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Original Research

Comparison Of Risk Factors and Clinicopathological Features Between Pre- and Post-Menopausal Patients with Breast Cancer

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Abstract

Background: Breast cancer is the most common cancer affecting women globally with an estimated 2.3 million new cases in 2020. In Nigeria, it constitutes about 12% of all new cancers and 25% of all cancers in women. The risk factors of breast cancer include both non-modifiable and modifiable factors. There are clinical and biological differences between patients with pre-menopausal and post-menopausal breast cancer. This study aims to evaluate the differences in risk factors, disease presentation and tumour characteristics between premenopausal and postmenopausal breast cancer patients.
Methodology: This is a 2-year prospective cross-sectional study conducted at the University of Port Harcourt Teaching Hospital between 1st January 2021 and 31st December 2022. All consecutive patients who presented with breast cancer that was histologically confirmed and gave informed consent were included in the study. Patients were divided into two groups which are pre-menopausal and post-menopausal based on their menopausal status. Relevant data were extracted and recorded in a data extraction form. Analysis was done using Statistical Product and Service Solution version 26.
Results: One hundred and thirty-three patients were recruited for the study. Seventy (52.6%) of them were pre-menopausal and 63 (47.4%) were post-menopausal. Their ages were from 19 to 78 with a mean of 46.94 ± 11.93. The peak age was 41-50 years and 30.8% of the patients were within this age range. Only late age at first pregnancy was significantly associated with pre-menopausal breast cancer.
Conclusion: Similar risk factors and tumour characteristics with a higher prevalence of triple-negative breast cancer were found in both groups but late age at first pregnancy occurred significantly in pre-menopausal breast cancer patients.

Keywords: *Breast Cancer; Pre-Menopausal; Post-Menopausal.*

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Introduction

Breast cancer is the most common cancer affecting women globally with an estimated 2.3 million new cases in 2020[1]. In Nigeria, it constitutes about 12% of all new cancers and 25% of all cancers in women[2]. The risk factors of breast cancer include both non-modifiable and modifiable factors. The non-modifiable risk factors include early menarche (< 12 years), late menopause (> 55 years), female sex, age, genetic factors, family history, personal history of breast cancer, and dense breast while the modifiable risk factors include nulliparity, late pregnancy (after 35 years), recent use of oral contraceptive pills, hormone replacement therapy, absence of breastfeeding, obesity and alcohol[3-5]. The protective factors of breast cancer include short duration of the effect of oestrogen, moderate exercise, longer periods of lactation and breastfeeding[6]. The protective effect of multiparity decreases along with post-menopausal breast cancer while the risk reduces with breast feeding[7].There are clinical and biological differences between patients with pre-menopausal and post-menopausal breast cancer. Pre-menopausal breast cancer develops an early peak while the peak in post-menopausal cancer is later in life[8].

Even though some studies have reported that menopause affects the hormonal receptors of breast cancer[8], further studies especially in Sub-Saharan Africa are needed to arrive at a conclusion. This study aimed to evaluate the differences in risk factors, disease presentation and tumour characteristics between premenopausal and postmenopausal breast cancer.

Patients and Methods

This was a 2-year prospective cross-sectional study conducted at the University of Port Harcourt Teaching Hospital between 1st January 2021 and 31st December 2022. All consecutive patients diagnosed with breast cancer who gave informed consent were included in the study. Relevant information which included risk factors, stage at presentation and tumor characteristics (histological type, grade and immunohistochemistry) were extracted and recorded in a data extraction form that was designed for the study. Tumours positive to oestrogen and/or progesterone receptors are regarded as hormone receptor-positive tumours. Patients were divided into two groups which are pre-menopausal and post-menopausal based on their menopausal status. Post-menopausal patients were regarded as those who had no menstrual flow for about 12 months and the rest were considered pre-menopausal. The association of BMI and hormonal risk factors like parity, early menarche, late age at first pregnancy, family history of breast cancer, oral contraceptive pills, and hormone replacement therapy with breast cancer was evaluated between the two groups. Exclusion criteria were male breast cancer, prior personal history of other cancers and previous hysterectomy. Statistical analysis was done using Statistical Package for Social Sciences (SPSS) version 26. The differences in risk factors and clinicopathological features were analyzed using the student's t-test in cases of quantitative variables and chi-square and Fisher's exact tests in categorical variables. P values of < 0.05 were considered significant.

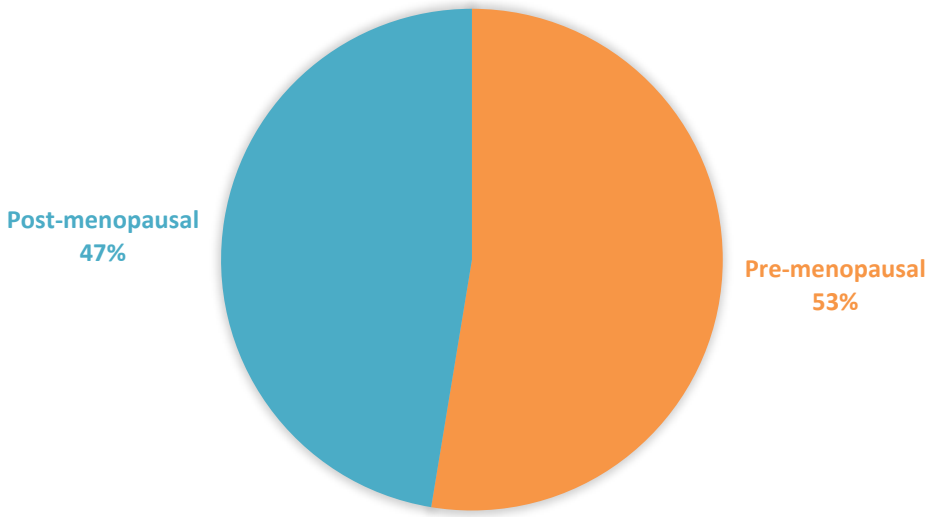
Results

One hundred and thirty-three patients were recruited for the study. Seventy (52.6%) of them were pre-menopausal and 63 (47.4%) were post-menopausal. Their ages were from 19 to 78 with a mean of 46.94 ± 11.93. See Figure 2. The peak age was 41-50 years with 30.8% of the patients within this age range. The ages for pre-menopausal patients were from 19 to 47 with a mean of 37.49 ± 6.18 and that for post-menopausal patients 45-78 with a mean of 57.02 ± 7.75. The age range of pre- and post-menopausal patients are as shown in Figures 3 and 4.

Only late age at first pregnancy was significantly associated with pre-menopausal breast cancer (P = 0.04). The results are presented in Table 1. Overall, 87 (65.4%) patients presented with stage 3 disease of which 43 (49.4%) of them were pre-menopausal and 44 (50.6%) post-menopausal. None of the patients presented in stage 1. There was no significant difference in the stage of presentation between the two groups (P = 0.189). See Table 2. Most of the patients (45 pre-menopausal and 47 post-menopausal) presented with grade 2 tumours. There was no significant difference in the histological grades between the two groups (P = 0.262). See Table 3. Regarding immunohistochemistry, 109 (81.2%) patients had triple-negative breast cancer while 6 (4.5%) patients had human epidermal growth factor receptor-2 (Her-2) positive disease. These are 5 (7.12%) pre-menopausal and 1 (1.6%) post-menopausal patient. However, there was no significant difference in the immunohistochemistry between the two groups (P = 0.296). See Table 4.

The predominant histological type was invasive ductal carcinoma, and this was seen in 82% of the patients. Fifty-eight (82.9%) of the pre-menopausal and 5 (81.0%) of the post-menopausal patients had invasive ductal carcinoma. No significant difference between the two groups (P = 0.847). See Table 5.

FIGURE 1: NUMBER OF PATIENTS



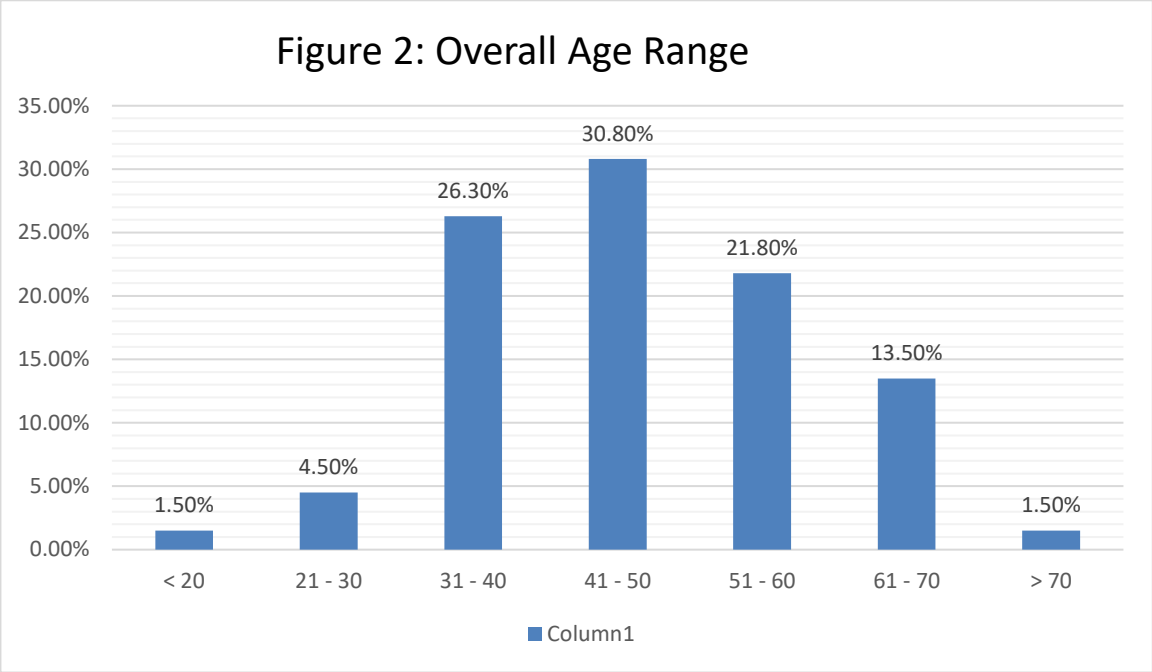


Figure 2: Overall Age Range
35.00%
30.00%
25.00%
20.00%
15.00%
10.00%
5.00%
0.00%
1.50%
4.50%
26.30%
30.80%
21.80%
13.50%
1.50%
< 20
21 - 30
31 - 40
41 - 50
51 - 60
61 - 70
> 70
Column1

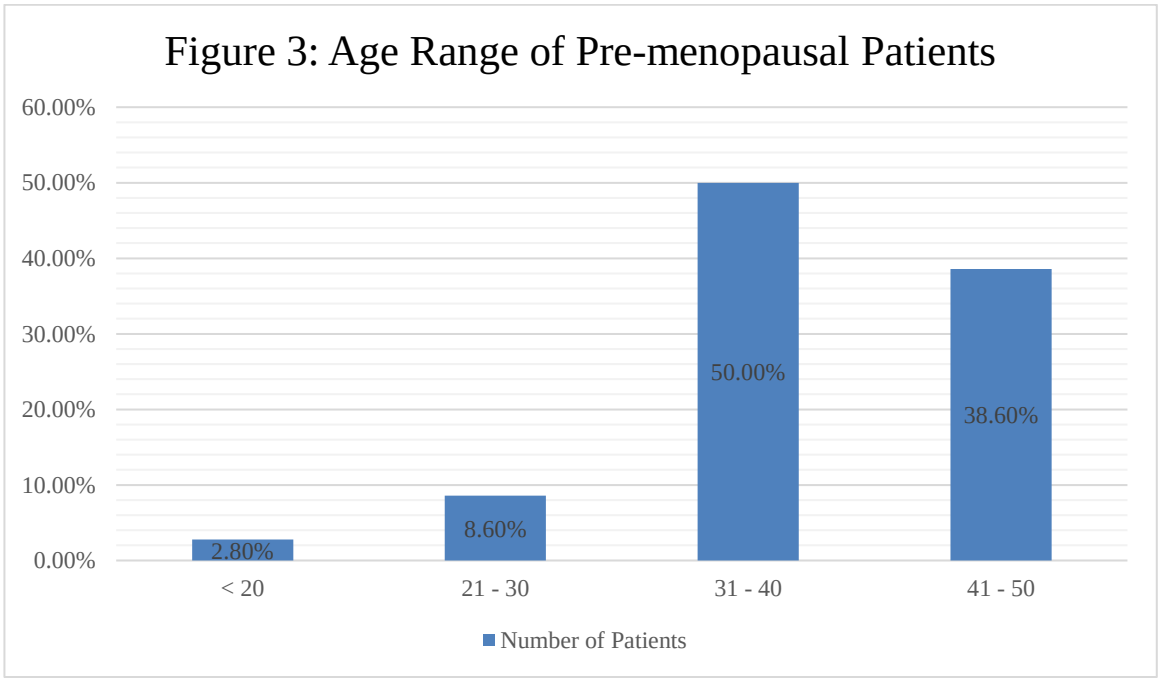


Figure 3: Age Range of Pre-menopausal Patients
60.00%
50.00%
40.00%
30.00%
20.00%
10.00%
0.00%
2.80%
8.60%
50.00%
38.60%
< 20
21 - 30
31 - 40
41 - 50
Number of Patients

Table 1: Comparison of Risk Factors for breast cancer among study subjects

Risk Factors		Pre-menopausal N (%)	Post-menopausal N (%)	Total N (%)	P
Parity	Nulliparous Parous Total	1(1.4) 69(95.6) 70(100.0)	1(1.6) 62(98.4) 63(100.0)	2(1.5) 131(98.5) 133(100.0)	0.06
Age at Menarche	< 12 ≥ 12 Total	10(14.3) 60(85.7) 70(100.0)	9(14.3) 54(85.7) 63(100.0)	19(14.3) 114(85.7) 133(100.1)	1.000
Age of first Pregnancy	< 18 18 – 35 >35 Total	0(0) 44(62.9) 26(37.1) 70(100.0)	1(1.6) 53(84.1) 9(14.3) 63(100.0)	1(0.8) 97(72.9) 35(26.3) 133(100.00	0.04
Family History	Negative Positive Total	58(82.5) 12(17.1) 70(100)	51(81.0) 12(17.0) 63(100.0)	109(82.0) 24(18.0) 133(100.0)	0.775
ORT	NO YES Total	63(90) 7(10) 70(100.0)	58(92.1) 5(7.9) 63(100.0)	121(91.0) 12(9.0) 133(100.0)	0.678
HRT	NO YES Total	69(98.6) 1(1.4) 70(100.0)	62(98.4) 1(1.6) 63(100.0)	131(98.5) 2(1.5) 133(100.0)	1.000
BMI	<30 ≥ 30 Total	42(60.0) 28(40.0) 70(100.0)	44(69.8) 19(30.2) 63(100.0)	86(64.7) 47(35.3) 133(100.0)	0.250

Table 2: Analysis of stage of disease among study participants

Stage	Pre-menopausal N (%)	Post-menopausal N (%)	Total N (%)	P
1	0(0)	0(0)	0(0)	0.189
2	13(18.6)	5(7.9)	18(13.5)	
3	43(61.4)	44(69.8)	87(65.4	
4	14(20.0)	14(22.2)	28(21.1)	
Total	70(100.0)	63(100.0)	133(100.0)	

Table 3: Comparison of grade of the tumour among study participants

Grade	Pre-menopausal N (%)	Post-menopausal N (%)	Total N (%)	P
1	18(25.7)	9(14.3)	27(0.3)	0.262
2	45(64.8)	47(74.6)	92(69.2)	
3	7(10.0)	7(11.1)	14(10.5)	
Total	70(100.0)	63(100.0)	133(100.0)	

Table 4: Comparison of immunohistochemistry pattern among study participants

Receptors	Pre-menopausal N (%)	Post-menopausal N (%)	Total N (%)	P
Hormone receptor-positive	9(12.9)	10(15.4)	19(14.3)	0.296
HER -2 Positive	5(7.1)	1(1.6)	6(4.5)	
Triple Negative	56(80.0)	52(82.5)	108(81.2)	
Total	70(100.0)	63(100.0)	133(100.0)	

Table 5: Comparison of histological findings among study participants

Histological type	Pre-menopausal N (%)	Post-menopausal N (%)	Total N (%)	P
Invasive Ductal Carcinoma	58(82.9)	51(81.0)	109(82.0)	0.847
Invasive Lobular Carcinoma	7(10.0)	5(7.9)	12(9.0)	
Ductal Carcinoma in situ	4(5.7)	5(7.9)	9(6.8)	
Lobular Carcinoma in situ	1(1.4)	2(3.2)	3(2.3)	
Total	70(100.0)	63(100.0)	133(100.0)	

Discussion

Some studies[8,9] have previously distinguished between pre- and post-menopausal breast cancer based on differences in risk factors like age, parity, age at first pregnancy, etc. Pre-menopausal patients with breast cancer predominate in this study accounting for 52.6 % of cases. Similar rates were found in other studies[8,9]. It has been documented those differences in the pathogenesis of breast cancer between pre-menopausal and post-menopausal patients relating to ethnicity, age at menarche, marital status, number of pregnancies, number of births and history of breastfeeding may be responsible for the dominance of pre-menopausal breast cancer[10,11].

The mean age of women with breast cancer in developing countries is about a decade lower than that in developed countries, leading to a higher disease burden in younger patients[12-14]. In agreement with these studies, most of our patients were between 31 and 50 years of age[15]. About 63.1% of our patients had breast cancer before the age of 50 years while only 23% of women in the western population present with breast cancer are younger than 50 years of age[16].

Previous studies have presented inconsistent reports on the association of risk factors with both pre- and post-menopausal breast cancer. A prospective cross-sectional study in India reported early menarche, older age at first pregnancy and nulliparity to be more common in pre-menopausal breast cancer patients. Butt et al[17] reported no significant difference in risk factors between pre- and post-menopausal breast cancers except nulliparity which increases the risk of post-menopausal breast cancer. In this study, only older age at first pregnancy was significantly more common in pre-menopausal patients. This tallies with the finding of Zhang et al[18] who reported an association between older age at first pregnancy and breast cancer in pre-menopausal patients. Furthermore, previous studies have documented that early age at first full-term pregnancy is inversely related to breast cancer risk[19]. First full-term pregnancy at an early age

induces irreversible changes that either render the breast tissue less susceptible to induction of cancer cells or reduce the carcinogenic stimulus on the breast[20].

The majority of both pre- and post-menopausal patients (> 60%) presented with stage 3 disease which agrees with the findings from other studies[4]. There was no significant difference between either groups. None of the groups had any patients that presented with stage 1 disease. This reflects the low awareness of the disease by the population and inadequate public health campaigns by the health authorities against breast cancer.

The grade of the tumour among the pre-menopausal patients was 64.8% for grade 2 and 10% for grade 3 while it was 74.6% and 11.1% for grade 2 and 3 tumours respectively for post-menopausal patients. Similar findings have been reported in other centres in the West African Sub Region[21,22]. It has been documented that triple-negative breast cancer is the most common molecular subtype in premenopausal African American and African women compared to women of European descent[23]. In this study, 80% of pre-menopausal patients had triple-negative breast cancer while Her-2 positive cases accounted for 7.1% and hormone receptor-positive 12.9%. This same pattern was observed in post-menopausal patients who recorded 82.5%, 1.6% and 15.9% for triple-negative, Her 2 positive and hormone receptor-positive breast cancer patients respectively and the difference was not statistically significant. This finding agreed with other findings[22-24].

Invasive ductal carcinoma remains the most common histological type in both pre- and post-menopausal breast cancer[8]. This was demonstrated in our study where invasive ductal carcinoma was seen in 82.9% and 81% of pre- and post-menopausal patients respectively.

Conclusion

Similar risk factors and tumour characteristics with a higher prevalence of triple-negative breast cancer were found in both groups but late age at first pregnancy occurred significantly in pre-menopausal breast cancer patients. An increase in public health campaigns and the introduction of breast cancer screening programmes will result in a presentation in the early stages.

References

1. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, Bray F. Global Cancer Statistics 2020. GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 cancers in 185 countries. CA Cancer J. Clin 2021; 71: 209-249.
2. Wichendu PN, Dodiyi-Manuel A. Advanced breast cancer in Nigeria: A single centre experience. Afr J Biol Health Res 2021; 4: 51-56.
3. Henderson IC. Risk factors for breast cancer development. Cancer 1993; 71 (6 Suppl): 2127-2140.
4. Surakasula A, Nagarjunapu GC, Raghavaiah KV. A comparative study of pre-menopausal breast cancer: Risk factors, presentation, characteristics and management. J Res Pharm Pract 2014; 3: 12-18.
5. Dodiyi-Manuel A, Wakama IE. Predispositions of carcinoma of the breast: A review. Nig J Med 2014; 23: 7-12.
6. Kruk I. Lifetime physical activity and the risk of breast cancer: a case-controlled study. Cancer Detect Prev 2007; 31: 18-28.
7. Campbell KL, Foster Schubert KE, Alfano CM, Wang C, Wang C, Duggan CR, et al. Reduced calorie dietary weight loss, exercise and sex hormones in post-menopausal women: randomized controlled trial. J Clin Oncol 2012; 30: 2314-2326.

8. Kocaoz S, Korukluoglu B, Parlak O, Dogan HT, Erdogan F. Comparison of clinicopathological features and treatment between pre- and post-menopausal female breast cancer patients: a retrospective study. Menopause Rev 2019; 18: 1-6.
9. Gharaibeh M, Al-Obeisat S, Hattab J. Severity of menopausal symptoms of Jordanian women. Climacteric 2010; 13: 385-394.
10. Gao YT, Shu XO, Dai Q, Potter JD, Brinton LA, Wen W, et al. Association of menstrual and reproductive factors with breast cancer risk: results from the Shangai breast cancer study. Int J Epidemiol 2000; 87: 295-300.
11. Bao PP, Shu XO, Gao YT, Zheng Y, Cai H, Deming SL, et al. Association of hormone-related characteristics and breast cancer risk by estrogen/progesterone receptor status in the Shangai breast cancer study. Am J Epidemiol 2011; 174: 661-671.
12. Olaogun JG, Omotayo JA, Ige JT, Omonisi AE, Akute OO, Aduayi OS. Socio-demographic pattern of presentation and management outcome. PAMJ 2020; 36: 363.
13. Rahman GA, Olatoke SA, Agodirin SO, Adeniji KA. Socio-demographic and clinical profile of immuno-histochemically confirmed breast cancer in a resource-limited country. PAMJ 2014; 17: 182.
14. Nimbalkar VP, Rajarajan S, VP S, Alexander A, Kalure R, Selvam S, et al. A comparative analysis of clinicopathological features and survival between pre- and post-menopausal breast cancer from an Indian cohort. Sci Rep 2023; 13: 3938.
15. Pathy NB, Yip CH, Taib NA, Hartman M, Saxena N, Lau P, et al. Breast cancer in a multiethnic Asian setting: Results from the Singapore-Malaysia hospital-based breast cancer registry. Breast 2011; 20 (suppl 2): S75-S80.
16. Edge S, Byrd DR, Compton CC, Fritz AG, Greene FL, Trotti A (editors). 7th ed. New York: Springer; 2010. AJCC Cancer Staging Manual; PP 347-369.
17. Butt Z, Haider SF, Arif S. A comparison between pre-menopausal and post-menopausal women. J Res Pharm. Pract 2014; 3: 12-18.
18. Zhang JY, Wang MX, Wang X, Li YL, Liang ZZ, Lin Y, et al. Association of reproductive factors with breast cancer prognosis and the modifying effects of menopausal status. Cancer Med 2020; 9:385-393.
19. Chie WC, Hsieh C, Newcomb PA, Longnecker MP, Mittendorf R, Greenberg ER, et al. Age at any full-term pregnancy and breast cancer risk. Am J Epidemiol 2000; 151: 715-722.
20. Kapil U, Bhodoria AS, Sareen N, Singh P, Dwivedi SN. Reproductive factors and risk of breast cancer: A review. Ind J Cancer 2014; 51: 571-576.
21. Bosompem K, Yorke J, Buckman TA, Brenu SG, Nyantakyi M, Somiah-Kwaw F, et al. Comparative analysis of breast cancer characteristics in young pre-menopausal and post-menopausal women in Ghana. Sci Rep 2024; 14: 2704.
22. Gukas ID, Jennings BA, Mandong BM, Igun GO, Girling AC, Manasseh AN, et al. Clinicopathological features and molecular markers of breast cancer in Jos, Nigeria. West Afr J Med 2005; 24: 209-213.
23. Dietze EC, Sistrunk C, Miranda-Carboni G, O'regan R, Seewaldt VL. Triple-negative breast cancer in African-American women: Disparities versus biology. Nat Rev Cancer 2015; 15: 248-254.
24. Nyagol J, Nyongo A, Byakika B, Muchiri L. Routine assessment of hormone receptor and her-2/neu status underscores the need for more therapeutic targets in Kenyan women with breast cancer. Anal Quant Cytol Histol 2006; 28: 97-103.