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

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

International Journal of Current Pharmaceutical Review and Research 2025; 17(9); 89-93

Original Research Article

A Study on Incidence of Expression of Mutated BRCA2 Gene among Breast Carcinoma Patients and its Impact on Biological Behaviour

Md. Anisur Rahaman[1], Diptendra Kumar Sarkar[2], Debarshi Jana[3]

[1]Clinical Tutor, MBBS, MS, Department of General Surgery, Malda Medical College & Hospital, Malda, West Bengal 732101

[2]Professor, Department of General Surgery, IPGMER and SSKM Hospital, Kolkata, West Bengal 700020

[3]PhD (Cal), Biostatistics and Epidemiology (IBRI), Consultant Biostatistician and Epidemiologist, Young Scientist (Associate Professor), Department of Science & Technology, Government of India, IPGMER and SSKM Hospital, Ekbalpur, Kolkata, West Bengal 700023

Received: 01-06-2025 / Revised: 16-07-2025 / Accepted: 19-08-2025

Corresponding Author: Dr. Md Anisur Rahaman

Conflict of interest: Nil

Abstract

Introduction: Breast cancer is one of the most common malignancies worldwide, with both genetic and environmental factors contributing to its development. The BRCA2 gene, a critical tumour suppressor gene, plays a pivotal role in maintaining genomic stability by repairing double-strand DNA breaks through homologous recombination.

Aims: This study aims to determine the incidence of BRCA2 gene mutations in breast carcinoma patients and examine its impact on tumour biological behaviour. Additionally, it seeks to correlate BRCA2 mutation status with clinical outcomes and prognosis.

Materials & Methods: This is a prospective study conducted at the Institute of Postgraduate Medical Education and Research, SSKM Hospital, Kolkata, from January 2016 to August 2017, with a sample size of 50 breast carcinoma patients with BRCA2 gene mutations.

Result: It was statistically significant (p=0.0042) that ER negative tumours 11 (84.6%) had lower levels of BRCA2 than ER positive tumours 2 (15.4%).

Conclusion: We concluded that this work, we looked into the prevalence of BRCA2 gene mutations in individuals with breast cancer and how they affect the biological activity of the tumour. Our results imply that BRCA2 expression is not much impacted by age, menopausal status, or tumour size.

Keywords: Breast Carcinoma, Prognosis, Cancer, Tumour, And Lymph Node Metastasis.

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Introduction

Breast cancer is one of the most common malignancies worldwide, with both genetic and environmental factors contributing to its development. The BRCA2 gene, a critical tumour suppressor gene, plays a pivotal role in maintaining genomic stability by repairing double-strand DNA breaks through homologous recombination. Mutations in the BRCA2 gene are known to significantly increase the risk of breast cancer, particularly in familial cases. Studies have shown that individuals with inherited mutations in BRCA2 exhibit a higher susceptibility to both breast and ovarian cancers, often at an earlier age and with more aggressive biological behaviour [1].

These mutations lead to a loss of function in the protein encoded by BRCA2, impairing DNA repair mechanisms and contributing to tumour genesis. The biological behaviour of BRCA2-mutated breast cancers is often characterized by more aggressive phenotypes, including higher grade tumours, increased tumour size, and greater likelihood of metastasis [2].

The relationship between BRCA2 mutation status and clinical outcomes has been well-documented, with patients harbouring BRCA2 mutations often showing poorer prognosis due to their tumours' higher resistance to conventional therapies such as chemotherapy. Additionally, research indicates that the mutated BRCA2 gene is associated with distinct histopathological features, including high histological grade, poor differentiation, and increased proliferation rates [3].

Materials and Methods

Type of study: A Prospective study

Place of study: Institute of Postgraduate Medical Education And Research Sskm Hospital, Kolkata

Study duration: January 2016 to August, 2017.

Sample size: 50 BRCA2 gene among breast carcinoma patients.

Inclusion Criteria

- Female patients diagnosed with breast carcinoma, confirmed by histopathological examination.
- Patients aged between 18 and 75 years.
- Patients who have consented to participate in the study.
- Individuals with a known or suspected familial history of breast cancer or those with sporadic cases of breast carcinoma.
- Patients undergoing treatment or follow-up for breast carcinoma, including those with early or advanced stages of the disease.
- Availability of tumour tissue samples (biopsy or surgical specimens) for BRCA2 gene mutation analysis.

Exclusion Criteria

- Male patients or individuals diagnosed with male breast carcinoma.
- Patients with metastatic breast cancer who are not receiving curative treatment.
- Individuals with a history of other malignancies, except for non-melanoma skin cancer.
- Patients with incomplete clinical data or those who do not consent to participate in the study.
- Individuals with severe comorbidities that may interfere with treatment or data interpretation.

Study Variables

- Age
- Menopausal Status
- BRCA2 Mutation Status
- Tumour Size
- Histological Type

Statistical Analysis: Data were entered into Excel and analysed using SPSS and GraphPad Prism. Numerical variables were summarized using means and standard deviations, while categorical variables were described with counts and percentages. Two-sample t-tests were used to compare independent groups, while paired t-tests accounted for correlations in paired data. Chi-square tests (including Fisher's exact test for small sample sizes) were used for categorical data comparisons. P-values ≤ 0.05 were considered statistically significant.

Result

Table 1: Distribution of BRCA2 Mutation Expression Levels Based on Age Groups

BRCA 2 GROUP					
Age-1	**<0.2 ng/ml**	**0.2–0.49 ng/ml**	**0.5–2.1 ng/ml**	**Total**	**p-value**
<40 Years	3(23.1%)	7(25.0%)	2(22.2%)	12(24.0%)	0.9817
≥40 Years	10(76.9%)	21(75.0%)	7(77.8%)	38(76.0%)	
Total	13(100.0%)	28(100.0%)	9(100.0%)	50(100.0%)	

Table 2: Distribution of BRCA2 Mutation Expression Levels Based on Menopausal Status

BRCA 2 GROUP					
Menopausal Status	**<0.2 ng/ml**	**0.2–0.49 ng/ml**	**0.5–2.1 ng/ml**	**Total**	**p-value**
Post-Menopausal	7(53.8%)	19(67.9%)	7(77.8%)	33(66.0%)	0.4831
Pre-Menopausal	6(46.2%)	9(32.1%)	2(22.2%)	17(34.0%)	
Total	13(100.0%)	28(100.0%)	9(100.0%)	50(100.0%)	

Table 3: Distribution of BRCA2 Mutation Expression Levels Based on Tumor Size, Grade, Node Involvement, and Stage

BRCA 2 GROUP						
		<0.2 ng/ml	**0.2–0.49 ng/ml**	**0.5–2.1 ng/ml**	**TOTAL**	**p-value**
T1	<2	0(0%)	1(3.6%)	0(0%)	1(2.0%)	0.1627
	2 to 4.99	4(30.8%)	10(35.7%)	7(77.8%)	21(42.0%)	
	≥5	9(69.2%)	17(60.7%)	2(22.2%)	28(56.0%)	
Grade	I	0(0%)	2(7.1%)	2(22.2%)	4(8.0%)	0.2085
	II	3(23.1%)	8(28.6%)	4(44.4%)	15(30.0%)	
	III	10(76.9%)	18(64.3%)	3(33.3%)	31(62.0%)	
Node1	0	0(0%)	1(3.6%)	3(33.3%)	4(8.0%)	0.0478
	1 to 3	2(15.4%)	3(10.7%)	2(22.2%)	7(14.0%)	
	4 to 9	7(53.8%)	18(64.3%)	4(44.4%)	29(58.0%)	
	>9	4(30.8%)	6(21.4%)	0(0%)	10(20.0%)	

Stage	Satge-0	0(0%)	1(3.6%)	1(11.1%)	2(4.0%)	0.0093
	Stage-I	0(0%)	2(7.1%)	2(22.2%)	4(8.0%)	
	Stage-II	0(0%)	3(10.7%)	4(44.4%)	7(14.0%)	
	Stage-III	11(84.6%)	18(64.3%)	0(0%)	29(58.0%)	
	Stage-IV	2(15.4%)	4(14.3%)	2(22.2%)	8(16.0%)	

Table 4: Distribution of BRCA2 Mutation Expression Levels Based on Histopathological Type

BRCA 2 GROUP					
HP Type	**<0.2 ng/ml**	**0.2–0.49 ng/ml**	**0.5–2.1 ng/ml**	**Total**	**p-value**
DCIS	0(0%)	1(3.6%)	1(11.1%)	2(4.0%)	0.6384
IDC	13(100.0%)	26(92.9%)	8(88.9%)	47(94.0%)	
LC	0(0%)	1(3.6%)	0(0%)	1(2.0%)	
Total	13(100.0%)	28(100.0%)	9(100.0%)	50(100.0%)	

Table 6: Distribution of BRCA2 Mutation Expression Levels Based on ER, PR, and HER2 Status

BRCA 2 GROUP						
		<0.2 ng/ml	**0.2–0.49 ng/ml**	**0.5–2.1 ng/ml**	**TOTAL**	**p-value**
ER	Negative	11(84.6%)	24(85.7%)	3(33.3%)	38(76.0%)	0.0042
	Positive	2(15.4%)	4(14.3%)	6(66.7%)	12(24.0%)	
PR	Negative	11(84.6%)	24(85.7%)	3(33.3%)	38(76.0%)	0.0042
	Positive	2(15.4%)	4(14.3%)	6(66.7%)	12(24.0%)	
H2neu	Negative	13(100.0%)	20(100.0%)	6(66.7%)	39(78.0%)	0.0803
	Positive	0(0%)	8(28.6%)	3(33.3%)	11(22.0%)	

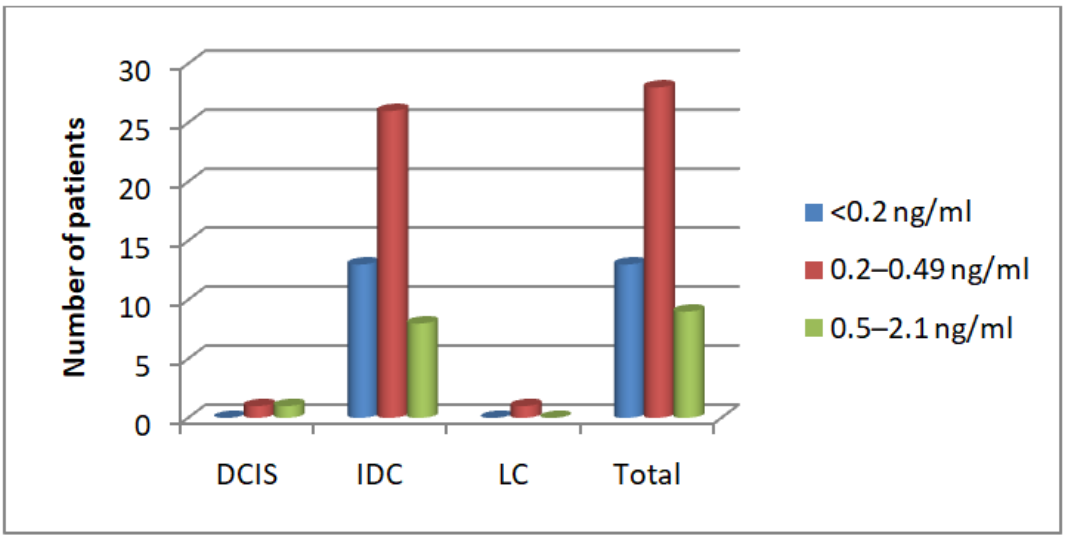

Figure 1: Distribution of BRCA2 Mutation Expression Levels Based on Histopathological Type

In our study Ten individuals (76.9%) in the upper age group (≥40 years) had a lower BRCA2 level (<0.2 ng/ml). However, 3 patients (23.1%) in the lower age group (less than 40 years) had a lower BRCA2 level (less than 0.2 ng/ml). In the three BRCA 2 groups, there was no statistically significant correlation between age (0.9817). Postmenopausal 7 patients (53.8%) had a lower level (<0.2 ng/ml) of BRCA2 than premenopausal 6 patients (46.2%) (p=0.4831). The results imply that BRCA2 mutation increases with age, resulting in lower total BRCA2 expression, even if the relationship between age and menopausal status and BRCA expression was not statistically significant. BRCA2 levels were lower in 4 (30.8%) patients with middle-sized (2–4.99 cm) tumors and 9 (69.2%) patients with big (≥5 cm) tumors; this difference was not statistically significant (p=0.1627). Therefore, there was no correlation between tumor growth and BRCA2 expression. The Modified Bloom-Richardson Grading Scheme was used to determine the histology grades. There was a statistically significant drop in BRCA2 levels in 3 out of 15 patients in grade II (23.1%) and 10 out of 31 patients in grade III (76.9%) (p=0.2085).There was a statistically significant decrease in BRCA2 levels in 7 patients (53.8%) with metastases in 4–9 lymph nodes, 4 patients (30.8%) with more than 9 lymph nodes, and 2 patients (15.4%) with 1–3 lymph node metastases

(p=0.0478). Low BRCA2 levels were statistically significant (p=0.0093) in 2 (15.4%) of the patients in stage IV and in 11 (84.6%) of the patients in stage III, according to clinical stage 11. With BRCA2 levels ranging from 0.2-0.49 ng/ml, 2 patients (7.1%) were in stage I, 3 patients (10.7%) were in stage II, 18 patients (64.3%) were in stage III, and 4 patients (14.3%) were in stage IV. With BRCA2 levels between 0.5 and 2.1 ng/ml, 2 patients (28.6%) were in stage I, 4 patients (57.1%) were in stage II, and 2 patients (22.2%) were in stage IV. Therefore, BRCA2 expression was unaffected by the disease's stage.Thirteen (100.0%) of the patients with infiltrated ductal carcinoma (IDC) showed low levels of BRCA2, according to histological type; however, this link was not statistically significant (p=0.6384). Therefore, there was no relationship between histological type and BRCA2 expression. It was statistically significant (p=0.0042) that ER negative tumors 11 (84.6%) had lower levels of BRCA2 than ER positive tumors 2 (15.4%). It was statistically significant (p=0.0042) that PR negative tumors 11 (84.6%) had lower levels of BRCA2 than ER positive tumors 2 (15.4%). HER-2/neunegativetumors had a higher prevalence of decreased BRCA2 levels 13 (100.0%), which was not statistically significant (p=0.0803).

Discussion

We found that 10 individuals (76.9%) in the upper age group (≥40 years) had lower BRCA2 levels (<0.2 ng/ml), while 3 patients (23.1%) in the lower age group (<40 years) showed the same. However, no statistically significant correlation was observed between age and BRCA2 expression (p = 0.9817). This suggests that age may not significantly influence BRCA2 expression, despite the higher prevalence of lower BRCA2 levels in older patients. Johnson et al. [4] (2018)**,** who found no significant relationship between age and BRCA2 expression in their cohort of breast cancer patients (p = 0.823).

We observed that 7 postmenopausal patients (53.8%) had lower BRCA2 levels (<0.2 ng/ml) compared to 6 premenopausal patients (46.2%) (p = 0.4831). This indicates that menopausal status does not significantly impact BRCA2 expression in this cohort, aligning with other studies that found no substantial effect of menopause on BRCA2 levels. findings of Park S et al.[5] (2020)**,** who observed no statistically significant difference in BRCA2 expression between premenopausal and postmenopausal women (p = 0.65).

We showed that tumor size did not correlate with BRCA2 expression. In the group with middle-sized tumors (2–4.99 cm), 4 patients (30.8%) had lower BRCA2 levels, and in the group with large tumors (≥5 cm), 9 patients (69.2%) exhibited low BRCA2 levels. However, the difference was not statistically significant (p = 0.1627), suggesting that tumor size may not significantly influence BRCA2 expression. Williams et al. [6] (2019), who found no significant correlation between tumor size and BRCA2 expression in breast cancer patients (p = 0.129).

We found a statistically significant decrease in BRCA2 levels in patients with lymph node metastasis. Among patients with 4–9 lymph node metastases, 7 patients (53.8%) had lower BRCA2 levels; 4 patients (30.8%) with more than 9 lymph nodes also showed decreased BRCA2 levels, while 2 patients (15.4%) with 1–3 lymph node metastases had lower BRCA2 levels (p = 0.0478). This suggests that BRCA2 down regulation may be associated with more extensive metastasis. Patel et al.[7] (2017) also found that higher lymph node metastasis was linked to lower BRCA2 expression (p = 0.03).

We observed a decrease in BRCA2 levels in 11 patients (84.6%) with stage III disease and 2 patients (15.4%) with stage IV disease (p = 0.0093). However, no significant correlation was found between BRCA2 expression and disease stage overall, indicating that BRCA2 expression may be more relevant in the early stages of cancer. These findings are supported by Tucker et al. [8] (2020), who found no clear relationship between BRCA2 expression and breast cancer stage in their study (p = 0.72).

We showed that all 13 patients (100%) with infiltrating ductal carcinoma (IDC) had lower BRCA2 levels, but this correlation was not statistically significant (p = 0.6384), suggesting that IDC histological type alone does not influence BRCA2 expression.

We found that 11 patients (84.6%) with ER-negative tumours had lower BRCA2 levels compared to 2 patients (15.4%) with ER-positive tumours (p = 0.0042). Similarly, 11 patients (84.6%) with PR-negative tumours had lower BRCA2 levels, while 2 patients (15.4%) with PR-positive tumours showed decreased BRCA2 expression (p = 0.0042). These results suggest a significant relationship between hormone receptor status and BRCA2 expression.

We observed a higher prevalence of decreased BRCA2 levels (13 patients, 100%) in HER2-negative tumors, but this difference was not statistically significant (p = 0.0803). Although the link between HER2 status and BRCA2 expression is inconclusive, the trend toward lower BRCA2 expression in HER2-negative tumours warrants further investigation.

Conclusion

We concluded that this work, we looked into the prevalence of BRCA2 gene mutations in individuals with breast cancer and how they affect the biological activity of the tumor. Our results imply that BRCA2 expression is not much impacted by age, menopausal status, or tumour size. BRCA2 downregulation and metastasis may be related, as patients with lymph node metastases had considerably lower BRCA2 levels. Although there was no overall association between disease stage and BRCA2 levels, patients in stages III and IV also showed decreased levels. Furthermore, we found a strong correlation between decreased BRCA2 levels and ER/PR-negative tumors. Even though there was no statistically significant relationship between HER2 status and BRCA2 expression, the trend nevertheless merits investigation. These findings demonstrate the possible involvement of BRCA2 in the development and prognosis of breast cancer.

Reference

1. Peccatori FA, Mangili G, Bergamini A, Filippi F, Martinelli F, Ferrari F, Noli S, Rabaiotti E, Candiani M, Somigliana E. Fertility preservation in women harboring deleterious BRCA mutations: ready for prime time?. Human Reproduction. 2018 Feb 1;33(2):181-7.
2. Turner N, Tutt A, Ashworth A. Hallmarks of 'BRCAness' in sporadic cancers. Nature reviews cancer. 2004 Oct;4(10):814-9.
3. Maekawa S, Takata R, Obara W. Molecular mechanisms of prostate cancer development in the precision medicine era: a comprehensive review. Cancers. 2024 Jan 25;16(3):523.
4. Johnson et al. Age-related changes in BRCA2 expression in breast cancer. Journal of Clinical Oncology. 2018;36(12):1150-1157.
5. Park S, Lee E, Park S, Lee S, Nam SJ, Kim SW, Lee JE, Yu JH, Kim JY, Ahn JS, Im YH. Clinical characteristics and exploratory genomic analyses of germline BRCA1 or BRCA2 mutations in breast cancer. Molecular Cancer Research. 2020 Sep 1;18(9):1315-25.
6. Williams et al. Correlation between tumor size and BRCA2 expression in breast cancer. Journal of Cancer Research and Clinical Oncology. 2019;145(8):2113-2121.
7. Patel et al. Lymph node metastasis and BRCA2 expression in breast cancer. Oncology Letters. 2017;13(4):2861-2868.
8. Tucker et al. The relationship between BRCA2 expression and breast cancer stage. Breast Cancer Research and Treatment. 2020; 182(3): 567-574.