e-ISSN: 0976-822X, p-ISSN:2961-6042

Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2026; 18(6); 1868-1878

Original Research Article

To Study Histomorphological Changes in Post Neoadjuvant Chemotherapy MRM (Modified Radical Mastectomy) Specimens

Jayanti Chandrakar[1], Varsha Pandey[2], Amit Banjara[3]

[1]Professor, Department of Pathology, Pt. JNM Medical College, Raipur, Chhattisgarh, India.
[2]Associate Professor, Department of Pathology, Pt. JNM Medical College, Raipur, Chhattisgarh, India
[3]Resident/Medical Officer, Department of Pathology, Pt. JNM Medical College, Raipur, Chhattisgarh, India

Received: 27-04-2026 / Revised: 26-05-2026 / Accepted: 28-06-2026
Corresponding Author: Amit Banjara
Conflict of interest: Nil

Abstract:

Background: Globally, breast cancer is the most common malignancy among women from being fourth in the list of most common cancers in India. The aim of neoadjuvant chemotherapy is to improve surgical outcome, downgrade the disease by obtaining tumour shrinkage, reduce the risk of distant metastasis, and prolong overall disease-free survival. Preoperatively, administered NACT currently represents the standard treatment option for locally advanced breast carcinoma. Histopathological tumour regression is considered as the gold standard for determining the Pathologic response.

Objectives: To study histomorphological changes in Post Neoadjuvant Chemotherapy modified radical mastectomy MRM) Specimens in a Tertiary Care Hospital at Raipur, Chhattisgarh.

Methodology: All well-preserved post-NACT MRM specimens will be enrolled and grossed as per CAP (College of American pathologists) guidelines. Macroscopic Examination, Specimen laterality, Specimen dimensions, Weight, Morphology of overlying skin, nipple areola complex, tumour site, tumour dimensions, tumour focality, involvement of surgical margins were recorded. Number and size of attached lymph nodes, satellite lesions (if any) noted & Microscopic evaluation (Post-NACT cytoplasmic, nuclear and stromal changes along with Lymphocyte response grade, Pathological Response according to Chevallier grading system) was noted.

Result: 51 cases of breast carcinomas were studied. Patient ages peak at 41-50 years (43%) The fundamental changes of effect of the therapy was graded in 60.8% pCR (Pathologic complete response), 23.5% pNR (no pathologic response) and 15.7% pPR (Partial pathologic response responses) and Cytoplasmic eosinophilia prevailed (75%), nuclear hyperchromasia (49%), and stromal fibrosis (59%) noted in post MRM breast specimen along with Modified Bloom-Richardson grade II was most common (51%) finding observed.

Conclusion: Histopathology is gold standard for evaluating response in breast cancer post NACT. The pathological assessment of therapeutic response predicts the distant relapse-free survival and further indicate the treatment protocol there by affecting overall prognosis of the patient. NACT is effective prior to MRM surgery.

Keywords: Breast cancer, Neoadjuvant chemotherapy, pathological evaluation, pathologic complete response, Modified radical mastectomy.

DOI: 10.25258/ijcpr.18.6.300

Introduction

The female breast has always been a symbol of beauty, fertility and femininity. The history of breast cancer is a complex maze of attempts to understand. The Edwin Smith Surgical Papyrus, dating back to 3,000–2,500 B.C., and possibly attributable to Imhotep (the Egyptian physician-architect), provides authentic accounts of breast cancer. In ancient Greece, a divinity was exhorted to offer relief from breast maladies, as evidenced by votive offerings in the shape of breasts.[1] Breast cancer represents the most common malignancy among women worldwide and remains a major public health concern due to its high incidence, variable clinical course, and significant impact on morbidity and mortality. [2]

In India, the epidemiological pattern has shifted significantly over the last three decades; from being fourth on the list of most common cancers during the 1990s, breast cancer has now emerged as the leading malignancy among women.[2] Breast cancer incidence rates have risen in most of the past four decades; with overall incidence increasing by ~0.5% annually during 2010–2019 [3]. It has now surpassed lung cancer as the leading cause of global cancer incidence in 2020, with an estimated 2.3

million new cases, representing 11.7% of all cancer cases. Epidemiological studies have shown that the global burden of breast cancer is expected to cross almost 2 million by the year 2030, As per the Globocan data 2020, in India, breast cancer accounted for 13.5% (178361) of all cancer cases and 10.6% (90408) of all deaths. [4] Current data indicate that the age-adjusted incidence rate of breast cancer in India is 25.8 per 100,000 women, with a mortality rate of 12.7 per 100,000 women. [5] It can occur at any age but the peak incidence is between 45 to 60 years in the developed world and 1 in 8 women in united states will be diagnosed with breast cancer in her lifetime. [6]

Breast cancer is a heterogeneous disease with variable responses to NACT. The histopathological reporting of post-NACT specimens is challenging due to therapy-induced changes in breast parenchyma, which can mimic atypical lesions, obscure residual disease, and complicate the assessment of tumour margins and nodal involvement. in vivo assessment of tumour response in post-NACT breast cancer specimens crucial for understanding the progression of the residual tumour post-chemotherapy depends on the proliferative capacity of the residual tumour cells, their interaction with the tumour microenvironment, and the chemotherapy-induced immunomodulation of the tumour immune landscape and guiding further management, thus Pathological complete response (pCR) is a robust predictor of favourable prognosis in breast cancer patients. [7] Assessment of response to chemotherapy can be done by two ways; assessment of clinical and pathologic response, later preferred as it provides the possibility of assessment of the treatment efficacy in vivo allowing modification of chemotherapeutic agent in patients with insignificant response and insight in the benefit of the same NACT continued postoperatively. Pathological response through Chevallier grading system is an important prognostic indicator, particularly the complete pathologic response associated with improved long-term outcome. [8]

Aim and Objective

Aim: To study histomorphological changes in Post-Neoadjuvant Chemotherapy modified radical mastectomy (MRM) Specimens.

Objectives

Primary Objective

- To study histomorphological changes in Post-NACT MRM Specimens.

Secondary Objectives

- To Study Pathological Response (PR) in Post NACT MRM Specimens according to Chevallier Grading system.
- To Study Cytoplasmic, Nuclear and Stromal changes in Post-NACT MRM Specimens.

Material and Methods

This study was an Observational Descriptive study conducted over a period of 2 years i.e. from March 2024 to February2026 at Department of Pathology, PT.J.N.M. Medical College, in association with DR.B.R.A.M. Hospital Raipur, Chhattisgarh. Prior approval from institutional ethical committee was taken to conduct this study (IEC/2023/034).

Inclusion Criteria	Exclusion Criteria
MRM resection specimens of patients with breast carcinomas who had received neoadjuvant chemotherapy (NACT) prior to surgery were included in the study.	Poorly preserved specimen

	Parameter	Score 1	Score 2	Score 3
1	Tumor tubule or gland formation	> 75% of tumour	10 – 75% of tumour	< 10% of tumour
2	Nuclear pleomorphism	Minimal variation in nuclear size and shape	Moderate variation in nuclear size and shape	Marked variation in nuclear size and shape
3	Mitotic count (per 10 high power fields)	< 7 mitosis/ 10 HPF	08-14 mitosis/ 10 HPF	>15 mitosis/ 10 HPF
	Total score	Grade I (Well differentiated) 3 – 5		
		Grade II (Moderately differentiated) 6 or 7		
		Grade III (Poorly differentiated) 8 or 9		

This study includes consecutive 51 MRM resection specimens of patients with breast carcinomas who had NACT prior to surgery sample specimens received at Department of Pathology. All well-preserved post-NACT MRM specimens enrolled and grossed as per CAP (College of American pathologists 2021) protocol and the tumour, node, metastasis (yPTNM) staging was done as per the American Joint Committee on Cancer, 8th Edition guideline. Macroscopic Examination Specimen laterality, Specimen dimensions, Weight, Morphology of overlying skin nipple areola complex, tumour site, tumour dimensions, tumour focality, involvement of surgical margins were

recorded Number and size of attached lymph nodes, satellite lesions (if any) noted & Microscopic Evaluation and categorisation was made according to the World Health Organisation (WHO) classification 5th edition 2019, encompass changes in tumour cellularity, nuclear/cytoplasmic alterations, stromal modifications. Post-NACT tumour grading using the Modified Scarff–Bloom–Richardson system as well as assessment of pathological response using the Chevallier grading system.

Table 1: Modified Scarff–Bloom–Richardson system [2]

Table 2: Chevallier grading system [2]

1	**Pathological response grade**	pCR- No residual invasive carcinoma or Ductal carcinoma in-situ (DCIS) in breast or lymph nodes.
		pPR- Presence of residual invasive carcinoma exhibiting stromal alterations.
		pNR- Little change in appearance or original carcinoma
2	**Lymphocytic response grade**	Grade 1- scattered lymphocytes in between tumour cells
		Grade 2-formation of microaggregates of lymphocytes.
		Grade 3-dense infiltration of lymphocytes destroying tumour cells or forming masses

pCR-Pathological Complete Response. pPR-Pathological Partial Response pNR- Pathological No Response

Finally, data were entered into Microsoft excel spread sheet and subjected for appropriate statistical analysis. Qualitative or categorical data presented as a frequency or percentage. Quantitative or continuous data presented as a mean +/-Standard deviation.

Observations and Results

A total of 51 cases of female breast carcinoma were evaluated in the present study shows that the largest single demographic group consisted of patients between 41 and 50 years old, representing 43.14% (22/51) of the cohort while with predominantly mean age 49.18 years. Out of a total of 51 participants, the majority (47 respondents; 92.16%) reported no family history, whereas only 4 respondents (7.84%) had a positive family history. A predominant Left Upper Outer Quadrant (LUOQ) observed in 12 patients (23.53%) along with Right Upper Inner Quadrant (RUIQ) in 12 patients (23.53%), making it equally prevalent to the LUOQ with 41 cases (80.39%) showed no involvement of the nipple areola complex, while 10 cases (19.61%) demonstrated positive NAC involvement.

The data reveals a bimodal distribution with peaks at 4 and 8 cycles, but the treatment protocols leaned heavily toward extended courses. The most common therapeutic course consisted of 8 cycles, which was administered to 37.25% (19/51) of the patients. The second most frequent regimen was 4 cycles, received by 19.61% (10/51) of the cohort. Collectively, more than half of the patients (54.9%) received 7 or 8 cycles of chemotherapy.

Among the 51 patients evaluated prior to NACT, the majority presented with medium-sized tumours (4–6.9 cm), comprising 26 cases (50.98%). Large tumours (≥7 cm) were observed in 18 patients (35.29%), while small tumours (<4 cm) accounted for 7 cases (13.73%). The mean pre-NACT clinical tumour size was 6.1 ± 2.3 cm, indicating that most patients had relatively large primary tumours at presentation whereas post-treatment pathological measurement revealed a decrease in the mean tumour size to 4.3 ± 2.4 cm, medium-sized tumours (3–5.9 cm) were most common, observed in 23 cases (45.10%). Small tumours (<3 cm) and large tumours (≥6 cm) were equally distributed, each accounting for 14 cases (27.45%) are shown in Table 3 & 4. Clinical TNM-T stage in among the 51 cases analysed, the most common stage was T4b, observed in 19 patients (37.25%), followed by T3 in 13 patients (25.49%) and T2 in 10 patients (19.61%) while post-treatment pathological TNM staging distribution shifted, with pT3 (41.18%) and pT2 (23.53%) becoming the most common post-treatment stages, indicating a general downstaging from the initial predominance of T4.

Microscopic examination of the resected tissue revealed that cytoplasmic eosinophilia was the predominant feature, seen in 38 cases (74.51%). Vacuolation was identified in 8 cases (15.68%), Among nuclear changes, hyperchromasia was the most prevalent, seen in 49.02% of cases. Other common features included prominent nucleoli (35.29%) and an increased nuclear-to-cytoplasmic (N:C) ratio (31.37%). The tumour stroma frequently showed treatment-related changes most notably fibrosis, which was present in 30 cases (58.82%)of cases, and necrosis, identified in 20 cases (39.22%). The post-NACT histomorphological changes are shown in Table 5,6 & 7. In 16 post-NACT grading showed that Grade II was the most common Modified Scarff–Bloom–Richardson grade, observed in 26 cases (50.98%). Grade I and no residual grade were each noted in 08 cases (15.69%), while Grade III was seen in 5 cases (9.80%). This distribution indicates a predominance of intermediate-grade tumours following NACT are shown in Figure 1.

Assessing the degree of pathological response is a primary endpoint for evaluating NACT efficacy and serves as a powerful surrogate for long-term clinical outcomes pPR dominated (60.8%), followed by pCR (23.5%) and pNR in (15.7%). Most received 8 cycles (37%). lymphocytic grading revealed that Grade 1 lymphocytic response was most common, observed in 34 cases (66.67%). Grade 2 response was noted in 12 cases (23.53%), while Grade 3 lymphocytic infiltration was seen in 5 cases (9.80%). This distribution indicates that mild lymphocytic response predominated following neoadjuvant chemotherapy. Pathological partial response was most frequently observed across all age groups, particularly in the 41–50 years category is shown in Figure 2 & 3.

pCR was more commonly associated with smaller post-NACT tumour size, absence of nipple–areola complex involvement, and negative tumour margins. Pathological no response showed a higher association with larger post-NACT tumour size. Overall, favourable pathological response correlated with reduced tumour size and absence of local invasive features following neoadjuvant chemotherapy. With respect to clinical TNM-T stage, pathological partial response was most frequently observed in advanced tumours (T3 and T4 stages), particularly T4b, while pathological complete response was more commonly seen in T2 and T3 stages. No pathological complete response was observed in T4c and T4d tumours. On pathological TNM staging, pathological complete response was predominantly associated with lower pathological T stages (T1a–T2), whereas pathological no response and partial response were more frequent in higher T stages (T3 and T4). These findings suggest that lower residual pathological tumour stage following NACT is associated with a better pathological response.

Table 3: Pre-NACT Clinical Tumour Size

Clinical Size of Tumour	**Frequency**	**Percentage**
Small (<4 cm)	7	13.73
Medium (4 - 6.9 cm)	26	50.98
Large (>= 7 cm)	18	35.29
Total	**51**	**100.00**
Mean, SD	**6.1 ± 2.3**	

Table 4: Post-NACT Grossly Tumour Size

Post NACT Size	**Frequency**	**Percentage**
Small (<3 cm)	14	27.45
Medium (3 - 5.9 cm)	23	45.10
Large (>= 6 cm)	14	27.45
Total	**51**	**100.00**
Mean, SD	**4.3 ± 2.4**	

Table 5: Post- NACT Cytoplasmic Changes

Cytoplasmic Features	**Frequency**	**Percentage**
Eosinophilia	38	74.51
Vacuolation	8	15.68
Others / No Change	8	15.69
Total	51	**100.00**

Table 6: Post- NACT Nuclear Changes

Nuclear Features	**Frequency**	**Percentage**
Hyperchromasia	25	49.02
Prominent nucleoli	18	35.29
Pleomorphic nuclei	15	29.41
Increased / high N:C ratio	16	31.37
Nuclear enlargement	7	13.73
Karyorrhexis	9	17.65
Karyolysis	5	9.80
Pyknosis	1	1.96
Total	51	**100.00**

Table 7: Post- NACT Stromal Changes		
Stromal Features	**n**	**%**
Fibrosis	30	58.82
Necrosis	20	39.22
Giant cells	14	27.45
Hyalinization	14	27.45
Degenerative changes	13	25.49
Calcification	12	23.53
Collagenization	7	13.73
Elastosis	3	5.88
Desmoplasia	1	1.96
Foamy histiocytes	1	1.96
Macrophages	1	1.96
Total	51	**100.00**

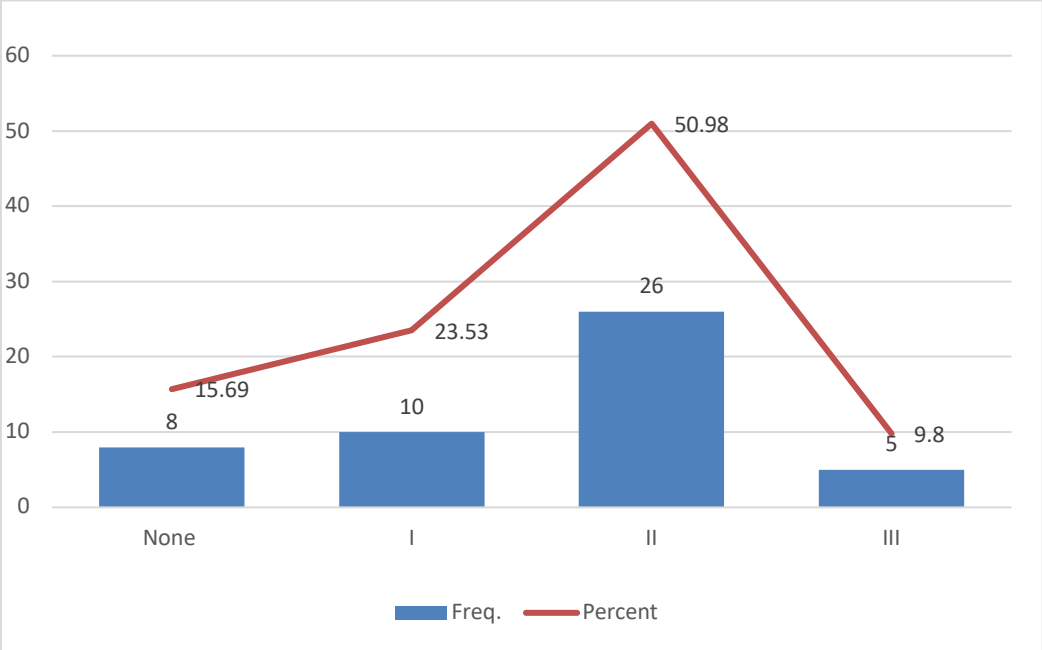

Figure 1: Modified Scarff–Bloom–Richardson Grade

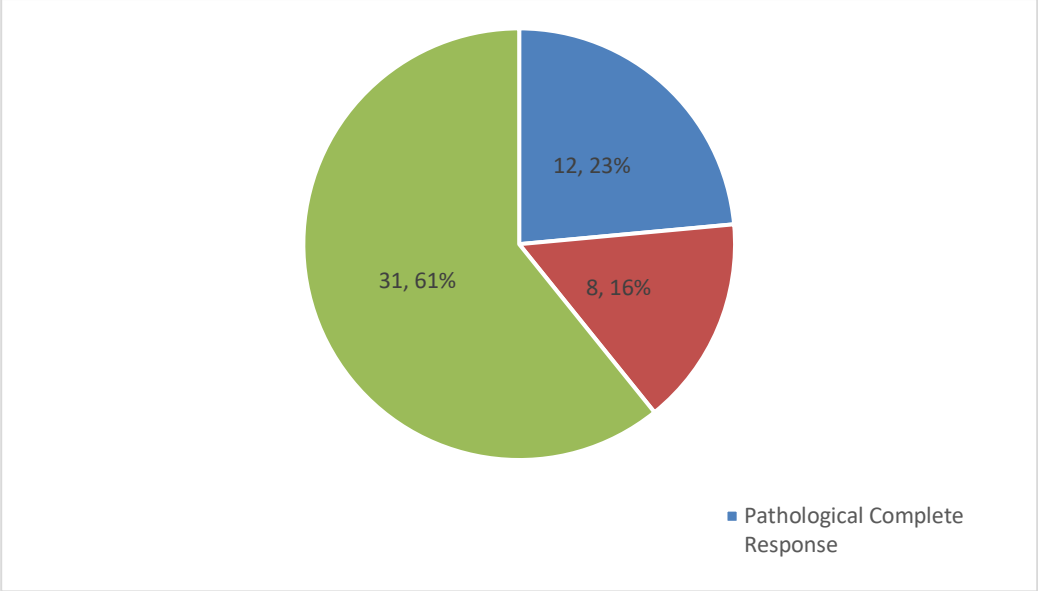

Figure 2: Pathological Response Grade

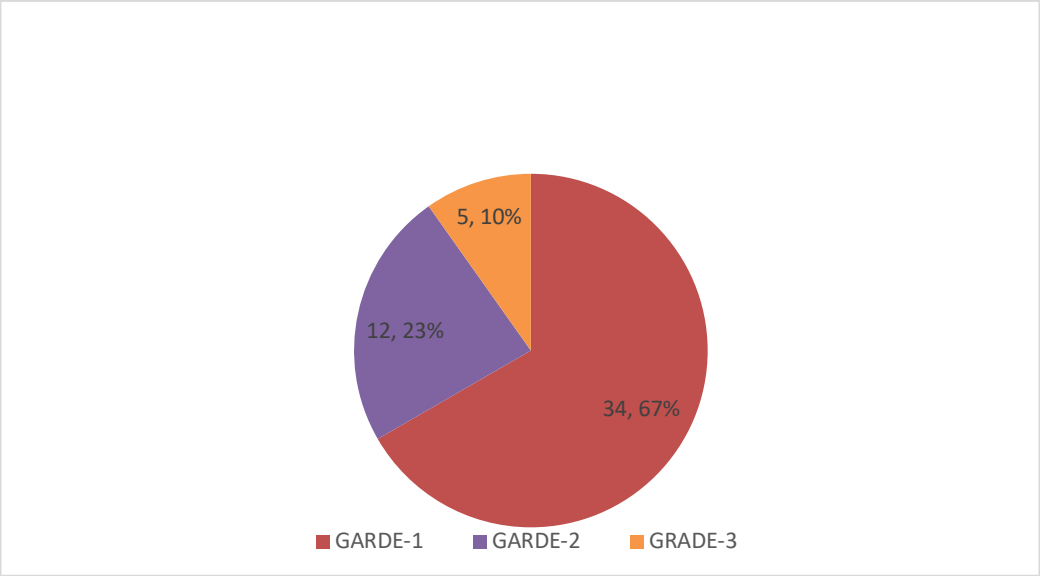

Figure 3: Lymphocytic Response Grade

Discussion

Neoadjuvant chemotherapy (NACT) has become an integral component in the management of locally advanced breast carcinoma, with the primary aim of reducing tumour burden, improving surgical resectability, and allowing better assessment of tumour biology and response to therapy. NACT include making inoperable breast cancers into operable one, downstaging the tumour size, and increasing breast-conserving surgery (BCS) rates and in vivo testing of chemosensitivity. [9]

Histopathological examination of post-NACT MRM specimens remains the gold standard for assessing tumour response. Chemotherapy induces a wide range of histomorphological alterations in both tumour cells and the surrounding stroma, including changes in cellularity, cytoplasmic and nuclear morphology, stromal fibrosis, necrosis, and inflammatory response. Accurate identification and interpretation of these therapy-induced changes are essential to differentiate residual viable tumour from treatment-related effects. The aim is to promote high-quality, standardised reporting of tumour response and residual disease after neoadjuvant treatment that can be used for subsequent management decisions for each patient. [10] The most broadly adopted grading classification system is the Nottingham grading system, modified by Elston and Ellis from the Bloome Richardson grading system, and its prognostic value has been validated in studies with varied populations. [2] pCR plays as a primordial prognostic value, it is of clinical value to emphasize that the role of residual in situ or isolated tumour cells did not adversely affect disease free survival and overall survival. Thus, it is necessary to compare the pathologic responses both in breast and in nodes. [11]

In the present study, the mean age of patients was 49.5 years, which is comparable to most Indian studies, where the mean age ranged between 46 and 50.5 years. Similar mean ages were reported by AS Ramaswamy, BN Kumarguru et al [12]. (49.79 years), Cheryl Sarah Philipose et al. [11] (49.5 years), Vasudevan D, Jayalakshmy P.S, et al. [13] Vasudevan et al. (50.58 years), and Sonal Bhati et al. (50.13 years). This indicates that breast cancer in the Indian population commonly presents in the fifth decade of life, consistent with existing literature.

With respect to laterality and quadrant involvement, the present study showed a predominance of upper outer quadrant involvement, with comparable right and left-sided distribution. Similar findings have been reported by Perubhotla L.M, Kodandapani S. et al [14] and Sonal Bhati et al [2]., where the upper outer quadrant was the most commonly involved site. This distribution is consistent with the known higher volume of breast tissue in the upper outer quadrant. The number of NACT cycles administered in the present study was received 3–8 cycles of NACT, which is comparable to the range reported in other studies, though variation exists due to institutional protocols and treatment response. which is comparable to AS Ramaswamy, BN Kumarguru et al [12]. and Vasudevan D, Jayalakshmy P.S, et al. [13]. Other studies reported a wider range of cycles, such as 3–11 cycles by Cheryl Sarah Philipose et al. [11]. and 6–8 cycles by Sonal Bhati et al[2]. Differences in the number of cycles may be related to institutional protocols, patient tolerance, and tumour response during treatment.

The pCR rate in the present study was 23.53%, which is comparable to AS Ramaswamy, BN Kumarguru et al [12] (22.7%), Cheryl Sarah Philipose et al. [11] (22.2%), and Perubhotla et al.

(18%). Higher pCR rates were reported by Vasudevan et al. (27.1%) and Sonal Bhati et al [2]. (26.6%), whereas Sheereen S, Lobo D. F et al. [15]. reported a lower pCR rate of 17.9%. These variations may be attributed to differences in tumour biology, chemotherapy regimens, and duration of treatment.

Pathological partial response (pPR) was the predominant response pattern in the present study (60.78%), which is comparable to Vasudevan D, Jayalakshmy P.S, et al. [13] (70.9%), Sonal Bhati et al [2]. (63.3%), and Perubhotla et al. (76%). However, Sheereen et al. reported a significantly lower pPR rate (15.4%), with a correspondingly higher non-response rate. The pathological non-response (pNR) rate in the present study was 15.69%, which is lower than that reported by Sheereen S, Lobo D. F et al. [15] (66.7%) and D. Sethi et al. (42.5%), but higher than Vasudevan D, Jayalakshmy P.S, et al. [13] (2%) and Perubhotla L.M, Kodandapani S. et al [14] (6%). The wide variation in non-response rates across studies may reflect differences in disease stage at presentation, biological aggressiveness, treatment compliance, and chemotherapy protocols. Overall, the findings of the present study are largely consistent with contemporary Indian literature and demonstrate satisfactory pathological response rates following neoadjuvant chemotherapy in Table 8.

Table 8: COMPARISONS OF CLINICOPATHOLOGICAL PARAMETERS IN POST-NACT MRM SPECIMEN

Parameters	D Sethi, R. Sen, S. Parsad et al. [16]	Vasudevan D, Jayalakshmy P.S, et al. [13]	Sheereen S, Lobo D. F et al. [15]	Cheryl Sarah Philipose et al. [11]	AS Ramaswamy, BN Kumarguru et al [12]	Perubhotla L.M, Kodandapani S. et al [14]	Sonal Bhati et al. [2]	Present Study
YEAR	2013	2015	2018	2019	2021	2021	2022	**2026**
N=	40	48	39	22	24	50	30	**51**
Mean age	46	50.58		49.5	49.79	50	50.13	**49.5**
Laterality	___	____	RIGHT UOQ	RIGHT = LEFT UOQ	Left central	Right UOQ	RIGHT=LEFT	**Left UOQ=RIGHT UIQ**
NACT	2-6	3	4-6	3-11	3	4	6-8	**3-8**
pCR	20%	27.1%	17.9%	22.2%	22.7%	18%	26.60%	**23.53%**
pPR	37.5%	70.9%	15.4%	77.3%	77.3%	76%	63.30%	**60.78%**
pNR	42.5%	2%	66.7%			6%	10%	**15.69%)**

The present study evaluated cytoplasmic, nuclear, and stromal changes and compared the findings with previously published studies by Pradhan and Chatterjee et al. (2023), Sheereen and Lobo et al. (2017), Cheryl Sarah Philipose et al. (2017), Gaur and Yadav et al. (2020), Perubhotla and Kodandapani et al. (2021), and Sonal Bhati et al. (2022) as shown in Table 9.

Cytoplasmic Changes: In the present study, cytoplasmic eosinophilia was the most frequently observed cytoplasmic alteration (74.51%). This finding is in agreement with Pradhan R and Chatterjee S et al., who reported a comparable prevalence (62.8%). Increased cytoplasmic eosinophilia reflects enhanced keratin production and altered protein synthesis, commonly seen in dysplastic and malignant epithelial cells. The lower incidence reported by Sheereen S and Lobo D.F et al. may be attributed to differences in case composition, grading criteria, or observer variability.

Cytoplasmic vacuolation was noted in 15.68% of cases, closely correlating with findings by Cheryl Sarah Philipose et al. (15%). Higher frequencies reported by other authors may indicate a greater degree of cellular degeneration or metabolic stress in their study populations. The relatively lower incidence in the present study suggests a predominance of less advanced lesions.

Nuclear Changes: Nuclear enlargement was observed in 13.73% of cases in the present study, which is considerably lower than the frequencies reported by Pradhan et al. (77.77%) and Sheereen et al. (89.7%). Hyperchromasia, a key indicator of cellular atypia, was noted in 49.02% of cases, which is lower than that reported in earlier studies, where values ranged from 71.4% to 87.2%. A high nuclear-to-cytoplasmic ratio was observed in 31.37% of cases in the present study, again lower than the proportions reported in comparable studies.

Prominent nucleoli were seen in 35.29% of cases, which is lower than the findings of Sheereen et al.

(76.9%) and Gaur et al. (65.7%). Features of nuclear degeneration such as karyorrhexis and karyolysis were observed in 27.45% of cases, while pyknosis was infrequent (1.96%), indicating relatively fewer advanced degenerative nuclear changes in the present cohort. Pleomorphic nuclei were identified in 29.41% of cases, which is lower than most comparative studies, suggesting variation in nuclear atypia across populations.

Stromal Changes: Among stromal alterations, necrosis was observed in 39.22% of cases in the present study compared to 80% in Sonal Bhati et al. On statistical comparison using the Chi-square test, this difference was statistically significant ($\chi^2 = 9.02$, df = 1, p = 0.003). Fibrosis was identified in 58.82% of cases, compared to 73.3% in Sonal Bhati et al.; however, this difference was not statistically significant ($\chi^2 = 1.58$, df = 1, p = 0.21). Calcification and giant cells showed comparable frequencies across studies, while hyalinization of blood vessel walls demonstrated marked variability. Giant cells were identified in 27.45% of cases, comparable to Sheereen et al. (35.9%) and Sonal Bhati et al. (30%). Degenerative stromal changes were noted in 25.49% of cases, while elastosis or collagenization was present in 19.61%, which is lower than that reported by Gaur et al. (48.6%). Calcification was seen in 25.53% of cases, comparable to Gaur et al. (31.4%).

Foamy histiocytes and hemosiderin-laden macrophages were infrequent findings in the present study, similar to earlier reports. Hyalinization of blood vessel walls was observed in 27.45% of cases, which is higher than that reported by Sheereen et al. (5.1%) but lower than Sonal Bhati et al. (54%), indicating variability in vascular stromal response.

The variation in cytological features observed across studies may be attributed to differences in study design, sample size, lesion spectrum, diagnostic criteria, and population characteristics. The present study demonstrates a moderate prevalence of cytoplasmic and stromal alterations with comparatively fewer nuclear atypical features, highlighting the heterogeneity of cytomorphological presentation. The findings of the present study reinforce the variability of cytological features reported in the literature and emphasize the importance of comprehensive evaluation of cytoplasmic, nuclear, and stromal changes for accurate diagnosis. Overall, the present study demonstrates statistically significant variation in certain stromal features, particularly necrosis, highlighting heterogeneity in cytomorphological presentation across populations.

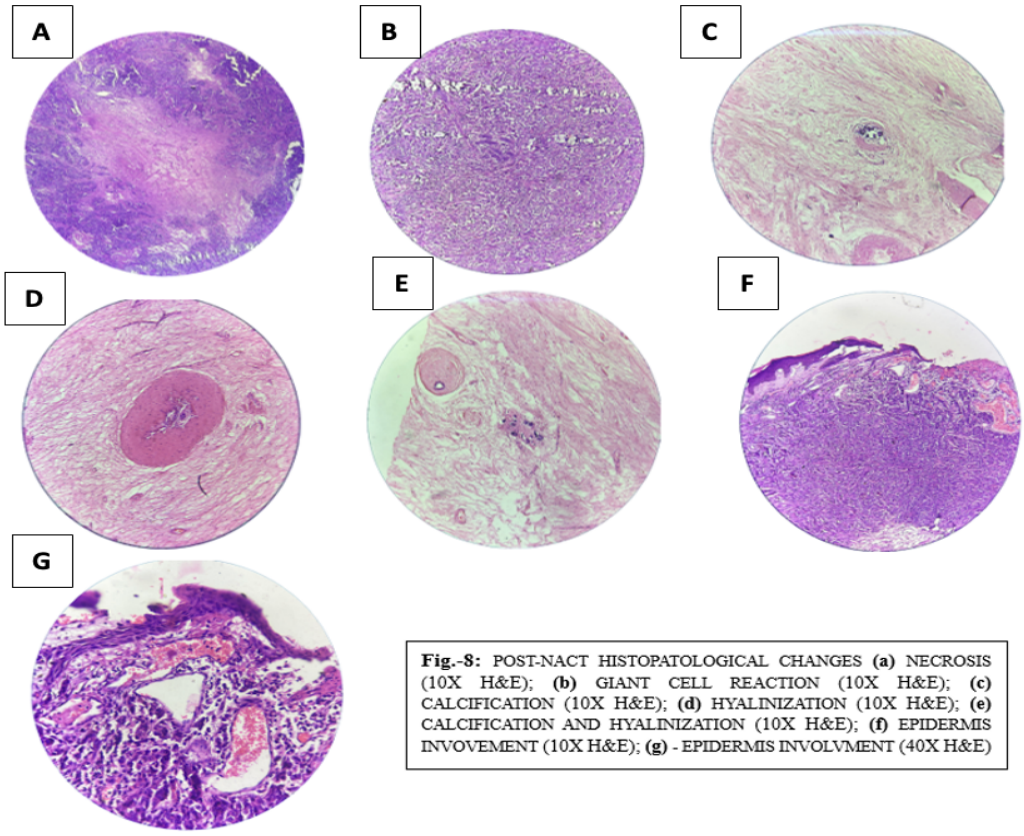

Fig.-8: POST-NACT HISTOPATOLOGICAL CHANGES **(a)** NECROSIS (10X H&E); **(b)** GIANT CELL REACTION (10X H&E); **(c)** CALCIFICATION (10X H&E); **(d)** HYALINIZATION (10X H&E); **(e)** CALCIFICATION AND HYALINIZATION (10X H&E); **(f)** EPIDERMIS INVOVEMENT (10X H&E); **(g)** - EPIDERMIS INVOLVMENT (40X H&E)

Table 9: Comparison of Post-Nact Histopathological Features Appreciated in Invasive Breast Cancer in Various Studies

	Parameters	Sheereen S, Lobo D. F et al. [15]	Cheryl Sarah Philipose et al. [11]	Gaur M, Yadav A et al. [14]	Perubhotla L.M, Kodandapani S. et al [14]	Sonal Bhati et al. [2]	Pradhan R, Chatterjee S et al [17]	Present Study
Years		2017	2017	2020	2021	2022	2023	**2026**
N=		39	22	35	50	30	36	**51**
Cytoplasmic Changes	Cytoplasmic eosinophilia			62.8	22			74.51
	Cytoplasmic vacuolation		15	28.6		36.6		15.68
Nuclear Changes	Nuclear Enlargement	89.7		74.3		46.6	77.77	13.73
	Hyperchromasia	87.2		71.4			72.22	49.02
	High N:C Ratio	84.6		71.4			63.88	31.37
	Presence of prominent nucleoli	76.9	____	65.7	____	____	_____	35.29
	karyorrhexis/ karyolysis	71.8	14	62.8			36.11	27.45
	Pyknosis	59	16	51.4				1.96
	Pleomorphic nuclei	61.5		60			77.77	29.41
Stromal Changes	Necrosis	74.4	16	60	46	80		39.22
	Fibrosis	64.1	5	68.7	10	73.3	33.33	58.82
	Desmoplasia	59		31.4		66.6		1.96
	Giant cells	35.9	5	34.3	6	30	8.33	27.45
	Degenerative changes				16			25.49
	Elastosis/ collagenization	35.9		48.6			8.33	19.61
	Calcification	23.1		31.4	16	16.6	13.88	25.53
	Foamy histocytes				38		5.88	1.96
	Hemosiderin laden macrophages	17.4	5	25.7	10	13.3	5.55	1.96
	Mucinous changes					10		
	Hyalinization of the walls of blood vessels	5.1	17	25.7	____	54	____	27.45

The present study evaluated the distribution of grades and compared the findings with previously published studies by Vasudevan D, Jayalakshmy P.S, et al [13], Sonal Bhati et al. [2], and Tiwari K, Verma N et al. [18]. In the present study, Grade 2 was the most prevalent (50.98%), followed by Grade 0 and Grade 1 (15.69% & 23.58% each), while Grade 3 constituted the smallest proportion (9.8%).

A similar predominance of Grade 2 was reported by Tiwari K, Verma N et al. [18], who observed Grade 2 in 50% of cases, indicating concordance with recent literature. In contrast, earlier studies by Vasudevan et al. and Sonal Bhati et al. demonstrated a higher prevalence of Grade 1, suggesting variation in disease severity or differences in population characteristics, diagnostic criteria, or study methodology.

The proportion of Grade 3 in the present study was higher than that reported by Vasudevan et al. (2.1%) and Sonal Bhati et al. (3.3%). This finding may reflect improved diagnostic accuracy, increased awareness, or delayed clinical presentation leading to identification of more advanced disease stages. Differences in sample size and demographic factors may also have contributed to the observed variation.

On statistical comparison using the Chi-square test, a significant difference in GRDE grade distribution was observed between the present study and Vasudevan et al. ($\chi^2 = 6.87$, df = 3, $p = 0.032$). The difference in distribution of GRDE grades between the present study and Vasudevan et al. was statistically significant This indicates a shift in grading patterns over time and underscores the influence of evolving diagnostic practices and population characteristics.

Table 10: Correlation of Post NACT MRBS in different studies.

Grade	Vasudevan D, Jayalakshmy P.S, et al [13] (2015)	Sonal Bhati et al. [2] (2023)	Tiwari K, Verma N et al. [18] (2024)	PRESNT STUDY %
n	48	30	34	**51**
0	27.1 (13)	26.60 (8)	2.94 (1)	**15.69 (08)**
1	27.1 (13)	43.30 (13)	38.24 (13)	**23.53 (12)**
2	43.8 (21)	26.60 (8)	50.00 (17)	**50.98 (26)**
3	2.1 (1)	3.30 (1)	8.82 (3)	**9.80 (5)**

In the present study, lymphocytic response was observed in all cases (100%). Grade 1 lymphocytic response was the most common pattern (66.67%), followed by Grade 2 (23.53%) and Grade 3 response (9.80%). In contrast, studies by Gundimeda et al [19]. and Sethi et al [16]. reported a predominance of Grade 2 lymphocytic response, accounting for 55.8% and 55% of cases respectively. Sonal Bhati et al [2] demonstrated a more even distribution, with 48% Grade 1, 32% Grade 2, and 20% Grade 3 responses.

The lymphocytic response is attributed by tumour biology, stage at presentation, and chemotherapy protocols. Previous studies have demonstrated that higher grades of lymphocytic response are associated with better pathological response, reflecting an effective host immune reaction to chemotherapy-induced tumour necrosis. Pathological complete response rates reported from 20% to 39% in following literature . The present study demonstrated a pCR rate of 23.53%, which is comparable to Sonal Bhati et al. (26.6%) and Sethi et al. (20%), though lower than that reported by Gundimeda et al. (39%). A trend toward improved pathological response was observed with increasing grades of lymphocytic response, with moderate and marked lymphocytic infiltration showing better pathological outcomes. Studies by Sethi et al. and Gundimeda et al. have demonstrated that higher grades of lymphocytic response are associated with increased rates of pCR and reduced non-response rates. Moderate and marked lymphocytic infiltration showed better pathological outcomes when compared to mild infiltration, indicating that lymphocytic response is an important morphological predictor of treatment response following NACT.

Table 11: Comparisons of Lymphocytic Response Grade with Various Study

Lymphocytic Response Grade	D Sethi, R. Sen, S. Parsad et al. [16]	Gundimeda V R N Krishna Kanth Nambiar Ajit et al. [19]	Sonal Bhati et al. [2]	Present Study
Year	2013	2019	2022	**2026**
N=	38/40	100/108	25/30	**51/51**
1	9 (22.5%)	30 (27.8%)	12(48%)	**34 (66.67%)**
2	22 (55%)	60 (55.8%)	8(32%)	**12 (23.53%)**
3	7 (17.5%)	10 (9.3%)	5(20%)	**5 (9.80%)**

Conclusion

Neoadjuvant chemotherapy (NACT) is an effective treatment modality for locally advanced breast carcinoma, facilitating tumour downstaging and improving surgical management. Histopathological examination of modified radical mastectomy (MRM) specimens following NACT demonstrates a wide range of tumoural and stromal alterations that reflect therapeutic response. In the present study, partial pathological response (pPR) was the most common outcome, whereas pathological complete response (pCR) was associated with favourable prognostic parameters, including smaller residual tumour size, absence of nipple–areola complex involvement, negative surgical margins, and lower pathological stage. Common histomorphological changes observed after NACT included fibrosis, necrosis, cytoplasmic eosinophilia, and lymphocytic infiltration. Notably, moderate to marked lymphocytic response was associated with better pathological outcomes, suggesting its potential role as a marker of treatment effectiveness. These findings underscore the significance of meticulous histopathological evaluation of post-NACT breast specimens, as it provides valuable information regarding treatment response, residual disease burden, and prognostic assessment, thereby contributing to optimal patient management.

Financial support and sponsorship: Nil.

Conflicts of interest: There are no conflicts of interest.

Acknowledgments: The authors are grateful to the faculty of the Pathology Department of Pt J. N. M. Medical College for their support in conducting this study.

References

1. Lakhtakia R. A brief history of breast cancer: Part I: Surgical domination reinvented. Sultan Qaboos Univ Med J. 2014;14(2):e166-169.

2. Bhati S, Bhatia G, Shrey, Goyal N. Evaluation of histomorphological changes in post-neoadjuvant chemotherapy MRM specimens – a tertiary care centre study. J Med Sci Health. 2023;9(3):288-295.
3. Giaquinto AN, Sung H, Miller KD, Kramer JL, Newman LA, Minihan A, et al. Breast cancer statistics, 2022. CA Cancer J Clin. 2022;72(6):524-541.
4. Mehrotra R, Yadav K. Breast cancer in India: Present scenario and the challenges ahead. World J Clin Oncol. 2022;13(3):209-218.
5. Kumar D, Batra U. Epidemiology of breast cancer in Indian women: Population and hospital based study. EAI Endorsed Trans Perv Health Technol. 2018.
6. Menon G, Alkabban FM, Ferguson T. Breast cancer. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025.
7. Rajesh A, Gurusamy DS, Manickam R, Saranya D. Evaluating the tumor burden, histological changes, and immune landscape of breast cancer post-neoadjuvant chemotherapy: Insights from 50 cases. Cureus. 2025;17(3).
8. Gaur M, Yadav A, et al. Neoadjuvant chemotherapy induced histopathological changes in breast cancer: A study of 35 cases in North India. Int J Curr Adv Res. 2022;11(3):497-501.
9. Pathak M, Deo SVS, Dwivedi SN, Sreenivas V, Thakur B, Julka PK, et al. Role of neoadjuvant chemotherapy in breast cancer patients: Systematic review and meta-analysis. Indian J Med Paediatr Oncol. 2019;40(1):48-62.
10. Bossuyt V, Provenzano E, Symmans WF, Webster F, Allison KH, Dang C, Gobbi H, et al. A dedicated structured data set for reporting of invasive carcinoma of the breast in the setting of neoadjuvant therapy: Recommendations from the International Collaboration on Cancer Reporting (ICCR). Histopathology. 2024; 84(7):1111-1129.
11. Philipose C, Umashankar T, Gatty R. A histomorphological study of changes in neoadjuvant chemotherapy in breast malignancies. J Clin Diagn Res. 2019.
12. Ramaswamy A, Kumarguru BN, Venkatappa S, Prashanth BM, Kumar U. Post-chemotherapy associated histopathological findings in invasive breast carcinoma: A camouflaged signature. Natl J Lab Med. 2021;10:11-17.
13. Vasudevan D, Jayalakshmy PS, Kumar S, Mathew S. Assessment of pathological response of breast carcinoma in modified radical mastectomy specimens after neoadjuvant chemotherapy. Int J Breast Cancer. 2015;2015:536145.
14. Perubhotla L, Kodandapani S, Murthy SS. Evaluation of pathological response in post-neoadjuvant chemotherapy breast carcinoma specimens using residual cancer burden system. J Clin Diagn Res. 2021;15(5).
15. Sheereen S, Lobo FD, Kumar B, Kumar SM, Reddy GS, Patel W, et al. Histopathological changes in breast cancers following neoadjuvant chemotherapy: Implications for assessment of therapy-induced cytological and stromal changes for better clinical outcome and effective patient care. Asian J Oncol. 2018;4(2):61-68.
16. Sethi D, Sen R, Parshad S, Khetarpal S, Garg M, Sen J. Histopathologic changes following neoadjuvant chemotherapy in locally advanced breast cancer. Indian J Cancer. 2013;50(1):58-64.
17. Pradhan R, Mondal S, Sikdar M, Chatterjee S. Histomorphological changes in breast cancer following neoadjuvant chemotherapy: Retrospective study in a tertiary care hospital. J Indian Med Assoc. 2023;121:44-48.
18. Tiwari K, Verma N. Post-chemotherapy changes in breast with evaluation of residual carcinoma burden. Asian J Med Sci. 2024;15:161-167.
19. Nambiar A. Evaluation of morphological predictors for response to neoadjuvant chemotherapy in breast cancer. J Med Sci Clin Res. 2019;7.