Journal of Cardiovascular Disease Research

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 09, 2024

EFFICACY OF GATA3 EXPRESSION IN BREAST CARCINOMA TISSUE FOLLOWING NEOADJUVANT CHEMOTHERAPY

R. Priyanka[1], Shashidhar. H. B[2], Raviteja C. N.[3], Naveen Kumar Ds[4]

[1]Post Graduate, Mysore Medical College and Research Institute, Department of Pathology- Karnataka, India.
[2]Professor, Mysore Medical College and Research Institute, Department of Pathology- Karnataka, India.
[3]Senior Resident, Chamarajanagar Institute of Medical sciences, Department of Pathology- Karnataka, India.
[4]Post Graduate, Mysore Medical College and Research Institute, Department of Pathology- Karnataka, India.

Received Date: 18/08/2024 Acceptance Date: 08/09/2024

Corresponding Author: Dr. Raviteja C. N., Senior Resident, Chamarajanagar Institute of Medical sciences, Department of Pathology- Karnataka, India.

Abstract

Background: Breast cancer is a leading cause of cancer-related mortality in women, with a rising incidence globally. Neoadjuvant chemotherapy(NACT) is a standard treatment approach for operable advanced loco-regional breast cancer, aiming to achieve tumor shrinkage, downstaging, and improved surgical outcomes. GATA3 expression has been identified as a significant marker for tumor differentiation, estrogen receptor status, and clinical outcomes in breast cancer. **Objectives:** To investigate the expression of GATA3 in post-NACT breast carcinoma cases and its utility in confirming histopathological diagnosis of partial and complete response, thereby guiding treatment strategies and predicting patient outcomes. **Methods:** A cross-sectional study of 60 breast carcinoma cases treated with NACT was conducted at Mysore Medical College and Research Institute. GATA3 expression was evaluated using immunohistochemistry, and its correlation with histopathological response to chemotherapy was assessed. **Results:** Among 60 cases, GATA3 was expressed in 87% of cases, with 91% of partial responders and 73% of complete responders showing immunopositivity. The study demonstrates GATA3 expression in post-NACT breast carcinoma cases, highlighting its potential as a predictive marker for treatment outcomes. **Conclusion:** GATA3 is a valuable marker for predicting response to NACT in breast cancer patients, supporting its utility in confirming histopathological diagnosis, guiding treatment strategies, and improving patient outcomes.

Keywords: GATA3, Breast carcinoma, Immunohistochemistry, Neoadjuvant Chemotherap

Introduction

Breast cancer represents the most prevalent site-specific malignancy among women and stands as the foremost cause of cancer-related mortality in females aged 20 to 59 years [1]. Among Indian women, breast cancer is the leading type of cancer in urban environments and the second most prevalent in rural contexts. A consistent rise in incidence, estimated at 0.5–2% per year, has been recorded across all geographic areas and age groups, with a significant

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 09, 2024

impact on younger women aged below 45 [2]. Breast cancer is characterized by its heterogeneity, encompassing various forms, from ductal carcinoma in situ (DCIS) to extensive metastatic disease. The treatment approach and prognosis are influenced by a variety of clinical and histopathological factors, such as tumor dimensions, tumor classification, hormonal receptor status, the therapeutic modalities employed, and, crucially, the stage at which the cancer is detected. Due to significant advancements in oncology, a range of treatment options for breast cancer is currently available, including surgical intervention, radiotherapy, chemotherapy, and more specialized therapies targeting hormonal and tumor receptors [3]. The current guidelines established by the National Comprehensive Cancer Network (NCCN) for the management of operable advanced loco-regional breast cancer advocate for the administration of neoadjuvant chemotherapy. This is typically followed by surgical intervention, which may involve mastectomy or lumpectomy accompanied by axillary lymph node dissection, and, if indicated, subsequent adjuvant therapy. Following neoadjuvant chemotherapy, the pathological response to the treatment is evaluated [1].

Neoadjuvant chemotherapy (NACT) refers to the systemic administration of chemotherapy agents aimed at reducing tumor size prior to surgical intervention. Initially, NACT was primarily utilized for advanced, inoperable carcinomas; however, its application has expanded to include operable cancers. This strategy is designed to achieve tumor shrinkage, downstaging of the disease, enhance surgical outcomes, lower the risk of distant metastasis, and prolong overall disease-free survival. Histopathological assessment of tumor regression is considered the gold standard for evaluating treatment efficacy in numerous solid malignancies [4]. The achievement of pathological complete response (pCR) following neoadjuvant chemotherapy is linked to markedly improved event-free survival and overall survival rates [5].

GATA-3, a transcription factor, is essential for the development of the mammary gland [6]. GATA3 is particularly significant in the differentiation of luminal epithelial cells and is preferentially expressed in luminal-type breast cancer [7]. The role of GATA3 in invasive breast cancer cells is to promote the reversal of epithelial-mesenchymal transition, thereby inhibiting the process of cancer metastasis [8]. GATA3 serves as a valuable tool for identifying metastatic lesions in the absence of other markers [6]. GATA3 may function as a novel prognostic marker for breast cancer and could be clinically relevant in predicting poor chemotherapy outcomes [7]. Currently, GATA3 IHC is employed in routine diagnostics as a surrogate marker for identifying breast and urothelial carcinoma origins in cases of unknown primary tumors [9].

Objectives

- To study the expression of GATA3 in breast carcinoma following neoadjuvant chemotherapy.
- To confirm the histopathological findings of complete response and partial response after neoadjuvant chemotherapy.

Methods

It was a cross-sectional study conducted in the Department of Pathology, Mysore Medical College and Research Institute from K.R. Hospital during the period of March 2022 – March 2023. All patients with breast carcinomas who had previously received NACT followed by Modified Radical Mastectomy (MRM) were included in the study. Specimens of benign lesions / in-situ carcinomas / metastatic lesions of the breast and autolyzed specimens were excluded from the study. The specimens were received in 10% formalin and the mastectomy

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 09, 2024

specimens were fixed in fresh formalin for 24 hours. The standard protocol for grossing surgical specimens was meticulously followed in each case. After conventional processing, paraffin sections of 5µm thickness were stained using hematoxylin and eosin to enable a thorough histopathological investigation.

Each stained section was evaluated for the following:

1. Histological type of the tumor
2. Pathological response to chemotherapy
3. Lymph node status
4. Lymphovascular invasion

Immunohistochemistry

Immunohistochemical staining was done with GATA-3 antibody. The presence of brown coloured end product at the site of the target antigen was indicative of positive reactivity. The immunoreactivity score for GATA-3 expression was determined by multiplying the proportion of immunoreactive cells, classified as Score 0 (absence of stained tumor cells), Score 1 (1–10% stained), Score 2 (11–50% stained), Score 3 (51–80% stained), and Score 4 (81–100% stained), by the intensity of the staining, categorized as Staining Score 0 (no tumor cells stained), and Scores 1, 2, and 3 representing weak, moderate, and strong staining, respectively. [12]

Statistical Analysis

Data was coded and placed into an Excel spreadsheet for statistical analysis. The data analysis was conducted using version 20 of SPSS (Statistical Package for Social Sciences). Quantitative data were represented through mean and standard deviation, whereas qualitative data were summarized in terms of proportions.

Results

Table 1: Age distribution of patients

Age	**No. of cases**	**% of cases**
≤40	10	17%
41-50	13	22%
51-60	19	32%
61-70	14	23%
≥70	4	6%
Total	**60**	**100%**

Table 2: Laterality of invasive breast carcinoma in patients

Laterality	**No. of cases**	**% of cases**
R	32	53%
L	28	47%
Total	**60**	**100%**

Table 3: Histological type of breast carcinoma in patients

Histological type	**No. of cases**	**% of cases**
IBC-NST	26	43%
IDC	31	52%
ILC	2	3%

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 09, 2024

IBC-mixed type	1	2%
Total	**60**	**100%**

Table 4: Lymph node involvement among patients

LN status	**No. of cases**	**% of cases**
LN(+)	33	55%
LN(-)	27	45%
Total	**60**	**100%**

Table 5: Lymphovascular invasion of breast carcinoma in patients

LV invasion	**No. of cases**	**% of cases**
(+)	23	38%
(-)	37	62%
Total	**60**	**100%**

Table 6: Response to chemotherapy for breast carcinoma in patients

Response to chemotherapy	**No. of cases**	**% of cases**
Partial	45	75%
Complete	15	25%
Total	**60**	**100%**

Table 7: Expression of GATA3 among invasive breast carcinoma patients

GATA3 score	**No. of cases**	**% of cases**
0(Negative)	8	13%
1(Weak)	7	12%
2(Moderate)	22	37%
3(Strong)	23	38%
Total	**60**	**100%**

Table 8: Expression of GATA3 among partial and complete pathological response in patients:

Response to chemotherapy	**GATA3(+ve)**	**GATA3(-ve)**
Partial	41(91%)	4(9%)
Complete	11(73%)	4(27%)
Total	**52**	**8**

Sixty patients were included in this study. Most of the study participants belong to the age group of 51–60 years (32%) with mean age of 54.05±12.19 years(Table 1). With respect to laterality of breast carcinoma, 53% of the cases had right sided carcinoma and 47% had left sided carcinoma(Table 2). Among the 60 cases, 43% of the cases were of IBC-NST type, 52% were IDC type, 3% were ILC type and 2% were IBC-mixed type(Table 3). Lymph node involvement was present in 33 out of 60 cases(55%)(Table 4). Lymphovascular invasion was present in 23 out of 60 cases(38%)(Table 5). With respect to pathological response to

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 09, 2024

chemotherapy, 45 cases(2/3rd) were reported as partial response and 15 cases(1/3rd) were reported as complete pathological response to chemotherapy in histopathological examination(Table 6). GATA-3 was not expressed in 13% of breast cancer cases. GATA-3 expression was weakly positive in 12% of the breast cancer cases. GATA-3 expression was moderately positive in 37% of the breast cancer cases. GATA-3 expression was strongly positive in 38% of the breast cancer cases(Table 7). 41 out of 45 cases(91%) reported as partial response showed GATA-3 immunopositivity. 11 out of 15 cases(73%) reported as complete response showed GATA-3 immunopositivity(Table 8).

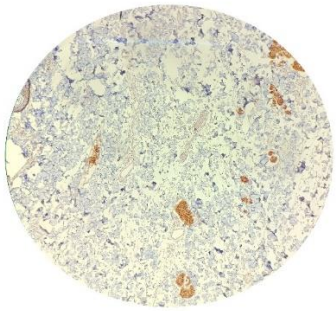

Figure 1: GATA3 staining(Nuclear score 1)

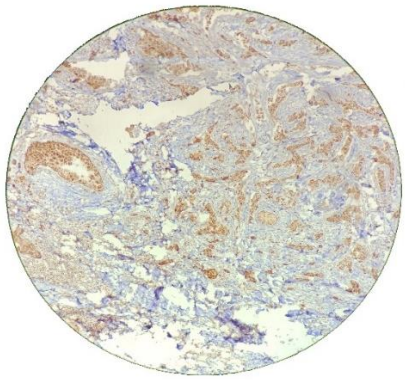

Figure 2A: GATA3 staining(Nuclear score 2)

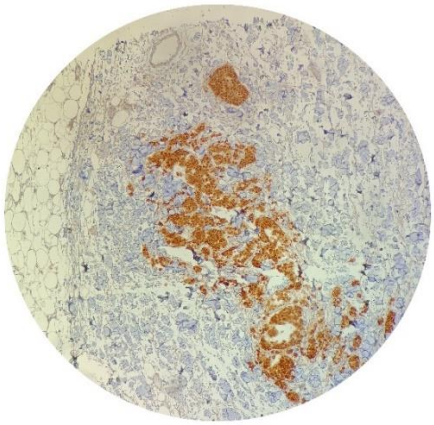

Figure 2B: GATA3 staining(Nuclear score 2)

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 09, 2024

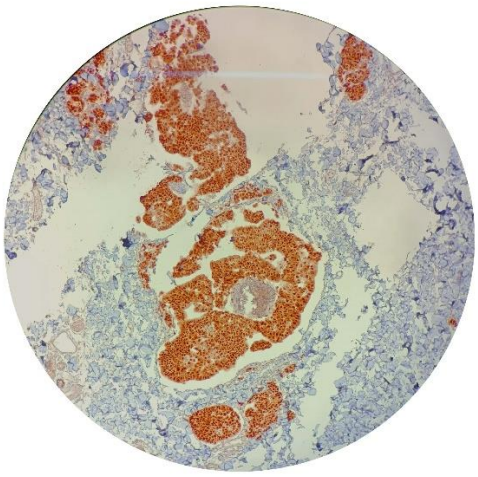

Figure 3A: GATA3 staining(Nuclear score 3)

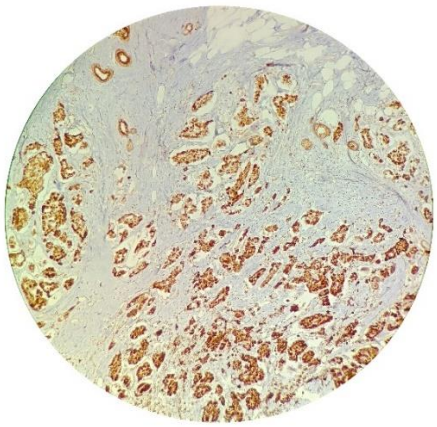

Figure 3B: GATA3 staining(Nuclear score 3)

Discussion

Breast cancer is the most prevalent cancer diagnosed in women and stands as the second most common cause of death among women globally. Although the majority of cases are diagnosed in women over the age of 50, it is not rare for younger women to develop this disease [3]. GATA-3 plays a pivotal role in the differentiation of luminal epithelial cells within the breast. Immunohistochemistry (IHC) for GATA-3 expression is chiefly utilized in surgical pathology to determine the breast or urothelial origin of carcinomas [2]. GATA-3 has been identified as a significant and independent marker for tumor differentiation, estrogen receptor status, and clinical outcomes in breast cancer [11]. A variety of studies examining the prognostic significance of GATA-3 in breast cancer treatment, whether in adjuvant or neoadjuvant scenarios, have produced somewhat contradictory results [10].

The study aimed to investigate the expression of GATA3 in post-neoadjuvant breast carcinoma cases and establish its utility in confirming the histopathological diagnosis of partial and complete response. A total of 60 cases of breast malignancies that received NACT were analyzed in the present study.

The age range of study participants was 30-78 years. Most of the study participants belong to the age group of 51–60 years (32%) with a mean age of 54.05 which is consistent with the studies conducted by H. E. Gulbahce *et al.* [10] and Banik *et al.* [12] which showed a mean age of 53.4 and 49.5 years respectively.

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 09, 2024

In the present study, 52% of the carcinomas are of ductal type. This proportion is lower compared to the studies conducted by Tominaga *et al.* [7] and Hemavathi *et al.* [13], which showed 92% and 90% respectively.

In the present study, lymphovascular invasion was seen in 38% of cases which is lower compared to the studies conducted by Banik *et al.* [12] and Cheryl Sarah Philipose *et al.* [4], which showed 62.7% and 59% respectively.

In the present study, lymph node metastasis was observed in 55% of cases which is lower compared to the studies conducted by Hemavathi *et al.* [13] and Cheryl Sarah Philipose *et al.* [4], which showed 73% and 77% respectively.

In the present study, 87% of cases were positive for GATA3 which is consistent with the studies conducted by Singh A *et al.* [2], Banik *et al.* [12], and H. E. Gulbahce *et al.* [10], which showed 87.50%, 88.10%, and 84.50% respectively. The study conducted by Tominaga *et al.* [7] showed GATA3 expression in only 57% of cases.

With respect to the pathological response to chemotherapy, 45 cases($2/3^{rd}$) showed partial response, and 15 cases($1/3^{rd}$) showed complete pathological response to chemotherapy on histopathological examination. In a study conducted by Hemavathi *et al.* [13], partial response was seen in 90% of cases, complete response was seen in 3.3% of cases, and no response was seen in 6.7% of cases. In a study by Singh A *et al.* [2], partial response was seen in 75.7% of cases, complete response was seen in 10.8% of cases, and 5.4% of cases showed no response.

41 out of 45 cases(91%) reported as partial response showed GATA-3 immunopositivity. 11 out of 15 cases(73%) reported as complete response showed GATA-3 immunopositivity.

Conclusion

GATA3 expression is a valuable marker for predicting response to NACT in breast cancer patients. Our findings support its utility in confirming histopathological diagnosis and guiding treatment strategies.

References

1. Subhendu BS, Shekhar R. The effect of neoadjuvant chemotherapy on pathological response and the hormone receptor profile in locally advanced breast carcinomas. South African Journal of Surgery. 2018;56(4):10-3.
2. Singh A, Karnik A, Anand A. Prevalence of GATA-3 in invasive breast cancer and its significance in predicting response to neoadjuvant chemotherapy: a tertiary center experience. International Surgery Journal. 2021 May 28;8(6):1833-8.
3. Sheereen, S., Lobo, F.D., Kumar, B., Kumar, M., Reddy, S., Patel, W. and Nayyar, A.S., 2018. 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 Journal of Oncology*, *4*(02), pp.061-068.
4. PHILIPOSE CS, Umashankar T, GATTY RC. A Histo-Morphological Study of Changes in Neoadjuvant Chemotherapy in Breast Malignancies. Journal of Clinical & Diagnostic Research. 2019 Mar 1;13(3).
5. Spring LM, Fell G, Arfe A, Sharma C, Greenup R, Reynolds KL, Smith BL, Alexander B, Moy B, Isakoff SJ, Parmigiani G. Pathologic complete response after neoadjuvant chemotherapy and impact on breast cancer recurrence and survival: a comprehensive meta-analysis. Clinical cancer research. 2020 Jun 15;26(12):2838-48.

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 09, 2024

6. Wasserman JK, Williams PA, Islam S, Robertson SJ. GATA-3 expression is not associated with complete pathological response in triple negative breast cancer patients treated with neoadjuvant chemotherapy. Pathology-Research and Practice. 2016 Jun 1;212(6):539-44.
7. Tominaga N, Naoi Y, Shimazu K, Nakayama T, Maruyama N, Shimomura A, Kim SJ, Tamaki Y, Noguchi S. Clinicopathological analysis of GATA3-positive breast cancers with special reference to response to neoadjuvant chemotherapy. Annals of oncology. 2012 Dec 1;23(12):3051-7.
8. Yan W, Cao QJ, Arenas RB, Bentley B, Shao R. GATA3 inhibits breast cancer metastasis through the reversal of epithelial-mesenchymal transition. Journal of Biological Chemistry. 2010 Apr 30;285(18):14042-51.
9. Querzoli P, Pedriali M, Rinaldi R, Secchiero P, Rossi PG, Kuhn E. GATA3 as an adjunct prognostic factor in breast cancer patients with less aggressive disease: a study with a review of the literature. Diagnostics. 2021 Mar 28;11(4):604.
10. Gulbahce HE, Sweeney C, Surowiecka M, Knapp D, Varghese L, Blair CK. Significance of GATA-3 expression in outcomes of patients with breast cancer who received systemic chemotherapy and/or hormonal therapy and clinicopathologic features of GATA-3–positive tumors. Human pathology. 2013 Nov 1;44(11):2427-31.
11. Kouros-Mehr H, Kim JW, Bechis SK, Werb Z. GATA-3 and the regulation of the mammary luminal cell fate. Current opinion in cell biology. 2008 Apr 1;20(2):164-70.
12. Banik L, Pal M, Mayur N. Study of GATA-3 Expression in Breast Carcinoma in a Tertiary Care Hospital in Eastern India: GATA3 expression in breast carcinoma. Archives of Breast Cancer. 2022 Jul 19:450-5.
13. Hemavathi N, Sridhar H. Histomorphological analysis of residual breast tumors following neoadjuvant chemotherapy. J Med Sci Health. 2021;7(2):90-5.