

Profile of female breast lesions along with histological grading and receptor study of malignant lesion**Hina Parikh*, Nupur Rastogi***Tertiary care center and medical college Baroda, Department of Pathology, Vadodara, Gujarat, India*

Received: 22-11-2019 / Revised: 28-01-2020 / Accepted: 05-02-2020

ABSTRACT

Background: The present study was done to understand the incidence and type of breast lesions along with histological grading of malignant lesions in correlation with IHC receptor, in Histopathology department of Baroda medical college, Gujarat, India between December 2017 to October 2018. **Method:** All patients of all age groups with breast lesions were included in the study. Resected specimen and biopsies of breast lesions were submitted to the Histopathology section, Baroda Medical College for histopathological examination. H & E sections were studied and most suitable tissue block was selected for IHC evaluation in malignant cases. **Results:** Out of 152 cases, 76 were benign, 10 were of Inflammatory pathology, 67 were malignant and 64 cases were submitted for IHC. Out of 46 MRM cases of breast carcinoma in this study, Grading was done only in 43 cases, as 1 case was of Invasive lobular carcinoma and 2 cases were of Metaplastic carcinoma. Grade I tumors show 75% positivity in IHC groups {ER/PR+, Her2-}, while 35.48% of Grade II tumors show {ER/PR+, Her2-} and 50% Grade III tumors show {ER/PR-, Her2-}. **Conclusion:** The spectrum of breast lesions consists of benign breast lesions as well as malignant breast lesions. Fortunately, most of the breast lesions are diagnosed as benign breast lesions. Breast carcinoma shows heterogeneity in its clinical behavior. Prognosis and management of breast carcinoma are influenced by classic variables such as histological type and grade, stage, tumor size, lymph node status, hormone receptor status of Estrogen (ER), Progesterone (PR) and Human epidermal growth factor receptor 2 (Her2/neu)

Key word: Breast lesions, Breast malignancy, Histological grade, Immuno Histochemistry.

©2020 The Author(s). This is an open access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

INTRODUCTION

The burden of breast cancer is increasing in both developed and developing countries, and in many regions of the world, it is the most frequently occurring malignant disease in women; comprising 18% of all female cancers, and worldwide, breast cancer is the fifth most common cause of cancer mortality. [1] In 2008, approximately 1.4 million women were diagnosed with breast cancer worldwide with a corresponding of 460,000 deaths. [2] In India, breast carcinoma forms the second most common malignancy after cervical carcinoma and is detected in 20/1,00,000 women. [3,4] Incidence of breast carcinoma is low in India compared to western countries, but it is associated with poor prognosis and high mortality, may be due to late presentation at advanced stages. [5]

The spectrum of breast lesions consists of benign breast lesions as well as malignant breast lesions. Fortunately, most of the breast lesions are diagnosed as benign breast lesions. Breast carcinoma shows heterogeneity in its clinical behavior. Prognosis and management of breast carcinoma are influenced by classic variables such as histological type and grade, stage, tumor size, lymph node status, hormone receptor status of Estrogen (ER), Progesterone (PR) and Human epidermal growth factor receptor 2 (Her2/neu). Though hormone receptor analysis is a prerequisite in this era, for management and prognosis, still histopathological grading can be taken up as an important variable for predicting prognosis. [6] Determining the estrogen receptor (ER), progesterone receptor (PR) and Her2/neu receptor status in breast carcinoma has become practice as survival advantage for patients with hormone receptor positive status by treatment with adjuvant hormonal or chemotherapeutic regimen. It is well known that strong ER-positive cases benefit from endocrine therapy alone, in contrast to those with low

Address for Correspondence

Dr. Hina Parikh

A-13, Punit Nagar Society, Old Padra Road, Vadodara-390020, India.

E-mail: parikhdrshailsh@yahoo.com

to moderate ER positivity. [7] PR status is independently associated with disease-free and overall survival. Patients with ER, PR positive tumors have a better prognosis than patients with negative expression of ER and PR tumors. [8]

MATERIALS AND METHODS

The present study was conducted at the Department of Pathology, Medical College Baroda and SSG hospital. The test population comprised of patients in all age group, with breast pathology, between December 2017 to October 2018. Resected specimen and biopsies of breast lesions were submitted to the Histopathology

section, Baroda Medical College for histopathological examination. Data for prospective study were obtained from tissue specimens received in the histopathology section in the specified period of study. The tissues of the test population submitted were evaluated by histopathological processing and examination (HPE), the most suitable tissue block was selected for IHC evaluation. During the HPE reporting, most of the cases were diagnosed by light microscopy and subsequently, ER, PR and Her2 were done on the best section representing the tumor. Cases were diagnosed as benign, malignant along with IHC performed on Malignant cases.

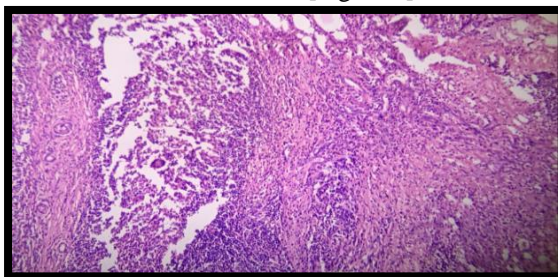
RESULTS

All 152 cases were evaluated histopathologically. 10 cases were of Inflammatory pathology [Table 1], 76 cases were benign [Table 2] and 67 cases were malignant [Table 3].

Table 1: Incidence of Inflammatory lesions

Type of lesion	No. Of cases	Percentage
Breast abscess	03	30%
Chronic mastitis	02	20%
Granulomatous mastitis	03	30%
Duct ectasia	02	20%
Total	10	

The most common inflammatory lesion was granulomatous mastitis [Figure 1] and breast abscess followed by chronic mastitis and duct ectasia [Figure 2].



**Figure 1: Granulomatous mastitis, H&E stain
10 X**

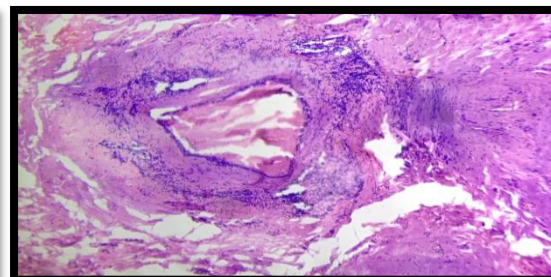


Figure 2: Duct ectasia, H & E stain, 10 X"

Table 2: Incidence of benign lesions

Type of lesion	No. of cases	Percentage
Fibroadenoma	49	64.47%
Fibrocystic disease	02	2.63%
Nodular adenosis	01	1.31%
Tubular adenoma	01	1.31%
Ductal adenoma	01	1.31%
Benign phyllodes tumor	11	14.47%
Intraductal papilloma	01	1.31%
usual ductal hyperplasia	03	3.95%
Atypical lobular hyperplasia	01	1.31%
Gynecomastia	06	7.9%
Total	76	100 %

The most common benign breast disease was fibroadenoma forming the major bulk with 49 cases out of the total 76 cases of benign breast diseases. It was followed by 11 cases of Benign Phyllodes tumor (11 cases) and 6 cases of gynecomastia . There were 3 cases of Usual ductal hyperplasia, 2 cases of Fibrocystic disease and 1 case each of nodular adenosis [Figure 3], tubular adenoma, ductal adenoma, atypical lobular hyperplasia and intraductal papilloma [Figure 4].

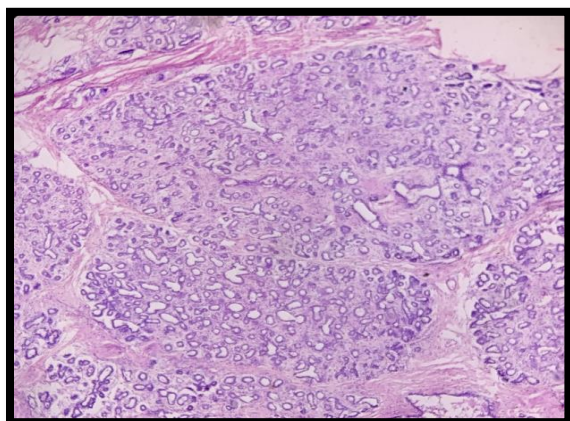


Figure 3: Nodular adenosis, H&E stain, 10 X

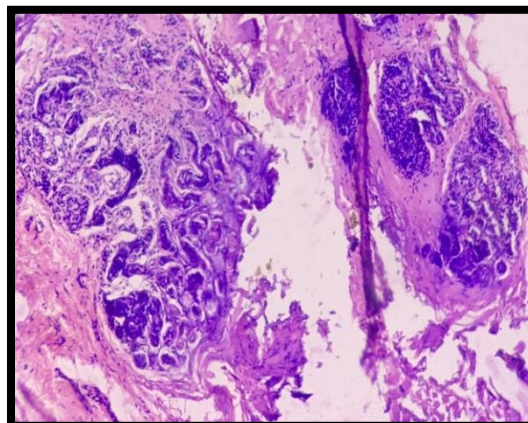


Figure 4: Ductal Papilloma, H&E stain, 10 X

Table 3: Incidence of malignant lesions

Type of lesion	No. of cases	Percentage
Ductal carcinoma in situ	01	1.49%
Invasive ductal carcinoma-nos	60	89.55%
Invasive lobular carcinoma	01	1.49%
Metaplastic carcinoma	02	2.98%
Malignant phyllodes	02	2.98%
Lymphoma	01	1.49%
Total	67	100 %

Out of the 67 cases of malignant lesion in our study, most common was IDC-NOS(60 cases)[Figure 5]. There were 2 cases of Metaplastic carcinoma and 1 case of Ductal carcinoma in situ [Figure 6].There were 2 cases of malignant phyllodes tumor and 1 case of diffuse large B-cell lymphoma.

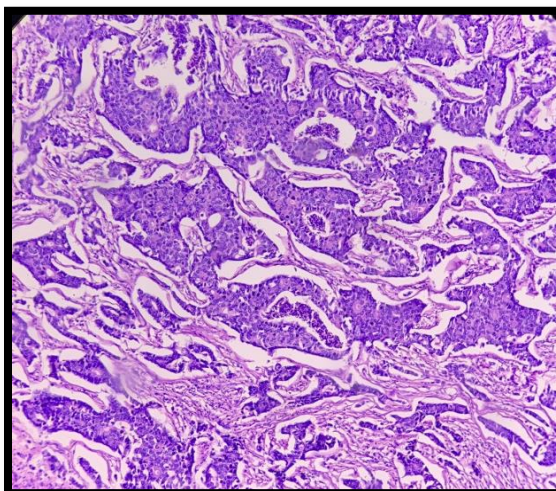


Figure 5: Invasive ductal carcinoma, H&E, 40 X

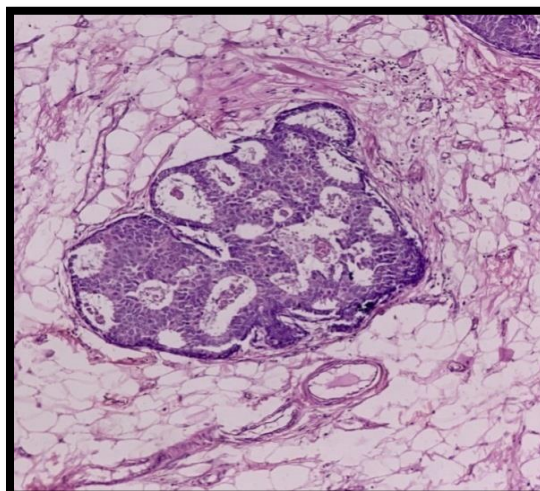


Figure 6: Ductal carcinoma in situ, H&E, 40 X

IHC was carried out in 64 cases out of 67 diagnosed malignant cases as 1 case was of lymphoma and 2 cases were metaplastic carcinoma of breast. There were 46 MRM specimen of breast carcinoma, 43 cases were of IDC NOS type, out of which 4 were of histological Grade I (9.30%) with 75 % positivity for ER/PR+ & Her2 -.31 were of histological Grade II (72.09%) with 35.48 % positivity for ER/PR & Her2 -. 8 cases were of histological Grade III (18.6% with 50 % showing negative results for ER/PR & Her2 . 2 cases were of Metaplastic carcinoma where histological

grading was not done but showed triple negativity in 1 cases for ER/PR and Her2/neu. 1 case was of Invasive lobular carcinoma where also histological grading was not done but was positive for ER/PR and negative for Her2/neu. Maximum numbers of Grade I tumors were seen in patients of 51-60 years of age group implying a better prognosis, while Grade II and Grade III tumors were more common in 41-50 years of age, with maximum number of triple negative cases implying a worse prognosis[Table 4].

Table 4: Distribution of cases according to Histological grade and IHC results

	Grade I	Grade II	Grade III	Total
ER/PR+,Her2+	01(25%)	06(19.35%)	00	07(16.28%)
ER/PR+,Her2-	03(75%)	11(35.48%)	02(25%)	16(37.21)
ER/PR-,Her2+	00	05(16.13%)	02(25%)	07(16.28%)
ER/PR-,Her2-	00	09(29.03%)	04(50%)	13(30.23%)
Total	04(100%)	31(100%)	08(100%)	43(100%)

DISCUSSION

In the present study, out of the 152 cases studied, 8 cases (5.26 %) were inflammatory lesions, the most common being granulomatous mastitis and breast abscess in age group 31-40 years. The probable reason behind this is that most of the inflammatory lesions in our tertiary set up are diagnosed by FNAC and managed conservatively so biopsy is not required. 76 cases (50 %) were benign. Most of the benign cases were in the age group of 21-30 years closely followed by 11-20 years . In accordance with the past studies, in the present study also, the most common benign breast lesion was found to be fibroadenoma constituting a total of 49 cases (64.47% of the total benign breast diseases and 32.23% of the total breast lesions). Fibroadenoma occupied 66.86% of the total benign cases studied by Mansoor et al^[9] 70.83% in study of Vissa Shanthi et al^[10] 71.3% in study of Aslam et al^[11]. This clearly concludes that Fibroadenoma is the most common benign breast lesion. In the present study, 67 cases were malignant (44.07%). The finding that breast cancer was higher in this study probably because being a tertiary health care facility, most of the patients admitted here are referred malignant cases from the periphery and the growing environment of private owned hospitals by general practitioners where most of the benign lesions are probably managed. In this study, most of the malignant cases were found to be in the age group of 41-50 years (n=20, 66.67%). The most common breast cancer was found to be infiltrating ductal carcinoma-not otherwise specified type (IDC-NOS) constituting a total of 60 cases (89.55%). This is similar to the past studies conducted

by Mansoor et al^[8] Vissa Shanthi et al^[10], Aslam et al.^[11] By seeing the above data we can conclude that IDC-NOS is the most common breast carcinoma. The age of patients ranged from 25 to 80 years, with a mean age group of 39.13 years. Maximum number of cases were seen in the age group of 41-50 years (31.25%) followed by 61-70 years (21.87%). In our study, mean age is slightly lower compare to other studies probably due to awareness programs has increased screening and early diagnosis of breast carcinoma in community.

Distribution pattern of breast cancer according to tumor grade and ER/PR, Her2/neu status

In our study ER positivity was expressed 100% (4cases) in Grade I, 48.39% (15cases) in Grade II and 37.5% (3cases) in Grade III tumors respectively. Similar results were observed by Azizun Nisa et al^[12] showing ER positivity in 70% cases in Grade I, 48.2% cases in Grade II and 3.5% cases in Grade III tumors respectively. In the study done by Bhagat et al^[20] showing ER positivity in 50% cases in Grade I, 56% cases in Grade II and 35.2 % cases in Grade III tumors respectively. In the study done by Amit et al^[13] ER positivity was expressed in 86.66% cases in grade I, 57.14% cases in grade II and 4% cases in grade III tumors while in study done by Rana et al^[14] ER positivity was seen in 84.21% of grade I and 78.26% cases of grade II tumors. All cases of grade III tumor was ER negative. In the study done by Nandam et al^[3] ER positivity was present in 100% cases in Grade I, 31.25% cases in Grade II and 25 % cases in Grade III tumors respectively [Table 5]

Table 5 : Distribution of cases according to tumor grade and ER status

Grade	ER+ Azizun Nisa <i>et al</i>	ER+ Bhagat <i>et al</i>	ER+ Amit <i>et al</i>	ER+ Rana <i>et al</i>	ER+ Nandam <i>et al</i>	ER+ Present study
I	70%	50%	86.66%	84.21%	100%	04(100%)
II	48.2%	56%	57.14%	78.26%	31.25%	15(48.39%)
III	3.5%	35.2%	4%	0%	25%	03(37.5%)

While PR positivity was expressed 100% (4cases) in Grade I, 54.84% (17 cases) in Grade II and 12.5% (1 case) in Grade III tumors respectively. Similar results were observed by Azizun Nisa *et al*^[12] showing PR positivity was expressed 70 %cases in Grade I, 36.1% cases in Grade II and 1.75% cases in Grade III tumors

respectively. In the study done by Bhagat *et al*^[15] showing PR positivity in 43.75 % cases in Grade I, 40% cases in Grade II and 29.1 % cases in Grade III tumors respectively. Similar results were also seen in studies done by Rana *et al*^[14] and Nandam *et al*^[3] [Table 6]

Table 6 : Distribution of cases according to tumor grade and PR status

Grade	PR+ Azizun Nisa <i>et al</i>	PR+ Bhagat <i>et al</i>	PR+ Amit <i>et al</i>	PR+ Rana <i>et al</i>	PR+ Nandam <i>et al</i>	PR+ Present study
I	70%	43.75%	86.66%	89.47%	50%	04(100%)
II	36.1%	40%	57.14%	60.87%	25%	17(54.84)%
III	1.75%	29.1%	8%	7.14%	25%	01(12.5%)

In our study Her2/neu positivity was expressed in 25%, 35.48% and 25% in Grade I, II and III respectively which correlate well with study done by Geethamala *et al*^[16] in which Her2/neu positivity was expressed 15.8%, 27.8% and 26.4 % in Grade I, II and III

respectively. In studies by Azizun Nisa *et al*^[12] 0%, 22.9%, 31.6% in Grade I, II and III respectively and Bhagat *et al*^[15] shows 0%, 28%, 52.94% in Grade I, II and III respectively were Her2/ neu positive. [Table 7]

Table 7: Distribution of cases according to tumor grade and Her2/neu status

Grade	Her2Neu+ Azizun Nisa <i>et al</i>	Her2Neu+ Bhagat <i>et al</i>	Her2Neu+ Geethamala K <i>et al</i>	Her2Neu+ Vissa Shanthi <i>et al</i>	Her2Neu+ Present study
I	0%	0%	15.8%	25%	01(25%)
II	22.9%	28%	27.8%	57.14%	11(35.48%)
III	31.6%	52.94%	26.4%	60%	02(25%)

Distribution pattern of breast cancer according to ER, PR and Her2/neu status: Her2/neu positivity in present study was 34.38% which is similar to the studies done by Vaidhyathanan *et al*^[17] with 43.2% and Munjal *et al*^[18] with 40.2% positivity in their study.

While studies done by Bhagat *et al*^[15] showed 27.58% positivity, Ambrose *et al*^[19] showed 27.10% positivity and Sharif *et al*^[6] showed 28% positivity respectively in their study. [Table 8,9]

Table 8 : Distribution of cases according to ER, PR status

	Bhagat <i>et al</i>	Ambrose <i>et al</i>	Amit <i>et al</i>	Present study
ER+PR+	36.20%	47.0%	45.16	43.75%
ER+PR-	12.06%	12.2%	4.84	9.38%
ER-PR+	1.72%	4.05%	6.45	9.38%
ER-PR-	48.27%	36.8%	43.55	37.5%

Table 9 : Distribution of cases according to Her2/neu status

	Bhagat <i>et al</i>	Munjhal <i>et al</i>	Ambroise <i>et al</i>	Sharif <i>et al</i>	Vaidhyanathan <i>et al</i>	Present study
Her2/neu+	27.58%	40.2%	27.10%	28%	43.2%	34.38%

The triple negative breast carcinoma is characterized by lack of ER, PR and Her2/neu expression. Present study showed 28.12% cases with Negative ER, PR and Her2/neu status

CONCLUSION

From the present study we can conclude that most common breast lesions are benign, in age group 21-30 years, fibroadenoma being the most common. This is followed by malignant lesions, Infiltrating Ductal Carcinoma-NOS type being the most common in age group 41-50 years. Inflammatory lesions are not so common constituting to only 5.26 % of all cases. Most common histological grade is Grade II for Infiltrating Ductal carcinoma (NOS) of Grade I tumors seen in patients of 51-60 years of age group imply a better prognosis than Grade II and Grade III tumors which were more common in 41-50 years of age. Based on the IHC profile of breast cancer in this study, ER/PR showed more positivity in Grade I than in Grade II & III tumors. Triple negative Grade III tumors are associated with poor prognosis. Thus Prognostic accuracy improves with incorporation of IHC into the histopathology report along with the traditional TNM staging and histological grading.

ACKNOWLEDGEMENT

Patients and their relatives.

REFERENCES

1. Bray, F., Ren, J.S., Masuyer and E., Ferlay, J. Global estimates of cancer prevalence for 27 sites in the adult population in 2008. *Int. J. Cancer*, 2012; 132: 1133-1145.
2. Ferlay, J., Shin, H., Bray, F., Forman, D., Mathers, C. Parkin, D. (2010). Cancer incidence and mortality worldwide. In: IARC Cancer Base No. 10 (version 2.0)
3. Mohan Rao Nandam, Histopathological Spectrum of Breast Lesions in Association with Histopathological Grade Versus Estrogen Receptor and Progesterone Receptor Status in Breast Cancers: A Hospital Based Study. *Annals of Pathology and Laboratory medicine*. 2003 ;4(5):A496-A501.
4. Desai M. Role of obstetrician and gynecologist in management of breast lump. *J Obstet Gynaecol India* 2003; 53:389-91.
5. Roy I, Othieno E .Breast carcinoma in Uganda: Microscopic study and receptor profile of 45 cases. *Arch Pathol Lab Med* .2011;135(2): 194-199.
6. Sharif MA, Mamoon N, Mustaq S, Khadim MT . Morphological profile and association of HER-2/Neu with Prognostic markers in Breast carcinoma in Northern Pakistan. *J Coll Physicians Surg Pak*2009; 19(2): 99-103.
7. Allred DC, Harvey JM, Berardo M, Clark GM. Prognostic and predictive factors in breast carcinoma by immunohistochemical analysis. *Mod Pathol* .1998;11(2): 155-168.
8. Bardou VJ, Arpino G, Elledge RM, Osborne CK, Clark GM. Progesterone receptor status significantly improves outcome prediction over estrogen receptor status alone for adjuvant endocrine therapy in two large breast carcinoma databases. *J Clin Oncol*.2003;3(4):98.
9. Abdul Aziz .Profile of Female Breast Lesions in Saudi Arabia. *J.PMA*.2001; 51:243.
10. Vissa Shanthi et al, clinicopathological study of breast lesions in females with assessment of correlation between tumor grade and prognostic factors. *JBiosciTech*,2011; 2 (5):367-378.
11. Aslam et al., diagnostic pathology 2013, clinicopathological profile of patients with breast diseases
12. 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 CarcinomaPrev* 2008; 9:553-6.
13. Amit M, C Prasad, Sreeramulu P, Sri nivasan D, Naveed ahmed k, Ruta U J. Histopathological Grade versus Estrogen and Progesterone Receptor Status in Carcinoma Breast- A Single Center Study. *Open Access J Surg*. 2017; 4(3): 555639.
14. Rana S, Rana RK, Kumar D, Baxla RG, Sharma RS, Mundu M. Carcinoma Breast and Correlation with Estrogen and Progesterone Receptor Status in Rajendra Institute of Medical Sciences, Ranchi. *Int J Sci Stud* 2016;4(6):133-138.

15. Bhagat Vasudha M, Jha Bharti M, Patel Prashant R. Correlation of Hormonal Receptor and Her-2/neu Expression in Breast Cancer: A Study at Tertiary Care Hospital in South Gujarat, 2012; 2(3):295-298.
16. Geehamala k et al. Histopathological grade versus hormone receptor in breast carcinoma IJBR 2015; 6(07):466-471.
17. Vaidyanathan K, Kumar P, Reddy CO. ErbB-2 expression and its association with other biological parameter of breast cancer among Indian women. *Ind. J. of Cancer.* 2010; 47(1):8-15.
18. Kavita Munjal, Abiy Ambaye, Mark F Evans, Jeannette Mitchell, Shirish Nandedkar, Kumarasen Cooper. Immuno histochemical Analysis of ER, PR, Her2 and CK5/6 in Infiltrative Breast Carcinomas in Indian Patients. *Asian Pacific Journal of Cancer Prevention*, 2009; 10: 773-778.
19. Ambroise M, Ghosh M, Mallikarjuna VS, Kurian. Immunohistochemical Profile of Breast Carcinoma Patients at a Tertiary Care Hospital in South India. *Asian Pacific J Carcinoma Prev* 2011; 12: 625-629.

How to cite this Article: Parikh H, Rastogi N. Profile of female breast lesions along with histological grading and receptor study of malignant lesion. *Asian Pac. J. Health Sci.*, 2020; 7(1):62-68.

Source of Support: Nil, **Conflict of Interest:** None declared.