A Surveillance of Estrogen Receptor (ER), Progesterone Receptor (PR) and Human Epidermal Growth Factor Receptor-2 (HER-2) Status in Malignant Female Breast Lesions in Bayelsa State, Nigeria.

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Abstract - A three (3) year retrospective study of Estrogen Receptor (ER), Progesterone receptor (PR) and Human Epidermal growth factor receptor-2 (HER2) status of previously diagnosed female breast cancers was done using immunohistochemistochemistry. Formalin fixed paraffin embedded (FFPE) tissue blocks of breast cancer cases from 2009-2011 were retrieved from the tissue block archives of the two major tertiary health institutions in the state; Federal Medical Centre, Yenagoa and Niger Delta University Teaching Hospital, Okolobiri. The result of this research work revealed the incidences of the receptor status as it occurred among 36 malignant female breast lesions in Bayelsa State as follows; ER+ve=13.8%, ER-ve=86.2%, PR+ve=19.4%, PR-ve=80.6%, HER2+ve=33.3% HER2-ve=66.7%, TR+=13.3% while TR-=55.7%. The statistical analysis of the result revealed that no significant relationship exists between the various age groups and the respective incidences of the receptor status. In the same vein, no significant relationship exists between the respective histopathologic diagnosis of the samples used and the incidences of the respective receptor status except for ER+ve and ER-ve whose incidences were found to have a significant relationship with the histopathologic diagnosis. This by implication means that the incidences of ER+ve and ER-ve respectively maybe dependent on the histopathologic diagnosis at $P < 0.05$. In conclusion, it is worthy of note here that while researches are on to tackle cancers and breast cancer in particular, there is need for even distribution of IHC facility or other molecular studies in the nation because of its role in breast cancer prevention strategies and patient management.

Index Terms -:Surveillance, Breast Cancer, Immunohistochemistry, Estrogen Receptor, Progesterone Receptor, HER-2

Introduction

Breast cancer is the commonest site-specific malignancy affecting women in Nigeria and worldwide with several reports indicating a rising incidence. In Nigeria, it has overtaken cervical cancer as the leading cause of cancer-based mortality in women [1]. Conventionally, it is diagnosed through microscopic evaluation of haematoxylin & Eosin stained sections of the affected tissue. It is furthermore subjected to investigations for the determination of the receptor status. Estrogen receptor (ER), Progesterone receptor (PR) and Human epidermal growth factor receptor-2 (HER-2) are the commonly assessed receptors in breast cancer. Receptor status is a critical assessment for all breast cancer as it encourages therapy specificity and monitoring of patients response to therapy and important for breast cancer prevention strategies [2]. Unfortunately, as important as these parameters are to breast cancer resolution, there is a notable unavailability of receptor status detecting Facilities in most of the health institutions in Nigeria. In Bayelsa State, there is paucity of work on the receptor status of malignant female breast lesions. Hence, the specific objective of the work were to (i) determine the expression of ER, PR and HER-2 in malignant female breast lesion and (ii) ascertain the pattern of occurrence of the respective receptor status in relation to the diagnostic outcome and age.

Literature Review

Most breast tumor markers are either proteins, part of proteins, or hormones. Some breast tumor markers are produced as a result of body's response to breast cancer but these can be frequently found in benign conditions as well. Additionally, there are some tumor markers that are specific for breast cancers, while some others are general. Presently, only three immunohistochemical marker, specifically estrogen receptor, progesterone receptor, and human epidermal growth factor 2 (HER2) levels are measured routinely in every breast cancer [3]. Studies of these markers in Sub-Saharan Africa (SSA) women with breast cancers have had extremely variable findings. Some studies reported percentages of estrogen receptor negative (ERN) tumors to range from 30% to 40% [4] to >70% [5]. In comparison, corresponding percentages in the United States are 35% in breast cancer patients aged 40 and decline to 15% to 20% by age 70, and are slightly higher in black than in white American women [6]. In SSA, for example, in 75 Ghanian breast cancer patients, 76% were ERN based on receptor testing carried out on formalin-fixed paraffin-embedded specimens obtained in Ghana and transported to the United States for receptor assessment [7]. Similarly, in 500 breast cancer tumor blocks used for immunohistochemical analysis from Nigeria and Senegal, half were triple negative, [8]. At the other end of the spectrum, 27% of tumors were ERN among 192 Nigerian breast cancer patients in a setting in which immunohistochemistry (IHC) was routinely conducted prospectively at diagnosis [4]. The latter study is consistent with

recent related results from breast cancers diagnosed in the United States in African-born women, of which 30% of tumors with known receptor status were ERN [9].

The Histological analysis conducted by Adisa *et al* for hormone receptors (estrogen and progesterone receptors), HER-2, and tumor infiltrating macrophages (ATM) on 17 breast cancer cases, obtained from Abia State Teaching hospital (Aba, Nigeria), between November 2008 and October 2009 indicated that majority of cases in this cohort were characterized as high grade (100% were grade III), triple negative (65%), and occur in young women (mean age 47 years) [10]. Other studies have shown that, the frequency of amplification or over expression of Her-2/neu is 10% to 52% in breast with average of 15% to 25% using various molecular and IHC procedure [11]. This supports the work done by Ugiagbe et al who discovered the immunopositivity of breast carcinomas for Her-2 /neu as 10.8% among patients of the University of Benin Teaching Hospital. Jones et al found no statistical significant different in Her-2/neu expression in breast carcinoma occurring in African Americans and Caucasians, having recorded figures of 38.7% & and 40% positivity for Her-2/neu respectively [12]. Also the 25% documented in Jos for Her2/neu over expression is in keeping with most studies [13]. However, a lower level of Her-2/neu expression (8.2%) was recorded in Ile-ife. Nevertheless, only a few studies have been done to ascertain the pattern of Her-2/neu status in African breast cancer cases. Further studies are required to establish the true incidence of Her-2/neu status among the African population [14]. Prati *et al.*, [15] while analyzing 199 cases of breast cancer in California, USA, found a mean age of 53.9 years and 57.6 years for Her-2/neu- positive and Her-2/neu-negative breast cancer patients, respectively. In a similar study, Rosen *et al*.[16] while studying 474 patients with lymph node negative breast cancer in New York, USA, observed that age did not predict or determine the likelihood of Her-2/neu positivity. As an adverse prognostic factor, Her-2/neu positivity has been associated with poorly differentiated high-grade tumors, high proliferation rate, metastasis to lymph node, resistance to certain types of chemotherapy [17]. Her-2/neu overexpression has been recognized as both a maker for aggressive disease and a target for treatment. There is often an inverse relationship between Her-2/neu positivity and hormone receptors. Studies have shown that women with Her-2/neu-positive breast cancers have relatively lower or absent hormone receptors in their tumors.[18] This is probably one of the reasons why women who over overexpress Her-2/neu in their breast cancer are resistant to tamoxifen. [19]. However, anthracycline-based adjuvant therapy is particularly beneficial to these patients [18].

About 35% of women with Her-2/neu positive breast cancer have been found to respond to trastuzumab (Herceptin) therapy (a humanized monoclonal antibody against Her-2,neu. [18]. Studies indicate that combining trastuzumab with either single or multiple chemotherapeutic agents increases the therapeutic efficacy and prolongs patient's survival [20]. Trastuzumab has not been shown to have clinical benefit in Her-2/neu-negative breast cancer [18]. However, trastuzumab has an adverse effect of causing cardiac dy sfunction. It is therefore essential to carefully determine the Her-2/neu status of patients with breast cancer before institution of trastuzumab therapy.

The primary risk factors for breast cancer are female sex and older age, [21]. Other potential risk factors include: genetics, [22], lack of childbearing or lack of breastfeeding, [23] higher levels of certain hormones, [24], certain dietary patterns, and obesity. Recent studies have indicated that exposure to light pollution is a risk factor for the development of breast cancer,[25].

There may be an association between use of oral Contraceptives and the development of premenopausal breast cancer, [26], but whether oral contraceptives use may actually cause premenopausal breast cancer is a matter of debate. If there is indeed a link, the absolute effect is small, [27]. In those with mutations in the breast cancer susceptibility genes BRCA1 or BRCA2, or who have a family history of breast cancer, use of modern oral contraceptives does not appear to affect the risk of breast cancer, [28].

The association between breast feeding and breast cancer has not been clearly determined; some studies have found support for an association while others have not, [29]. In the 1980s, the abortion-breast cancer hypothesis posited that induced abortion increased the risk of developing breast cancer, [30]. This hypothesis was the subject or extensive scientific inquiry which concluded that neither miscarriages nor abortion are associated with a heightened risk for breast cancer, [31].

There is a relationship between diet and breast cancer, including an increased risk with a high fat diet, [32], alcohol intake, [33] and obesity [34] related to higher cholesterol levels.[35] Dietary iodine deficiency may also play a role [36]. Other risk factors include radiation [37] and shift-work [38]. A number of chemicals have also been linked including: polychlorinated biphenyls, polycyclic aromatic hydrocarbons, organic solvents, [39] and a number of pesticides, [40]. Although the radiation from mammography is a low dose, it is estimated that yearly screening from 40 to 80 years of age will cause approximately 223 cases of fatal breast cancer per million women screened,[41].

Some genetic susceptibility may play a minor role in most cases,[42]. Overall however, genetics is believed to be the primary cause of 5-10% of all breast cancer cases, [43]. In those with zero, one or two affected relatives, the risk of breast cancer before the age of 80 is 7.8%, 13.3%, and 21.1% with a subsequent mortality of 2.3%, 4.2%, and 7.6% respectively, [44]. In those with a first degree relative with the disease the risk of breast cancer between the age of 40 and 50 is double that of the general population, [45].

In less than 5% of causes, genetics plays a more significant role by causing a hereditary breast-ovarian cancer syndrome.[42] This mutations account for up to 90% of the total genetic influence with a risk of breast cancer of 60-80% in those affected, [43]. Other significant mutations include: p53 (Li-Fraumeni syndrome), PTEN (Cowden syndrome), and STK 11 (Peutz-Jeghers syndrome), CHEK2, ATM, BRIPI, and PALB2, [43]. In 2012, researchers said that there are four genetically distinct types of the breast cancer and that in each type, hallmark genetic changes lead to many cancers,[46]. Breast changes like atypical ductal hyperplasia as noted in the national cancer institute report in 2014 and lobular carcinoma insitu, [47], found in benign breast conditions such as fibrocystic breast changes are correlated with an increased breast cancer risk. Diabetes mellitus might also increase the risk of breast cancer, [48].

In the United States, 10% to 20% of patients with breast cancer and patients with ovarian cancer have a first or second degree relative with one of these diseases. The familial tendency to develop these cancers is called hereditary breast-ovarian cancer syndrome. The best known of these, the BRCA mutations, confer a lifetime risk of breast

cancer of between 60% and 85% and a lifetime risk of ovarian cancer between 15% and 40%. Some mutations associated with cancer, such as p53, BRCA1 and BRCA2, occur in mechanisms to correct errors in DNA. These mutations are either inherited or acquired after birth. Presumably, they allow further mutations, which allow uncontrolled division, lack of attachment, and metastasis to distant organs, [38]. However there is strong evidence of residual risk variation that goes well beyond hereditary BRCA gene mutations between carrier families. This is caused by unobserved risk factors, [49]. This implicates environmental and other causes as trigger for breast cancers. The inherited mutation in BRCA1 or BRCA2 genes can interfere with repair of DNA cross links and DNA double strand breaks.[15]. The later damages often requires repair by pathways containing BRCA1 and BRCA2, [50]. However, mutations, in BRCA genes account for only 2% to 3% of all breast cancers. Levin et al have noted that cancer may not be inevitable for all carriers of BRCA1and BRCA2 mutations.[51]. About half of hereditary breast-ovarian cancer syndromes involve unknown genes. GATA-3 directly controls the expression of estrogen receptor (ER) and other genes associated with epithelial differentiation, and the loss of GATA-3 leads to loss of differentiation and poor prognosis due to cancer cell invasion and metastasis, [52].

High mammographic breast density, which is a marker of increased risk of developing breast cancer, may not mean an increased risk of death among breast cancer patients, according to a 2012 report of a study involving 9232 women by the national cancer institute, [53].

Younger women tend to have a poorer prognosis than post-menopausal women due to several factors. Their breasts may change with their menstrual cycles, infant nursing, and they may be unaware of changes in their breasts. Therefore, younger women are usually at a more advanced stage when diagnosed. There may also be biologic factors contributing to a higher risk disease recurrence for younger women with breast cancer, [54]Also since breast cancer in males is usually detected at later stages, outcome are typically worse, [55].

Women may reduce their risk of breast cancer by maintaining healthy weight, drinking less alcohol, being physically active and breastfeeding their children. The benefits with moderate exercise such as brisk walking are seen at all age groups including postmenopausal women, [56]. Marine onega-3 polyunsaturated fatty acids appear to reduce the risk, [57].

Removal of both breasts before any cancer has been diagnosed or any suspicious lump or other lesion has appeared (a procedure known as prophylactic bilateral mastectomy), may be considered in people with BRCA1 and BRCA2 mutations, which are associated with a substantially heightened risk for an eventual diagnosis of breast cancer, [58]. BRCA testing is recommended in those with a high family risk after genetic counseling but not recommended routinely, [59]. This is because there are many different forms of changes in BRCA genes, ranging from harmless polymorphisms to obviously dangerous frame shift mutations. The effect of most identifiable changes in the genes is uncertain. Testing in an average-risk person is particularly likely to return one of these indeterminate, useless results.

The selective estrogen receptor modulators (Such as tamoxifen) reduce the risk of breast cancer but increase the risk of thromboembolism and endometrial cancer, [60]. However, there is not overall change in the risk of death, [61] . They are thus not recommended for the prevention of breast cancer in women at average risk but may be offered for those at high risk, [62]. The benefit of breast cancer education continues for at least five years after stopping a course of treatment with these medications, [61].

Knowledge of the receptor-status distribution among breast cancer patients in Bayelsa State is needed, given the paucity of literature on this subject.

METHODOLOGY

This was an experimental study conducted in Federal Medical Centre Yenagoa and Niger Delta University Teaching Hospital Okolobiri, Bayelsa State. Previously diagnosed malignant female breast lesion cases between 2009 and 2011 were retrieved from the tissue block archives and their ER, PR and HER2 statuses determined. A total of 36 formalin fixed paraffin embedded (FFPE) tissue blocks were used for the study. The investigations were done using the immunoperoxidase technique which involved the following stages; sectioning, deparaffinization, rehydration, epitope retrieval blocking of endogenous peroxidase, application of primary antibody, application of Horseradish peroxidase labeled secondary antibody, application of chromogen-substrate complex and counterstaining. The sections were thereafter dehydrated, cleared and mounted for light microscopy. Lack of nuclear staining of malignant cells was regarded as negative for ER and PR while nuclear staining of 1% and above of malignant cells was taken as positive for ER and PR respectively. Lack of membrane staining or weak, incomplete membrane staining in any proportion of malignant cells was regarded as HER-2negative while uniform intense membrane staining of > 10% was regarded as HER-2 positive. Data were analyzed using the chi-square. Probability was considered significant at $P< 0.05$.

RESULT

The positive receptor status occurred as follows: ER, 13.8% PR, 19.4% and HER2, 33.3% while the negative receptor status occurrences were 86.2% for ER, 80.6% for PR and 66.7% for HER2 as shown figure 1. The least occurrences of both the positive and negative receptor status occurred mostly at 66 years and above with ER, 0%, PR, 0% and HER2, 1% for the positive receptor status and ER, 11.2%, PR, 11.1% and HER2, 8.3% for the negative status (as shown in Table 1). However, no significant relationship was found to exist between the occurrence of these receptor status and age.

When the positive receptor status occurrences were related with the histopathological subtype, it revealed that the highest occurrences of ER were in Mucinous carcinoma with the value of 5.5% (Table 2.1), PR and HER2 were in Infiltrating Ductal Carcinoma with the values of 11.1% and 22.2% (Table 2.2 & 2.3) respectively. The highest occurrences of all the negative receptor status were in infiltrating ductal carcinoma with ER. 63.9%, PR, 55.5% and HER2, 44.4% Table 2.1, 2.2 &2.3)

There are non-occurrence of ER and PR positive status in insitu papillary carcinoma, medullary carcinoma and infiltrating lobular carcinoma, HER-2- positive status in medullary carcinoma, ER and PR negative status in ductal carcinoma lobular carcinoma and ductal carcinoma insitu. The positive and negative ER statuses were the only status found to have a significant relationship with the diagnostic outcome.

TABLE 1: showing the pattern of occurrence of the respective receptor status in relationship to age.

Age-Groups	Total Number of Cases Treated	%ER+ve Cases	% ER-ve Cases	% PR+ve Cases	% PR-ve Cases	% HER-2 Cases	% HER-2-ve Cases	Triple + ve	Triple - ve
20-35 yrs	7(19.4%)	0 (0%)	7 (19.4%)	1 (2.8%)	6 (16.88&)	2 (5.5%)	5 (13.9%)	0 (0%)	4 (11.1%)
36-45yrs	12 (33.3%)	3 (8.3%)	9 (25%)	4 (11.1%)	8 (22.2%)	5 (13.9%)	7 (19.5%)	2 5.5%)	6 (16.8%)
46-65yrs	13 (36.2%)	2 (5.5%)	11 (30.5%)	2 (5.5%)	11 (30.5%)	4 (11.1%)	9 (25%)	1 (2.8%)	7 (19.5%)
>66yrs	4 (11.1%)	0 (0%)	4 (11.2%)	0 (0%)	4 (11.1%)	1 (2.8%)	3 (8.3%)	0 (0%)	3 (8.3%)
Total	36	5 (13.8%)	31 (86.2%)	7 (19.4%)	29 (80.6%)	12 (33.3%)	24(66.7%)	3 (8.3%)	20 (55.7%)

PEARSON'S CHI SQUARE VALUES FOR THE VARIOUS RECEPTOR STATUS ARE: ERP & ERN = 0.3386, PRN & PRP = 0.440, HER2N & HER2P = 0.894, TRN = 0.552, RELATIONSHIP SIGNIFICANT AT P > 0.05

TABLE 2.1: SHOWING THE PATTERN OF DISTRIBUTION OF THE ESTROGEN RECEPTOR STATUS IN RELATIONSHIP TO THE MADE HISTOPATHOLOGICAL SUBTYPE.

PEARSON'S CHI SQUARE VALUES FOR ERN & ERP = 0.018 RESPECTIVELY, RELATIONSHIP SIGNIFICANT AT P < 0.05 KEY: IDC-INFILTERATING DUCTAL CARCINOMA, MUC. CA-MUNCINOUS CARCINOMA, INSITU PC-INSITU PAPILLARY CARCINOMA, MED CA-MEDULLARY CARCINOMA, INF LC – INFILTRATING LOBULAR CARCINOMA, DUC IS – DUCTAL CARCINOMA INSITU, INV DC-INVASIVE DUCTAL CARCINOMA, LOB CA-LOBULAR CARCINOMA

TABLE 2.2: SHOWING THE PATTERN OF DISTRIBUTION OF THE PROGESTERONE RECEPTOR STATUS IN RELATIONSHIP TO THE MADE HISTOPATHOLOGICAL SUBTYPE

		Histological Diagnosis								
		IDC	MUC CA	INSITU PC	MED CA	INF LC	DUC IS	INV DC	LOB CA	TOTAL
PR Receptor	Negative	20 (55.5%)	5 (13.8%)	1 (2.8%)	1 (2.8%)	1 (2.8%)	0 (0%)	1 (2.%)	0 (0%)	29 (80.5%
	Positive	4 (11.1%)	1 (2.8%)	0 (0%)	0 (0%)	0 (0%)	1 (2.8%)	0 (0%)	1 (2.8%)	7 (17.5%)
Total		24	6	1	1	1	1	1	1	36

PEARSON'S CHI SQUARE VALUES FOR PRN & PRP = 0.225 RESPECTIVELY RELATIONSHIP INSIGNIFICANT AT P > 0.05

TABLE 2.3: SHOWING THE PATTERN OF DISTRIBUTION OF THE HUMAN EPIDERMAL GROWTH FACTOR RECEPTOR-2 STATUS IN RELATIONSHIP TO THE MADE HISTOPATHOLOGICAL SUBTYPE.

		Histological Diagnosis								
		IDC	MUC CA	INSITU PC	MED CA	INF LC	DUC IS	INV DC	LOB CA	TOTAL
HER-2 Receptor	Negative	16 (44.4%)	5 (13.8 %)	0 (0%)	1 (2.8%)	0 (0%)	0 (0%)	1 (2.%)	1 (2.8%)	24 (66.56%
	Positive	8 (22.2%)	1 (2.8%)	1 (2.8%)	0 (0%)	1 (2.8%)	1 (2.8%)	0 (0%)	1 (2.8%)	12 (33.3%)
Total		24	6	1	1	I	1	1	1	36

PEARSON'S CHI SQUARE VALUES FOR HER-2N & HER-2 P = 0.311 RESPECTIVELY RELATIONSHIP INSGNIFICANT AT P > 0.05

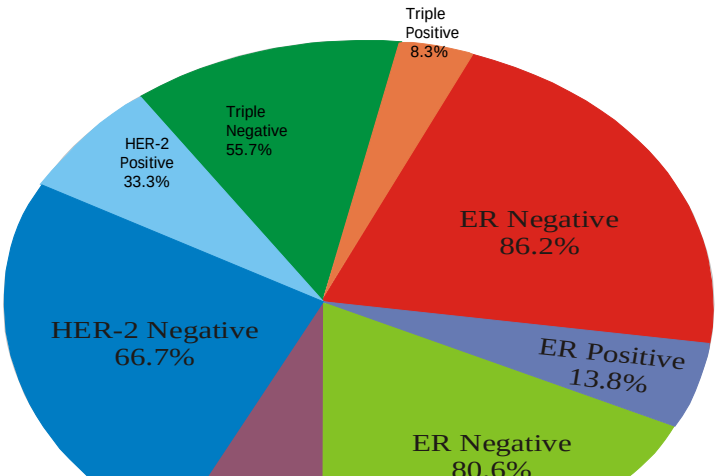


FIGURE 1.0

PIE CHART SHOWING THE INCIDENCES OF THE RESPECTIVE RECEPTOR STATUS RESPECTIVE RECEPTOR STATUS

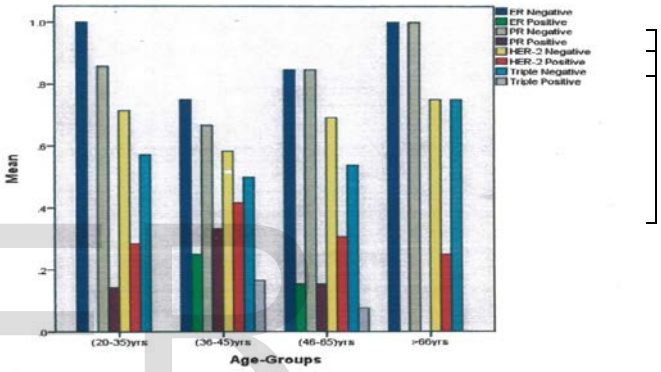
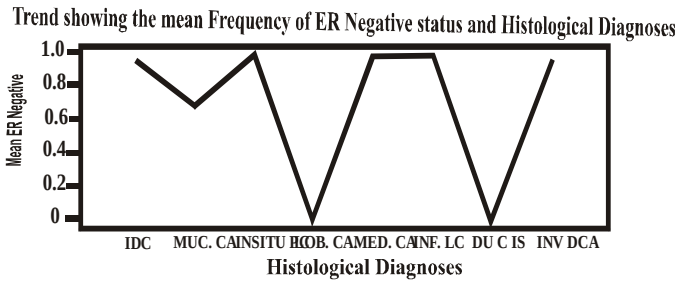


FIGURE 2.0 A BAR CHART SHOWING A COMPARATIVE PRESENTATION OF THE MEAN FRQUENCIES OF THE RECEPTOR STATUS IN RELATIONSHIP TO AGE RANGES RESPECTIVELY

FIG. 3: GRAPHS SHOWING THE TREND OF OCCURRENCE OF THE RESPECTIVE RECEPTOR STATUS IN RELATIONSHIP TO THE MADE DIAGNOSES



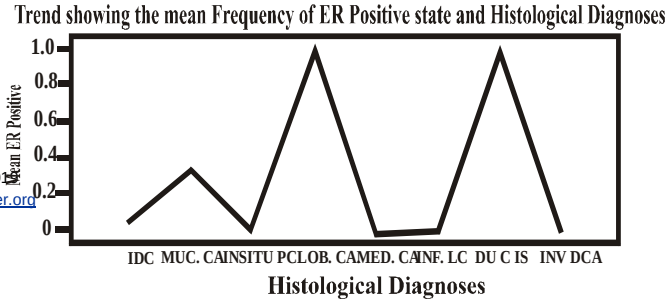
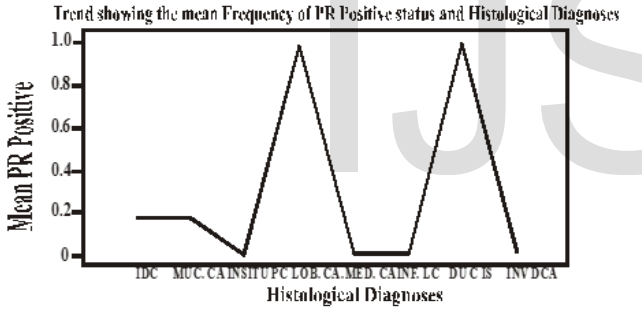
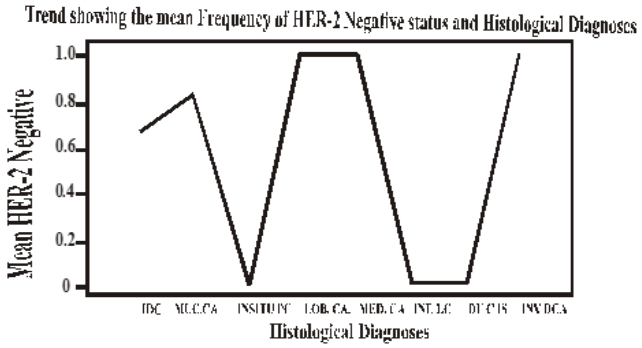
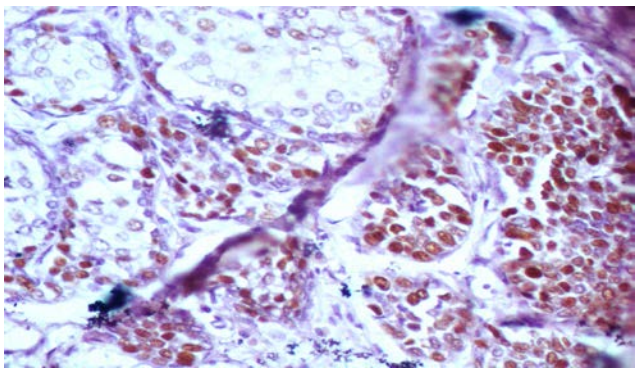


FIG 4.0 Section of breast tissue treated with immunoperoxidase staining techniqueshowing strong nuclear immunostaining or Estrongen Receptor







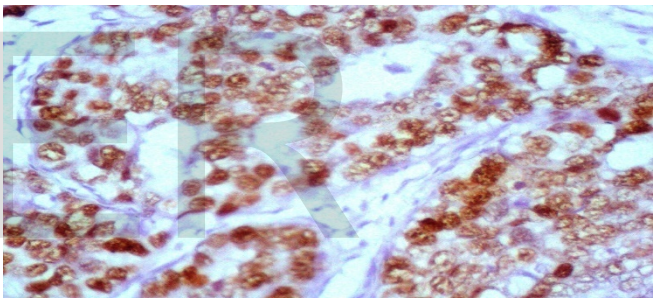


FIG. 6.0 Section of Breast Tissue Treated with Immunoperoxidase staining technique. Showing strong membrane immunostaining for progesterone receptor.

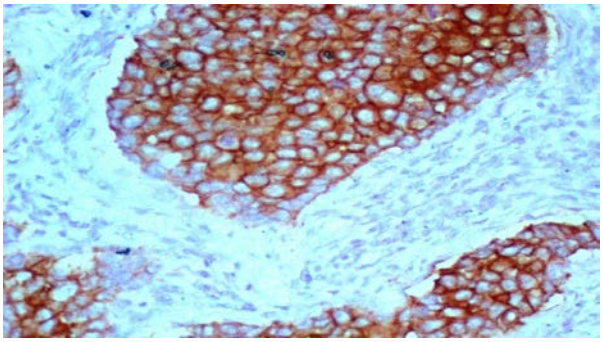


FIG. 8.0 Section of Breast Tissue Treated with Immunoperoxidase staining technique. showing strong membrane immunostaining HER-2/neu.

DISCUSSION

The importance of receptor status evaluation cannot be overemphasized because it is a tool needed to excite hope in the minds of despairing women diagnosed positive for breast cancer. Cancer has been a serious health menace that requires solution and in a bid to achieve this, the place of a proper epidemiological data bank cannot be sidetracked. This is so because it gives a wide view of possible areas and angles which can serve as link to a solution. This study has contributed its quota to adding to this epidemiology databank and has also provided a means of comparing the Bayelsa environment with other areas in Nigeria and the world at large. This is achieved during the course of comparing results obtained in the later region and other areas. Studies of these markers in women with breast cancer in Sub-Saharan African (SSA) have had extremely variable findings; reported percentages of estrogen negative (ERN) tumours ranges from 30% to 40% [4] to > 70% [13].In comparison, corresponding percentages in the United States are 35% of breast cancer patients aged 40 and decline to 15% - 20% by age 70 and are slightly higher in Black than in White American women [6].

Comparatively, the results obtained in this study are relatively in line with what is obtained in other parts of Nigeria and in the world at large.

The incidence rate of 87.5% realized for ERN is in line with previous findings of a research carried out on African women which gave the range of the incidence of ERN as spanning from 30% to >70%[5].

Also the incidence rates of 35% realized from this research for Her2 positive cases is in accord with the 10-52% range recorded for work studies worldwide using various molecular and immunohistochemical procedure [11].

Moreover, the average mean age for the various receptors status were evaluated and found to be 51 years for ER positive, 44.8 years for PR positive and 45.2 years for Her-2 positive. The 47.5 years for ER negative, 48.6 years for PR negative and 49.4 years for Her-2 negative cases respectively are somewhat close to the 53.9 and 57.6 years recorded by Prati et al who discovered this mean ages while analyzing 199 cases of breast cancer in California, USA [15].

RECOMMENDATIONS

All hands must be on deck to ensure the even distribution of immunohistochemical or other forms of receptor status detecting facilities in the country. Also health care providers involved in managing breast cancer patients should imbibe the culture of using target oriented therapeutic approach in managing their patients. Women diagnosed positive for breast cancer should be given hope for survival and shielded from the wrong psychological and societal attitudes to cancer by the reorientation of the later audience. A mass literacy campaign should be encouraged to dissuade women who are at risk of developing cancer from indulging in life style that may make them vulnerable to this monster.

Since genetic mutation play a role in breast carcinogenesis, molecular diagnostic facilities for detecting such mutations should be made available alongside the receptor status detecting facilities nationwide. This to enable early detection of cancer tendencies and nip it in the bud before it springs up.

As a way of advancing in this research, further work is recommended to find out if any significant relationship exists between environment and the incidences of these receptor status. Finally, the relationship between the receptor status and the histological grading is also recommended for research.

CONCLUSION

Although researches are on to break new grounds for breast cancer resolution, the fight against breast cancer cannot be actualized without the availability of immunohistochemistry or other receptor status detecting facilities in the nation. This will assist in targeted therapy for effective management.

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