IOSR Journal of Pharmacy and Biological Sciences (IOSR-JPBS)
e-ISSN:2278-3008, p-ISSN:2319-7676. Volume 21, Issue 5 Ser. II (Sep. – Oct. 2026), PP 50-54
www.Iosrjournals.org

Correlation of clinical features and pathology of breast cancer with immunohistochemistry.

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Abstract
Purpose – This study aimed to asses the relationship between clinical presentation of breast cancer with its immunohistochemistry profile.
Methodology – A prospective Observational study was conducted at Gandhi Medical college and Hamidia Hospital, Bhopal, from histopathology and immunohistochemistry and to utilise study as clinical features with histology can be predictor of biomarker.July 2022 to July 2024.A total of 80 patient of all group with complaints of breast lump and pain evaluated with radiological examination followed by confirmation with histopathology.Patient with male gender,histologically undiagnosed,involved in other study,multiple malignancy,lack of compliance,and with previous histry of chemoradiotherapy.
postmenopausal status,mainly sporadic, with clinical symptoms of lump >5cm and skin changes were triple negative,basal molecular type of breast cancer.
Key Words – *Breast cancer, Immunohistochemistry, Histopathology, molecular subtypes.*

Date of Submission: 17-10-2026 Date of Acceptance: 31-10-2026

I. INTRODUCTION

Breast cancer is the most common malignancy and leading cause of death among women resulting in more than 1,00,000 cases found worldwide annually.[1] Breast cancer has been classified into five main molecular groups which differs markedly in terms of distinct races / ethnicities, risk factors distributons, prognosis, therapeutic treatment responsiveness, clinical outcomes and both overall survival (os) and relapse free survival , and types are Luminal type A and B both of which have simila profiles to those of normal luminal cells breast gland, basal cell like(BCL) , Triple negative which have genetic expression similar to basal cells / myoepithelial cells.Erb-B2 tumors which have amplification of her2neu and normal brast like group.[1,2,3,4] Routine IHC evaluation of breast cancers may therefore provide not only crucial information to guide clinical management but also represents a valid alternative to costly genotyping assays.The relationship between IHC markers and responsiveness to therapeutic treatments has been extensively studied [5,6,7,8,9.]. However, only a few population-based studies have investigated the relationship between molecular subtypes as defined by immunohistochemistry and clinicopathologic characteristics [8,10].This study aims to assessment of variation in clinicopathological effect Of breast Cancer with various immunohistochemical marker profileat Dept of General Surgery Gandhi Medical College Bhopal and Associated Hamidia Hospital Bhopal.

II. Materials and Methods

This prospective observational study was conducted in the Department of General Surgery, Gandhi Medical College & Hamidia Hospital, Bhopal, from July 2022 to July 2024 after approval from the Institutional Ethics Committee.

The study included all patients who presented to the department during the study duration (sample size= 80); all age groups presenting with lump in breast,pain,nipple discharge skin changes. Exclusion criteria included Histologically undiagnosed cases,Participation in another intervention-trial with interference of intervention and outcome of this study,Multiple malignancies,Expected lack of compliance,Male patients with breast cancer,Patients who have received Prior chemoradiation,Pagets disease,Postoperative cases of carcinoma of breast,Patients having distant metastasis,Patients who have received chemotherapy.

After obtaining written informed consent, eligible patients were evaluated through Triple Assesment which include examination,radiological Assesment (USG for BIRAD scoring,X-ray Chest, and CT thorax) and histopathologial examination. Immunohistochemical analysis of tissue for ER,PR,Her2Neu receptors

Data were collected and analysed using Epi Info Version 6. Frequency distribution and cross-tabulation were employed to summarize the data. Continuous variables were expressed as mean ± standard deviation, while categorical data were presented as percentages. The Pearson Chi-Square test was used for normally distributed data, and the student's t-test for non-normally distributed data, with a p-value of <0.05 considered statistically significant.

III. RESULT

Table – 1 Distribution of study participants based on status of Immunohistochemical markers

Sl. No.	Marker	Frequency	Percent
1	**ER**		
a	Positive	39	48.7
b	Negative	41	51.3
2	**PR**		
a	Positive	37	46.3
b	Negative	43	53.7
3	**HER2/neu**		
a	Positive	38	47.5
b	Negative	42	52.5
Total	80	100	

Table 2 : Distribution of ER and PR + study participants based on Examination findings of lump.

	Variable	ER and PR n (%)		Total, n	Chi sq., p
		Positive	Negative	(%)	Value
Lump Consistency	Hard	32 (82.1)	25 (61)	57 (71.3)	4.334, **0.037**
	Firm	7 (17.9)	16 (39)	23 (28.8)	
Local Rise in Temperature	Present	7 (17.9)	7 (17.1)	14 (17.5)	0.011, 0.918
	Absent	32 (82.1)	34 (82.9)	66 (82.5)	
Tenderness	Present	14 (35.9)	11 (26.8)	25 (31.3)	0.765, 0.382
	Absent	25 (64.1)	30 (73.2)	55 (68.8)	
Nipple Retraction	Present	3 (7.7)	8 (19.5)	11 (13.8)	2.355, 0.125
	Absent	36 (92.3)	33 (80.5)	69 (86.3)	
Skin Involvement	Present	5 (12.8)	7 (17.1)	12 (15)	0.284, 0.594
	Absent	34 (87.2)	34 (82.9)	68 (85)	
Fixity to chest wall	Present	6 (15.4)	6 (14.6)	12 (15)	0.009, 0.925
	Absent	33 (84.6)	35 (85.4)	68 (85)	
Lymph nodes	Present	20 (51.3)	26 (63.4)	46 (57.5)	1.204, 0.273
	Absent	19 (48.7)	15 (36.6)	34 (42.5)	
Total	39 (100)	41 (100)	80 (100)		

Table-3 Distribution of ER+ study participants based on histopathological findings.

Histopathological Examination	ER, n (%)		Total, n (%)	Chi sq, p value
	Positive	Negative		
Ductal Carcinoma In Situ	3 (7.7)	4 (9.8)	7 (8.8)	

Infilterating Ductal Carcinoma	28 (71.8)	29 (70.7)	57 (71.3)	
Infiterating Lobular Carcinoma	3 (7.7)	3 (7.3)	6 (7.5)	
Medullary Carcinoma	5 (12.8)	3 (7.3)	8 (10)	3.389,
Mucinous Carcinoma	0 (0)	2 (4.9)	2 (2.5)	0.495
Total	39 (100)	41 (100)	80 (100)	

Table -4 Distribution of PR+ study participants based on histopathological findings.

Histopathological Examination	PR, n (%)		Total, n (%)	Chi sq., p value
	Positive	Negative		
Ductal Carcinoma In Situ	2 (5.4)	5 (11.6)	7 (8.8)	
Infilterating Ductal Carcinoma	27 (73)	30 (69.8)	57 (71.3)	
Infiterating Lobular Carcinoma	3 (8.1)	3 (7)	6 (7.5)	4.314,
Medullary Carcinoma	5 (13.5)	3 (7)	8 (10)	0.365
Mucinous Carcinoma	0 (0)	2 (4.7)	2 (2.5)	
Total	37 (100)	43 (100)	80 (100)	

Table 5: Distribution of HER2/neu+ study participants based on histopathological findings.

Histopathological Examination	HER2NEU, n (%)		Total, n (%)	Chi sq., p value
	Positive	Negative		
Ductal Carcinoma In Situ	2 (5.3)	5 (11.9)	7 (8.8)	
Infilterating Ductal Carcinoma	30 (78.9)	27 (64.3)	57 (71.3)	
Infiterating Lobular Carcinoma	1 (2.6)	5 (11.9)	6 (7.5)	7.475,
Medullary Carcinoma	3 (7.9)	5 (11.9)	8 (10)	0.113
Mucinous Carcinoma	2 (5.3)	0 (0)	2 (2.5)	
Total	38 (100)	42 (100)	80 (100)	

IV. Result

The findings of this prospective observational study offer compelling evidence that severe clinical symtoms does have higher BIRAD score and higher histologic grade and most common type being Infilterating ductal Carcinoma and immunohistochemistry remains to be tripple negative.

These results suggest that patients with the Basal cell type,tripple negative subtypes are more likely to have higher-histologic-grade tumors and medullary cancer. The HER2 subtype was typically associated with a higher BI-RADS category

V. DISCUSSION

Breast carcinoma is one of the leading cause of death in women worldwide. It has been ranked the most common cancer in Indian females1. The most common age group for IDC breast that was observed in our study was 51-60 years i.e. the perimenopausal and post menopausal age group. The mean age came out to be 58.68 years. These findings are consistent with the studies conducted by other Indian studies like Vedashree et al, [6] Geethamala K, [7] Chandrika Rao[8] and Lakhmini et al[9] while it is in contrast with western studies such as study conducted by Rhodes et al10 in which he observed the most common age group for invasive breast carcinomas to be >50 years with mean age of 64 years. In the present study of 80 patients, majority (75 out of 80 i.e. 93.7%) of participants were postmenopausal while only 6.25% reported premenopausal menstrual history and among ER+, 53.8% of participants reported right breast carcinoma which was followed by left breast (46.2%) involvement. Similarly, among ER-, majority (53.7%) had right breast carcinoma followed by left breast (43.9%), Among ER+, upper outer quadrant 112 | P a g e (61.5%) was involved in majority of the carcinomas which was then followed by lower outer quadrant (23.1%)> Upper inner quadrant (20.5%)> Lower inner quadrant (15.4%)> central quadrant (10.3%). 43.6% reported breast pain with mean duration of pain to be 5.24 ± 9.59 months. Among ER- females, pain was reported by 39.0% of females and its mean duration was 7.75 ± 16.14 months, Out of 39 ER+ females, 82.1% (32) had firm consistency while only 17.9% (7) were hard lumps. Out of 41 ER- females, 61% (25) were 113 | P a g e firm lumps while 39% (16) were hard lumps. p-value of 0.037 indicates that there is a significant association between ER status and lump consistency. Out of 39 ER+

females, local rise in temperature was found in 17.9 % (7) of participants which was reported to be 17.1% (7 out of 41) among ERfemales. Tenderness was observed in 35.9% (14/39) of ER+ females and 26.8% (11/41) of ER- females. Nipple retraction was observed in 7.7% (3 out of 39) of ER+ females and 19.5% (8 out of 41) of ER- females.Among ER+ females, skin involvement, fixity to chest wall and involvement of lymph nodes was observed in 12.8%, 15.4% and 51.3% of participants respectively. Among ER-females, skin involvement, fixity to chest wall and involvement of lymph nodes was observed in 17.1%, 14.6% and 63.4% respectively. Majority (51.3%) of ER+ females had BIRADS score 5 followed by BIRADS 4 (35.9%)> BIRADS 3 (12.8%). Among ER- females, majority (46.3%) reported BIRADS 5 followed by BIRADS 4 (31.7%)> BIRADS 3 (19.5%)> BIRADS 2 (2.4%).Which indicates higher BIRAD score higher is the possibility of estrogen receptor positivity.

PR+, 51.4% of participants reported right breast carcinoma which was followed by left breast (48.6%) involvement. Similarly, among PR-, majority (55.8%) had right breast carcinoma followed by left breast (41.9%). Out of 37 PR+ females, 81.1% (30) had firm consistency while only 18.9% (7) were hard lumps. Out of 43 PR- females, 62.8% (27) were firm lumps while 37.2% (16) were hard lumps. Out of 37 PR+ females, local rise in temperature was found in 18.9% (7) of participants which was reported to be 16.3% (7 out of 43) among PR- females. Tenderness was observed in 37.8% (14/37) of PR+ females and 25.6% (11/43) of PR- females. Nipple retraction was observed in 8.1% (3 out of 37) of PR+ females and 18.6% (8 out of 43) of PR- females. Among PR+ females, skin involvement, fixity to chest wall and involvement of lymph nodes was observed in 13.5%, 16.2% and 51.4% of participants respectively. Among PR- females, skin involvement, fixity to chest wall and involvement of lymph nodes was observed in 16.3%, 14.0% and 62.8% respectively. T2 (39.5%).Similarly, out of 43 PR- females, 34 (79.1%) had ill defined borders and 33 (76.7%) had heterogenous texture of the lesion. Among PR+ females, Infilterating Ductal Carcinoma was the most common (73%) type followed by medullary carcinoma (13.5%), infilterating lobular carcinoma (8.1%) and Ductal carcinoma in situ (5.4%). Similarly, among PR Negative females, Infilterating Ductal Carcinoma was the most common (69.8%) type. Among HER2/neu+ females, the mean lump diameter was 4.33 ± 1.76 cm with majority (65.8%) reporting of >2 to 5 cm followed by >5cm diameter (21.1%). Among HER2/neu- females, the mean lump diameter was found to be 4.06 ± 1.96 cm with majority (64.3%) reporting size to be >2cm to 5 cm. Figure 30: Distribution of HER2/neu+ study participants based on size of lump. Out of 38 HER2/neu+ females, 63.2% (24) had firm consistency while only 36.8% (14) were hard lumps. Out of 42 HER2/neu- females, 78.6% (33) were having hard lumps while 21.4% (9) were with firm lumps. Out of 38 HER2/neu+ females, local rise in temperature was found in 21.1% i.e 8 of all participants which was reported to be 14.3% (6 out of 42) among HER2/neu- females. Tenderness was observed in 34.2% (13/38) of HER2/neu+ females and 28.6% (12/42) of HER2/neu- females. Nipple retraction was observed in 15.8% (6 out of 38) of HER2/neu+ females and 11.9% (5 out of 42) of HER2/neu- females. Among HER2/neu+ females, skin involvement, fixity to chest wall and involvement of lymph nodes was observed in 18.4%, 13.2% and 57.9% of participants respectively. Among HER2/neu- females, skin involvement, fixity to chest wall and involvement of lymph nodes was observed in 11.9%, 16.7% and 57.1% respectively. Majority (55.3%) of HER2/neu+ females had BIRADS score 5 followed by BIRADS 4 (31.6%)> BIRADS 3 (10.5%)> BIRADS 2 (2.6%). Among HER2/neu- females, majority (42.9%) reported BIRADS 5 followed by BIRADS 4 (35.7%)> BIRADS 3 (21.4%). 35 (92.1%) had ill defined borders and 33 (86.8%) had heterogenous texture of the lesion. Similarly, out of 42 HER2/neu- females, 28 (66.7%) had ill defined borders and 28 (66.7%) had heterogenous texture of the lesion. On comparision of type of lesion border with presence of HER2/neu+ marker, a statistically significant (p= 0.005) association was observed between them. Similary, on comparison of lesion texture with presence of HER2/neu+ marker, a statistically significant (p= 0.034) association was observed between them.

VI. CONCLUSION

Immunohistochemistry (IHC) markers (ER, PR, HER 2neu) are positively correlated with increasing age, tumor size, tumor grade and positive axillary lymph nodes, also there is statistically significant correlation between HER 2neu overexpression and hormone receptor (ER, PR) negativity in study population(0.113). In our study, maximum prevalence in 51-60 years age group all types of molecular cancer have more predilection to right sided and outer quadrantand pathology was Infiltrating Ductal Carcinoma, which is the commonest carcinoma where Chi sq and p-value are 4.314 & 0.365 respectively, also reported worldwide. ER and PR positivity was seen more in grade I tumors and less pain while higher grade tumors were negative for ER/PR/her2ne and more pain and it showed more predilection for higher grades (Grade II & Grade III). Tumors showing ER and PR positivity carry a good prognosis and respond to hormonal therapy and Her2 neu tumors, though carry a bad prognosis but are particularly responsive to transtuzumab. ER negative and triple negative tumors carry poor prognosis and don't respond to hormonal therapy.

VII. STUDY LIMITATIONS

While this study provides valuable insights into the relationship between breast cancer and its histopathology and its immunochemistry, it is essential to acknowledge certain limitations that may impact the generalizability and interpretation of the findings. First and foremost, the study's relatively small sample size of 80 patients might limit the statistical power to detect subtle associations between clinical features and expected histopathology and immunohistochemistry profile. Additionally, the single-centre design of the study raises the possibility of selection bias and limits the applicability of the results to other populations or healthcare settings. Furthermore,Male breast cancer patients,females involved in other studies Future studies with larger, multi-centre cohorts and extended inclusion criterias are warranted to address these limitations and provide a more comprehensive understanding.

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