2020; 11(11): 935-944

URL: <https://www.wjgnet.com/2218-4333/full/v11/i11/935.htm>

DOI: <https://dx.doi.org/10.5306/wjco.v11.i11.935>

INTRODUCTION

Female breast cancer is the most common malignancy worldwide, with over two million cases diagnosed in 2018^[1]. Prognostic indicators are features that are unrelated to adjuvant therapy that determines the outcome of disease, while predictive indicators are related to response to therapy^[2]. The treatment and outcome of this disease entity vary depending on the biological characteristics. Hence, modalities for treatment employ those features to individualized breast cancer therapy^[3]. These characteristics can also determine the prognosis and outcome^[2]. In the last three decades, tremendous progress has been made in the biological characterization of breast cancers with the advent of immunohistochemistry and immunophenotyping. Various biomarkers such as hormone receptors, vascular endothelial growth factors, epidermal growth factor, tumor suppressor genes, multidrug resistant genes and adhesion molecules have been identified^[2,4].

Currently, determination of estrogen receptor (ER), progesterone receptor (PR) and human epidermal receptor growth factor 2 (HER2/neu) receptor is routine in the diagnosis of breast cancer^[5,6]. The International Breast Cancer Study Group classified breast cancer into three^[6,7] categories based on the proportion of cells that are receptor positive [responsive (10%), response uncertain (1%-9%) and nonresponsive (0%)]. At least 1% positivity is necessary for commencement of hormone therapy. Molecular assays give an insight into the current status of the tumor, which often differs from the primary when it metastasizes. A comparative study involving 658 and 418 of ER/PR samples showed a dissonant rate of 29% and 27%, respectively, for primary and metastatic tumors^[8,9].

ER is a biomarker found in over 65% of invasive breast cancer and contributes significantly to its pathobiology. ER positivity makes it responsive to hormonal therapy, resulting in a more favorable outcome. PR, like ER, is also a transcription factor, which is largely controlled by ER and to a lesser extent by growth factors. About 55% to 65% of invasive breast cancers show PR positivity. PR commonly coexists with ER. Both receptors require at least 1% nuclear staining to be considered positive according to the American Society of Clinical Oncology/College of American Pathologists guidelines^[11,12]. Allred scoring and H-scoring are two other commonly used systems for ER and PR evaluations^[9-11].

HER2/neu has the potential of enhancing proliferation and survival of tumor cells.

Hence its overexpression, which occurs in about 12%-20% of inflammatory breast cancer, results in a more aggressive growth and poor response to treatment. According to the American Society of Clinical Oncology/College of American Pathologists guidelines, membrane staining of 10% or more is considered positive and an indication of a favorable response to anti-HER2/neu therapy^[11,13]. HER2/neu can be evaluated either by immunohistochemistry or fluorescence in situ hybridization. Although there are many ways to test for this receptor, the above two are the only approved methods^[14-16].

This study aimed to determine the molecular expression of biomarkers in breast cancer in Sokoto, Nigeria and their correlation with tumor variables.

MATERIALS AND METHODS

This prospective study was designed to analyze expression patterns of ER, PR and HER2/neu in breast cancer patients. The dataset was taken from the Department of Radiotherapy and Oncology of Usmanu Danfodiyo University Teaching Hospital Sokoto, Nigeria from 1 January 2015 to 2 December 2019. The dataset had 259 records and 7 attributes. The data analyzed demographic and other clinicopathological characteristics as categorical variables. The mean and standard deviation were determined for the quantitative variable. All variables were coded as binary dummy variables. For example tumor site (right breast = 1, left breast = 2). Patients were grouped according to age < 50 years and ≥ 50 years. Histological grading stratification of tumor size was performed in three groups (< 2 cm, 2-5 cm and > 5 cm), and lymph nodes were grouped as 1-3 and ≥ 4 based on tumor node metastasis staging for breast carcinoma.

Data were presented as charts, and frequency distribution was generated for all categorical variables. Descriptive and inferential statistics [chi-squared, Fisher exact test, bi-variate correlation (Kendall's test) and multivariate logistic regression analysis] were used to explore association, the strength of the association and odds ratio (OR) or relative risk between clinicopathological variables and biomarkers expressed (ER, PR and HER2/neu). $P \leq 0.05$ was considered statistically significant. SPSS version 23.0 (Chicago, IL, United States) was used.

RESULTS

Two hundred and fifty-nine subjects that fulfilled the inclusion criteria were recruited into the study. The mean age was 48.3 ± 11.0 . The ages ranged between 26 and 80 years, and the median age was 46 years. Most of the patients 144 (55.6%) were less than 50 years at diagnosis (Figure 1). The left side was the predominant site of breast cancer 151 (58.3%) (Figure 2). The morphological categories were invasive ductal carcinoma (258 patients, 99.6%) and invasive lobular carcinoma (1 patient, 0.4%). Sixty-two (23.9%) cases were grade I, 131 (50.6%) were grade II and 66 (25.5%) were grade III. Tumor sizes were stratified into three categories: 62 patients (23.9%) were < 2.0 cm, 131 patients (50.6%) were 2-5 cm and 66 patients (25.5%) were > 5.0 cm (Table 1).

ER positivity increased in 73 patients (50%) under the age of 50 years, and PR positivity increased in 34 patients (23.6%) under the age of 50 years. HER2/neu positivity decreased in 8 patients (5.6%) under the age of 50 years ($P < 0.01$). ER positivity was found in 35 patients (56.5%), 55 patients (42.0%) and 23 patients (34.8%) with grade I, II and III carcinomas, respectively. PR positivity was found in 3 patients (3.2%), 29 patients (22.1%) and 10 patients (15.2%) with grade I, II and III carcinomas, respectively. HER2/neu positivity was found 3 patients (4.8%), 13 patients (9.9%) and 7 patients (10.6%) with grade I, II and III carcinomas, respectively. ER and PR positivity were much less in high-grade tumors than in those with intermediate grade (ER 34.8% vs 42%; PR 15.2% vs 22.1%).

The patients were categorized into three groups based on tumor size: Group 1 (tumor size ≤ 2 cm); group 2 (2-5 cm); and group 3 (≥ 5 cm). The total number of group 1 tumors was 62 [35 ER positive (56.5%); 3 PR positive (4.8%); and 3 HER2/neu positive (4.8%)]. The total number of group 2 tumors was 131 [55 ER positive (42.0%); 29 PR positive (22.1%); and 13 HER2/neu positive (9.9%)]. The total number of group 3 tumors was 66 [23 ER positive (34.8%); 10 PR positive (15.2%); and 7 HER2/neu positive (10.6%)]. ER expression in the HER2/neu positive, large-sized tumors was significantly decreased compared with smaller tumors ($P < 0.05$). Metastasis in axillary lymph nodes was seen in 237 (91.5%) patients. Among the ER positive cases, 86

Table 1 Clinico-pathological and molecular characteristics of the breast cancer patients (259)

Histologic type	Frequency	Percentage
Invasive ductal carcinoma	258	99.6
Invasive lobular carcinoma	1	0.4
Grading		
I	62	23.9
II	131	50.6
III	66	25.5
Tumour size		
< 2.0 cm	62	23.9
2-5 cm	131	50.6
> 5.0 cm	66	25.5
Lymph node involvement		
No	22	8.5
1-3	196	75.7
≥ 4	41	15.8
Hormonal receptors		
ER + ve	113	43.6
ER - ve	52	20.1
PR + ve	42	16.2
PR - ve	12	4.6
HER/2 neu + ve	23	8.9
HER/2 neu - ve	17	6.6
Total	259	100

ER: Estrogen receptor; PR: Progesterone receptor; Human epidermal growth factor receptor-2.

(43.9%) had axillary lymph node involvement ranging from 1-3. Among the PR positive cases, 37 (17.3%) had positive axillary lymph nodes positive for metastasis. Nineteen (9.7%) participants with HER2/neu positive disease were positive for axillary lymph nodes metastasis. Tumors with axillary lymph node metastasis showed significant association with ER, PR and HER2/neu ($P < 0.03$) (Table 2).

Age was significantly correlated with ER, PR and HER2/neu ($P < 0.05$). However, there was no significant correlation in PR negative disease ($P > 0.05$). We found that ER and HER2/neu expression compared to tumor grade was statistically significant ($P < 0.05$) while PR expression was not significant ($P > 0.05$) (Table 3).

This study also found that women younger than 50 years are likely to present with ER positive disease ($P = 0.01$, OR = 8.517, 95% confidence interval: 2.309-31.413) and PR negative disease ($P = 0.04$, OR = 14.00, 95% confidence interval: 2.300-85.218). Similarly, most of the tumors that presented with grade I disease were 15 times more likely to be ER positive than those in grade II or III ($P = 0.01$, OR 15.2, 95% confidence interval 1.296-12.252) (Table 4 and 5).

DISCUSSION

This study revealed that most of the patients (56%) were less than 50 years at diagnosis, and the mean age of the study participants was 48 years. This corresponds to what was reported by Sengal *et al*^[17] and Errahhali *et al*^[18] where the mean ages of the participants were 48 years. On the contrary, a similar study by Chand *et al*^[19] reported a mean age of 55 years. In this study, the most predominant histologic type was invasive ductal carcinoma. A similar study in Sudan also reported invasive ductal carcinoma as

Table 2 Association of estrogen receptor and progesterone receptor with prognostic markers (n = 259)

Age	Hormonal receptors						Total	P value
	ER + ve	ER - ve	PR + ve	PR - ve	HER/2 neu + ve	HER/2 neu - ve		
< 50	73 (50.70%)	17 (11.80%)	34 (23.60%)	9 (6.30%)	8 (5.60%)	3 (2.10%)	144	0.01
≥ 50	40 (34.80%)	35 (30.40%)	8 (7.00%)	3 (2.60%)	15 (13.00%)	14 (12.20%)	115	
Grading								
I	35 (56.50%)	18 (29.00%)	3 (4.80%)	2 (3.20%)	3 (4.80%)	1 (1.60%)	62	0.02
II	55 (42.00%)	23 (17.60%)	29 (22.10%)	5 (3.80%)	13 (9.90%)	6 (4.60%)	131	
III	23 (34.80%)	11 (16.70%)	10 (15.20%)	5 (7.60%)	7 (10.60%)	10 (15.20%)	66	
Tumour size								
< 2.0 cm	35 (56.50%)	18 (29.00%)	3 (4.80%)	2 (3.20%)	3 (4.80%)	1 (1.60%)	62	0.02
2-5 cm	55 (42.00%)	23 (17.60%)	29 (22.10%)	5 (3.80%)	13 (9.90%)	6 (4.60%)	131	
> 5.0 cm	23 (34.80%)	11 (16.70%)	10 (15.20%)	5 (7.60%)	7 (10.60%)	10 (15.20%)	66	
Lymph node involvement								
No	11 (50.00%)	3 (13.60%)	3 (13.60%)	2 (9.10%)	2 (9.10%)	1 (4.50%)	22	0.03
1-3	86 (43.90%)	43 (21.90%)	34 (17.30%)	6 (3.10%)	19 (9.70%)	8 (4.10%)	196	
≥ 4	16 (39.00%)	6 (14.60%)	5 (12.20%)	4 (9.80%)	2 (4.90%)	8 (19.50%)	41	

ER: Estrogen receptor; PR: Progesterone receptor; HER/2 neu: Human epidermal growth factor receptor-2.

Table 3 Bi-variate correlation of clinicopathological parameters and hormonal receptors

Clinic pathologic feature	Estimators	Hormonal receptors					
		ER + ve	ER - ve	PR + ve	PR - ve	Her-2 + ve	Her-2 - ve
Age	R	-0.159 ^a	0.231 ^b	-0.224 ^b	-0.086	0.131 ^a	0.202 ^b
	P value	0.01	0.01	0.01	0.167	0.036	0.001
Grading	R	-0.144 ^b	-0.101	0.089	0.07	0.067	0.184 ^b
	P value	0.015	0.087	0.133	0.236	0.26	0.002
Tumour size	R	-0.144 ^a	-0.101	0.089	0.07	0.067	0.184 ^b
	P value	0.015	0.087	0.133	0.236	0.26	0.002
Lymph node	R	-0.051	-0.018	-0.024	0.045	-0.047	0.184 ^b
	P value	0.401	0.761	0.689	0.455	0.438	0.002
Total		259	259	259	259	259	259

^a: Strongly significant.

^b: Significant.

ER + ve: = Estrogen receptor positive; ER - ve = Estrogen receptor negative; PR + ve =Progesterone receptor positive; PR - ve =Progesterone receptor negative, HER/2 neu + ve= Human epidermal growth factor receptor-2 positive, HER/2 neu - ve= Human epidermal growth factor receptor-2 negative.

the most common histological type^[17]. The majority of the ER (50%) and PR (23.6%) positive cases were seen in an age less than 50 years. This report agreed with other similar investigations in Sudan and the northern region of India^[17,20]. HER2/neu positivity was observed in patients > 50 years. Our report was not in line with Alzaman *et al*^[21] in Bahrain. There was a significant correlation between the age and ER, PR and HER2/neu positivity ($P < 0.05$). This was consistent with a similar study conducted by Ramic *et al*^[22].

The majority of ER positive cases (57.0%) were observed in grade I carcinomas. Most PR positive cases (22.0%) were seen in grade II, and most HER2/neu positive cases (10.6%) were seen in grade III. This finding did not correspond to Siadati *et al*^[23] where

Table 4 Multivariate logistic regression analysis of hormonal receptor and age patients

Hormonal receptors		P value	OR	95% confidence interval	
				Lower bound	Upper bound
ER + ve	< 50 yr	0.001	8.517	2.309	31.413
	≤ 50 yr	1			
ER - ve	< 50 yr	0.243	2.267	0.573	8.965
	≤ 50 yr	1			
PR + ve	< 50 yr	0	19.833	4.58	85.883
	≤ 50 yr	1			
PR - ve	< 50 yr	0.004	14	2.3	85.218
	≤ 50 yr	1			
HER/2 neu + ve	< 50 yr	0.238	2.489	0.548	11.308
	≤ 50 yr	1			

ER: Estrogen receptor; PR: Progesterone receptor; OR: Odd ration; HER/2 neu: Human epidermal growth factor receptor-2.

Table 5 Multivariate logistic regression analysis of hormonal receptor and tumor grading

Hormonal receptors	Grading	P value	OR	95% confidence interval	
ER + ve	Grade I	0.012	15.217	1.823	127.02
	Grade II	0.016	3.986	1.296	12.252
	Grade III	1			
ER - ve	Grade I	0.012	16.364	1.835	145.95
	Grade II	0.049	3.485	1.007	12.057
	Grade III	1			
PR + ve	Grade I	0.375	3	0.265	33.974
	Grade II	0.013	4.833	1.397	16.725
	Grade III	1			
PR - ve	Grade I	0.301	4	0.288	55.471
	Grade II	0.532	1.667	0.336	8.258
	Grade III	1			
HER/2 neu + ve	Grade I	0.246	4.286	0.366	50.197
	Grade II	0.105	3.095	0.789	12.144
	Grade III	1			

ER: Estrogen receptor; PR: Progesterone receptor; OR: Odd ration; HER/2 neu: Human epidermal growth factor receptor-2.

most of the ER positive cases were grade II^[23]. A significant association was established between tumor grade, ER positivity and HER2/neu negativity ($P < 0.05$). A study conducted by Dodiya *et al*^[24] in the western region of India showed that ER and PR correlated with the grade but not HER2/neu.

One hundred and thirty-one cases had a tumor size ranging from 2-5 cm. We observed that 42.0% were ER positive, 22.1% were PR positive and 9.9% were

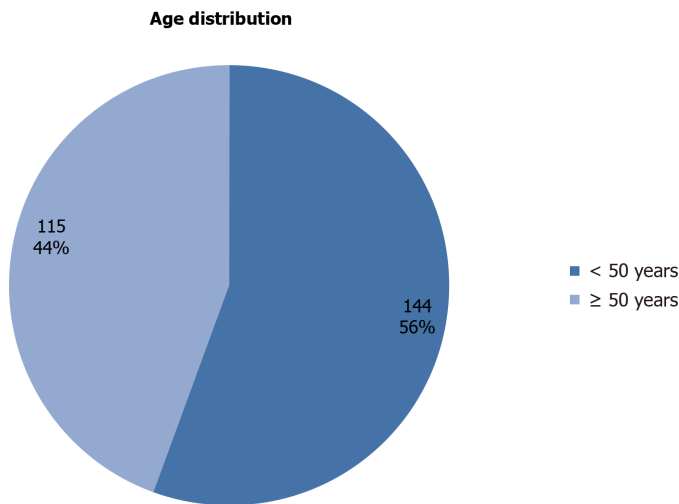


Figure 1 Age distribution of the study participants.

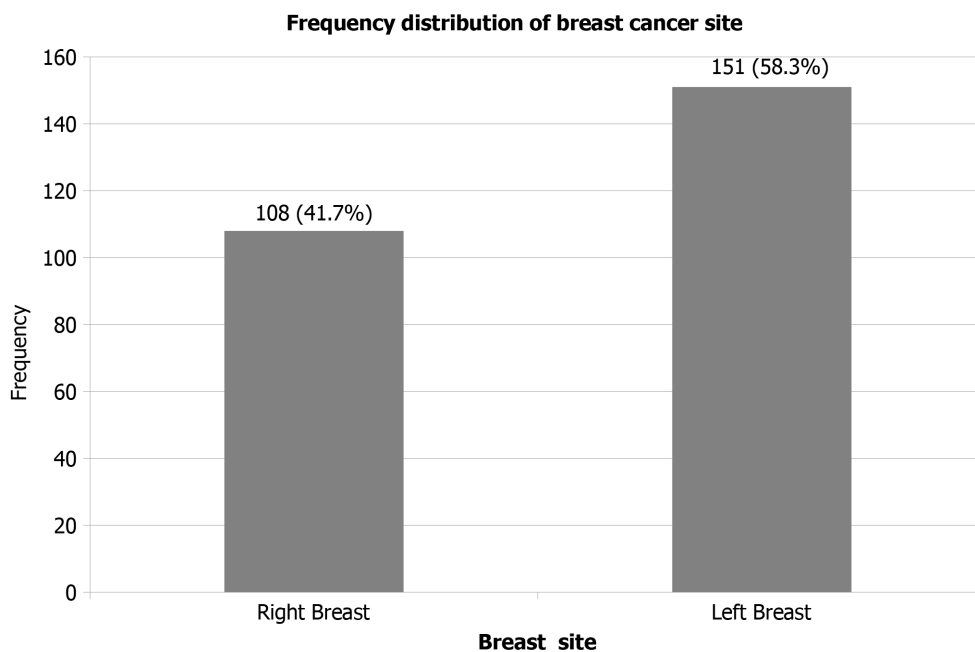


Figure 2 Frequency distribution of breast cancer site among the study participants.

HER2/neu positive. Our finding indicated that there was a negative correlation in ER positivity status and a positive correlation in HER2/neu positivity status with the tumor size ($r = -0.144$, $P = 0.02$). This agreed with a study by Almasri *et al*^[25] that reported a significant correlation between tumor size and hormone receptors.

Metastasis in axillary lymph nodes was observed to be higher in ER positive cases (49.3%), while metastasis to axillary lymph nodes was present in 17.3% of the PR positive cases and 9.7% of HER2/neu positive cases. Tumors with axillary lymph node metastasis showed significant association with ER, PR and HER2/neu ($P < 0.03$). These findings agreed with other similar studies that showed a significant association between axillary lymph node and hormone receptors^[19,26,27].

This study also found that women younger than 50 years were more likely to be present with ER positive and PR negative breast cancer. Similarly, most of the tumors that presented with grade I disease were 15 times more likely to be ER positive than those in grade II or III. On the contrary, Sengal *et al*^[17] reported that younger women are 2 times more likely to develop ER negative disease, and grade III tumors are 2 times more likely to be ER negative compared with grade I or II tumors.

CONCLUSION

Our study showed that ER, PR and HER2/neu expression had a strong correlation with age, tumor grade, tumor size and lymph node status. Hence, hormone receptor assessment is highly recommended because of its significance in clinical management and prognostication.

ARTICLE HIGHLIGHTS

Research background

Female breast cancer is the leading type of cancer worldwide with an incidence of approximately 2.1 million in 2018. Hormone receptor status plays a vital role in its management.

Research motivation

Expression of biomarkers to treat breast cancer play a significant role in its management.

Research objectives

To determine the molecular expression pattern of biomarkers in breast cancer and their correlation with tumor variables.

Research methods

This prospective study was designed to analyze expression patterns of estrogen receptor(ER), progesterone receptor (PR) and HER2/neu in breast cancer patients. The dataset was taken from the Department of Radiotherapy and Oncology of Usmanu Danfodiyo University Teaching Hospital Sokoto, Nigeria from 1 January 2015 to 2 December 2019. The dataset had 259 records and 7 attributes. SPSS version 23.0 was used for statistical analysis. The data analyzed demographic and other clinicopathological characteristics as categorical variables. The mean and standard deviation were determined for the quantitative variable.

Research results

A total of 259 breast cancer cases were included in the study. The mean age was 48.3 ± 11.0 , with an age range of 26-80 years and a median age of 46 years. The morphological categories were invasive ductal carcinoma (99.6%) and invasive lobular carcinoma (0.4%). Estrogen receptor positivity increased in 73 patients (50.0%) under the age of 50 years. Progesterone receptor positivity increase in 34 patients (23.6%) under the age of 50 years. Human epidermal receptor growth factor 2 positivity decreased in 8 patients (5.6%) under the age of 50 years. Hormone receptors were statistically significant with clinicopathological characteristics ($P < 0.05$).

Research conclusions

Our study showed that ER, PR and HER2/neu expression had a strong correlation with age, tumor grade, tumor size and lymph node status. Therefore, assessment of hormone receptors for clinical management of a breast cancer patient is strongly recommended to provide prognostic information and therapeutic measurement.

Research perspectives

In low-resource countries, there are paucities in the evaluation of the molecular expression of biomarkers in breast cancer. Therefore, there is a need for further studies to improve prevention and early detection of breast carcinoma in developing countries.

REFERENCES

- 1 **Musa AA**, Aliyu UM. Application of Machine Learning Techniques in Predicting of Breast Cancer Metastases Using Decision Tree Algorithm, in Sokoto Northwestern Nigeria. *J Data Mining Genomics Proteomics* 2020; **11**: 220 [DOI: [10.35248/2153-0602.20.11.220](https://doi.org/10.35248/2153-0602.20.11.220)]
- 2 **Leong AS**, Zhuang Z. The changing role of pathology in breast cancer diagnosis and treatment. *Pathobiology* 2011; **78**: 99-114 [PMID: [21677473](https://pubmed.ncbi.nlm.nih.gov/21677473/) DOI: [10.1159/000292644](https://doi.org/10.1159/000292644)]

- 3 **Rodenhiser DI**, Andrews JD, Vandenberg TA, Chambers AF. Gene signatures of breast cancer progression and metastasis. *Breast Cancer Res* 2011; **13**: 201 [PMID: 21345283 DOI: 10.1186/bcr2791]
- 4 **Leong AS**, Lee AK. Biological indices in the assessment of breast cancer. *Clin Mol Pathol* 1995; **48**: M221-M238 [PMID: 16696013 DOI: 10.1136/mp.48.5.m221]
- 5 **Zaha DC**. Significance of immunohistochemistry in breast cancer. *World J Clin Oncol* 2014; **5**: 382-392 [PMID: 25114853 DOI: 10.5306/wjco.v5.i3.382.]
- 6 **Barnes DM**, Harris WH, Smith P, Millis RR, Rubens RD. Immunohistochemical determination of oestrogen receptor: comparison of different methods of assessment of staining and correlation with clinical outcome of breast cancer patients. *Br J Cancer* 1996; **74**: 1445-1451 [PMID: 8912543 DOI: 10.1038/bjc.1996.563]
- 7 **Fisher ER**, Anderson S, Dean S, Dabbs D, Fisher B, Siderits R, Pritchard J, Pereira T, Geyer C, Wolmark N. Solving the dilemma of the immunohistochemical and other methods used for scoring estrogen receptor and progesterone receptor in patients with invasive breast carcinoma. *Cancer* 2005; **103**: 164-173 [PMID: 15565575 DOI: 10.1002/encr.20761]
- 8 **Franco A**, Col N, Chlebowski RT. Discordance in estrogen (ER) and progesterone receptor (PR) status between primary metastatic breast cancer: a meta-analysis. *J Clin Oncol (Meeting Abstracts)* 2004; **22** (14_suppl): 539 [DOI: 10.1200/jco.2004.22.90140.539]
- 9 **Harvey JM**, Clark GM, Osborne CK, Allred DC. Estrogen receptor status by immunohistochemistry is superior to the ligand-binding assay for predicting response to adjuvant endocrine therapy in breast cancer. *J Clin Oncol* 1999; **17**: 1474-1481 [PMID: 10334533 DOI: 10.1200/jco.1999.17.5.1474]
- 10 **McCarty KS Jr**, Miller LS, Cox EB, Konrath J, McCarty KS Sr. Estrogen receptor analyses. Correlation of biochemical and immunohistochemical methods using monoclonal antireceptor antibodies. *Arch Pathol Lab Med* 1985; **109**: 716-721 [PMID: 3893381]
- 11 **Tang P**, Tse GM. Immunohistochemical Surrogates for Molecular Classification of Breast Carcinoma: A 2015 Update. *Arch Pathol Lab Med* 2016; **140**: 806-814 [PMID: 27472239 DOI: 10.5858/arpa.2015-0133-ra]
- 12 **Hammond ME**, Hayes DF, Wolff AC, Mangu PB, Temin S. American society of clinical oncology/college of american pathologists guideline recommendations for immunohistochemical testing of estrogen and progesterone receptors in breast cancer. *J Oncol Pract* 2010; **6**: 195-197 [PMID: 21037871 DOI: 10.1200/jop.777003]
- 13 **Wolff AC**, Hammond ME, Hicks DG, Dowsett M, McShane LM, Allison KH, Allred DC, Bartlett JM, Bilous M, Fitzgibbons P, Hanna W, Jenkins RB, Mangu PB, Paik S, Perez EA, Press MF, Spears PA, Vance GH, Viale G, Hayes DF; American Society of Clinical Oncology; College of American Pathologists. 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. *J Clin Oncol* 2013; **31**: 3997-4013 [PMID: 24101045 DOI: 10.1200/jco.2013.50.9984]
- 14 **Yeh IT**, Mies C. Application of immunohistochemistry to breast lesions. *Arch Pathol Lab Med* 2008; **132**: 349-358 [PMID: 18318578 DOI: 10.1043/1543-2165(2008)132
- 15 **Carlson RW**, Moench SJ, Hammond ME, Perez EA, Burstein HJ, Allred DC, Vogel CL, Goldstein LJ, Somlo G, Gradishar WJ, Hudis CA, Jahanzeb M, Stark A, Wolff AC, Press MF, Winer EP, Paik S, Ljung BM. HER2 testing in breast cancer: NCCN Task Force report and recommendations. *J Natl Compr Canc Netw* 2006; **4** Suppl 3: S1-S22; quiz S23 [DOI: 10.6004/jnccn.2006.2003]
- 16 **Wolff AC**, Hammond ME, Schwartz JN, Hagerty KL, Allred DC, Cote RJ, Dowsett M, Fitzgibbons PL, Hanna WM, Langer A, McShane LM, Paik S, Pegram MD, Perez EA, Press MF, Rhodes A, Sturgeon C, Taube SE, Tubbs R, Vance GH, van de Vijver M, Wheeler TM, Hayes DF; American Society of Clinical Oncology; College of American Pathologists. American Society of Clinical Oncology/College of American Pathologists guideline recommendations for human epidermal growth factor receptor 2 testing in breast cancer. *J Clin Oncol* 2007; **25**: 118-145 [PMID: 17159189 DOI: 10.5858/arpa.2013-0953-SA]
- 17 **Sengal AT**, Haj-Mukhtar NS, Elhaj AM, Bedri S, Kantelhardt EJ, Mohamedani AA. Immunohistochemistry defined subtypes of breast cancer in 678 Sudanese and Eritrean women; hospitals based case series. *BMC Cancer* 2017; **17**: 804 [PMID: 29191181 DOI: 10.1186/s12885-017-3805-4]
- 18 **Elidrissi Errahhali M**, Elidrissi Errahhali M, Ouarzane M, El Harroudi T, Afqir S, Bellaoui M. First report on molecular breast cancer subtypes and their clinico-pathological characteristics in Eastern Morocco: series of 2260 cases. *BMC Womens Health* 2017; **17**: 3 [PMID: 28068979 DOI: 10.1186/s12905-016-0361-z]
- 19 **Chand P**, Garg A, Singla V, Rani N. Evaluation of Immunohistochemical Profile of Breast Cancer for Prognostics and Therapeutic Use. *Niger J Surg* 2018; **24**: 100-106 [PMID: 30283220 DOI: 10.4103/njs.njs_2_18]
- 20 **Kaul R**, Sharma J, Minhas SS, Mardi K. Hormone receptor status of breast cancer in the himalayan region of northern India. *Indian J Surg* 2011; **73**: 9-12 [PMID: 22211030 DOI: 10.1007/s12262-010-0121-5]
- 21 **AlZaman AS**, Mughal SA, AlZaman YS, AlZaman ES. Correlation between hormone receptor status and age, and its prognostic implications in breast cancer patients in Bahrain. *Saudi Med J* 2016; **37**: 37-42 [PMID: 26739972 DOI: 10.15537/smj.2016.1.13016]
- 22 **Ramić S**, Asić K, Balja MP, Paić F, Benković V, Knežević F. Correlation of phosphorylated HER2 with clinicopathological characteristics and efficacy of trastuzumab treatment for breast cancer. *Anticancer Res* 2013; **33**: 2509-2515 [PMID: 23749902]
- 23 **Siadati S**, Sharbatdaran M, Nikbakhsh N, Ghaemian N. Correlation of ER, PR and HER-2/Neu with other Prognostic Factors in Infiltrating Ductal Carcinoma of Breast. *Iran J Pathol* 2015; **10**: 221-226 [PMID: 26351488]
- 24 **Dodiya H**, Patel A, Patel D, Kaushal A, Vijay DG. Study of hormone receptors and epidermal growth factor expression in invasive breast cancers in a cohort of Western India. *Indian J Clin Biochem* 2013; **28**: 403-409 [PMID: 24426244 DOI: 10.1007/s12291-012-0294-8]
- 25 **Almasri NM**, Al Hamad M. Immunohistochemical evaluation of human epidermal growth factor receptor 2 and estrogen and progesterone receptors in breast carcinoma in Jordan. *Breast Cancer Res* 2005; **7**: R598-R604 [PMID: 16168103 DOI: 10.1186/bcr1200]

- 26 **Ali EM**, Ahmed RH, Ali AM. Correlation of breast cancer subtypes based on ER, PR and HER2/neu expression with axillary lymph node status. *Cancer Oncol Res* 2014; **2**: 51-57
- 27 **Azizun-Nisa**, Bhurgri Y, Raza F, Kayani N. Comparison of ER, PR and HER-2/neu (C-erb B 2) reactivity pattern with histologic grade, tumor size and lymph node status in breast cancer. *Asian Pac J Cancer Prev* 2008; **9**: 553-556 [PMID: [19256737](#)]



Published by **Baishideng Publishing Group Inc**
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-3991568
E-mail: bpgoffice@wjgnet.com
Help Desk: <https://www.f6publishing.com/helpdesk>
<https://www.wjgnet.com>

