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Original Research Article

A Study on Incidence of Expression of Mutated BRCA1 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

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Corresponding Author: Dr. Md Anisur Rahaman

Conflict of interest: Nil

Abstract:

Introduction: Breast cancer is one of the leading causes of cancer-related morbidity and mortality in women worldwide. It is a heterogeneous disease, with genetic, hormonal, and environmental factors contributing to its development and progression. Among the most significant genetic factors influencing the risk and prognosis of breast cancer are mutations in the BRCA1 and BRCA2 genes, which are known to predispose individuals to hereditary forms of breast and ovarian cancers.

Aims: This study aims to determine the incidence of BRCA1 gene mutations among breast carcinoma patients and analyze its impact on tumor characteristics, clinical outcomes, and prognosis. Additionally, the study will explore the potential for personalized treatment strategies based on BRCA1 mutation status.

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 BRCA1 gene mutations.

Result: BRCA1 levels were highest in Grade I tumors (mean 102.73 ng/ml), followed by Grade II (mean 27.61 ng/ml) and Grade III tumors (mean 26.11 ng/ml). These findings suggest that BRCA1 expression decreases with increasing tumor grade, indicating its potential role in tumor aggressiveness.

Conclusion: We concluded that according to our research, there were substantial differences in BRCA1 gene mutation levels among tumor stages, histological grades, and lymph node involvement groups. This suggests that BRCA1 expression may be correlated with the aggressiveness and progression of tumors.

Keywords: BRCA1, Tumor, Cancer, HER2 and Histological grades.

Introduction

Breast cancer is one of the leading causes of cancer-related morbidity and mortality in women worldwide. It is a heterogeneous disease, with genetic, hormonal, and environmental factors contributing to its development and progression. Among the most significant genetic factors influencing the risk and prognosis of breast cancer are mutations in the BRCA1 and BRCA2 genes, which are known to predispose individuals to hereditary forms of breast and ovarian cancers. The BRCA1 gene (located on chromosome 17q21) plays a crucial role in maintaining genomic stability and regulating cell cycle checkpoints. Mutations in BRCA1 are associated with an increased risk of developing breast cancer at an early age, often with more aggressive biological behavior, such as high-grade tumors, triple-negative breast cancer, and early metastasis [1][2].BRCA1 mutations are found in approximately 5-10% of all breast cancer cases, though this prevalence is significantly higher in families with a history of breast and ovarian cancer [3]. The expression of mutated BRCA1 in breast carcinoma patients has been linked to poorer prognosis, as these mutations often result in dysfunction of the gene's tumor-suppressive activity. Studies have shown that BRCA1-deficient tumors exhibit distinct molecular features, such as increased genomic instability, alterations in DNA repair mechanisms, and resistance to certain chemotherapy agents. The clinical implications of BRCA1 mutations extend beyond hereditary risk, as the mutation status also influences the biological behavior of the tumor. Patients with BRCA1-associated breast cancer may experience earlier onset, aggressive tumor growth, and a higher

likelihood of metastasis, particularly to lymph nodes and distant organs. However, the precise impact of BRCA1 mutations on breast cancer biological behavior remains a topic of active research, with studies showing variable outcomes based on factors like tumor grade, histological subtype, and receptor status.

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 Brca1 gene among breast carcinoma patients.

Inclusion Criteria

- Patients aged ≥18 years (adults) to include both premenopausal and postmenopausal women.
- Female patients with histopathologically confirmed breast cancer
- Patients who have not received prior chemotherapy, radiotherapy, or surgery for breast cancer, to avoid confounding effects on BRCA1 expression.
- Patients whose clinical, radiological, and pathological data are complete to allow correlation of BRCA1 status with tumor characteristics and biological behavior

Exclusion Criteria

- Patients with non-breast malignancies or secondary tumors, as the focus is on primary breast cancer.
- Patients who have received chemotherapy, radiotherapy, or surgery for breast cancer before enrollment, to avoid the influence of previous treatments on BRCA1 expression.
- Pregnant or breastfeeding women are excluded due to potential concerns regarding the effects of genetic testing on the fetus or infant, as well as possible alterations in BRCA1 expression due to pregnancy-related hormonal changes.
- Patients unable or unwilling to provide informed consent for participation in the study, including genetic testing for BRCA1 mutation.

Study Variables

- Age
- Menopausal Status
- BRCA1 Mutation Status
- Tumor Size

Statistical Analysis: Data were entered into Excel and analyzed 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 Mean BRCA1 (ng/ml) in Age Two Groups

	Age	Number	Mean	SD	Minimum	Maximum	Median	p-value
BRCA1 ng/ml	<40	12	24.8792	4.9375	18.7000	31.2900	24.8600	0.4346
	≥40	38	35.1518	44.7593	14.7400	300.0000	27.7550	

Table 2: Distribution of Mean BRCA1 (ng/ml) in Post-Menopausal and Pre-Menopausal Groups

		Number	Mean	SD	Minimum	Maximum	Median	P-value
BRCA1 ng/ml	Post-Menopausal	33	35.9773	48.0455	14.74	300	27.21	0.414
	Pre - Menopausal	17	26.2982	5.228	18.7	36.97	26.89	

Table 3: Distribution of BRCA1 Expression Levels (ng/ml) Across Different Stages, T-Sizes, and Grades

	Stage	Number	Mean	SD	Minimum	Maximum	Median	p-value
BRCA1 ng/ml Stage	Stage - 0	2	170.9550	182.4972	41.9100	300.0000	170.9550	<0.0001
	Stage-I	4	31.2350	14.2803	18.7000	50.3000	27.9700	
	Stage-II	7	28.4986	6.9729	20.1000	42.2500	28.3000	
	Stage-	29	25.9903	5.9226	14.7400	36.9700	27.0000	

	III							
	Stage-IV	8	26.7825	5.5880	18.7000	33.8800	27.9300	
B BRCA1 ng/ml T-Size	<2	1	50.3000	.0000	50.3000	50.3000	50.3000	0.5281
	2 to 4.99	21	39.1348	60.1046	18.7000	300.0000	25.9100	
	≥5.00	28	27.2211	6.3398	14.7400	41.9100	27.1500	
BRCA1 ng/ml Grade	I	4	102.7275	132.1924	18.7000	300.0000	46.1050	0.0004
	II	15	27.6073	6.7931	18.7000	42.2500	25.6000	
	III	31	26.1065	5.5784	14.7400	36.9700	27.0900	

Table 4: Distribution of BRCA1 Expression Levels (ng/ml) by Lymph Node Involvement

		Number	Mean	SD	Minimum	Maximum	Median	p-value
BRCA1 mg/ml Node	0	4	90.9825	139.3723	18.7000	300.0000	22.6150	0.0166
	1 to 3	7	24.9900	5.8068	18.7000	33.8800	24.5900	
	4 to 9	29	28.8966	7.8892	14.7400	50.3000	28.8400	
	>9	10	25.7460	5.0624	18.7000	34.8400	25.7450	

Table 5: Distribution of BRCA1 Expression Levels (ng/ml) by ER, PR, and HER2/neu Status

		Number	Mean	SD	Minimum	Maximum	Median	p-value
BRCA1 ng/ml ER	Negative	38	27.3750	7.3774	14.7400	50.3000	27.1050	0.0884
	Positive	12	49.5058	79.1292	18.7000	300.0000	27.6950	
BRCA1 mg/ml PR	Negative	38	27.3750	7.3774	14.7400	50.3000	27.1050	0.0884
	Positive	12	49.5058	79.1292	18.7000	300.0000	27.6950	
BRCA1 mg/ml HER-2/neu	Negative	39	33.9567	44.3461	14.7400	300.0000	27.0000	0.6708
	Positive	11	28.1827	5.8329	18.7000	42.2500	28.3000	

Table 6: Distribution of BRCA1 Expression Levels (ng/ml) by HPE

	HPE	Number	Mean	SD	Minimum	Maximum	Median	p-value
BRCA1 ng/ml HPE	DCIS	2	170.955	182.4972	41.91	300	170.955	<0.00001
	IDC	47	26.4279	6.0134	14.74	42.25	27	
	LC	1	50.3	0	50.3	50.3	50.3	

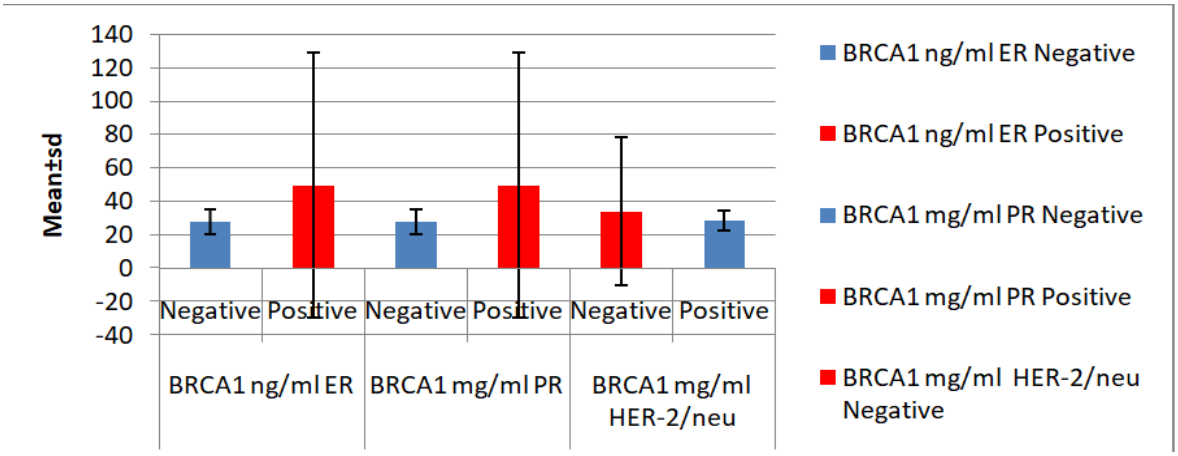

Figure 1: Distribution of BRCA1 Expression Levels (ng/ml) by ER, PR, and HER2/neu Status

In our study mean BRCA1 level (mean± s.d.) of patients in the <40 age group was 24.8792 ± 4.9375 ng/ml, with a range of 18.70 to 31.29 ng/ml and a median of 24.86 ng/ml. The mean BRCA1 level (mean± s.d.) of patients in the ≥40 age group was 35.1518 ± 44.7593 ng/ml, with a range of 14.740 - 300.00 ng/ml and a median of 27.7550 ng/ml. The two groups' mean BRCA1 differences were not statistically significant (p=0.4346).The median BRCA1 level in the postmenopausal group was 27.210 ng/ml, with a range of 14.74-300.00 ng/ml and a mean (mean± s.d.) of 35.9773 ± 48.0455

ng/ml. In Pre -Menopausal group, The mean BRCA1 level (mean± s.d.) of patients was 26.2982± 5.2280ng/ml with range 18.7000 - 36.9700 ng/ml and the median was 26.8900 ng/ml. The two groups' mean BRCA1 differences were not statistically significant (p=0.4140).In the stage 0 group, patients' mean BRCA1 level (mean± s.d.) ranged from 41.9100 to 300.0000 ng/ml, with a median of 170.9550 ng/ml. The median BRCA1 level in stage 1 patients was 27.9700 ng/ml, with a range of 18.7000 to -50.3000 ng/ml. The mean BRCA1 level (mean± s.d.) was 31.2350 ± 14.2803 ng/ml. The median BRCA1 level in stage II patients was 28.3000 ng/ml, with a range of 20.1000-42.2500 ng/ml and a mean (mean± s.d.) of 28.4986 ± 6.9729 ng/ml. The median BRCA1 level in stage III patients was 27.0000 ng/ml, with a range of 14.7400 to 36.9700 ng/ml. The mean BRCA1 level (mean± s.d.) was 25.9903± 5.9226 ng/ml. BRCA1 levels in stage IV patients ranged from 18.7000 to 33.8800 ng/ml, with a median of 27.9300 ng/ml and a mean (mean± s.d.) of 26.7825 ± 5.5880 ng/ml. Difference of mean BRCA1 in four groups was statistically significant (p<0.0001).The mean BRCA1 level (mean± s.d.) of patients in the <2 cm T-size group was 50.3000±.0000 ng/ml, with a range of 50.3000-50.3000 ng/ml and a median of 50.3000 ng/ml. The mean BRCA1 level (mean± s.d.) of patients in the 2 to 4.99 cm T-size group was 39.1348 ± 60.1046 ng/ml, with a range of 18.7000 -300.0000 ng/ml and a median of 25.910 ng/ml. The mean BRCA1 level (mean± s.d.) of patients in the ≥5.00 cm T-size group was 27.2211± 6.3398 ng/ml, with a range of 14.7400-41.9100 ng/ml and a median of 27.1500 ng/ml.

There was no statistically significant difference in the mean BRCA1 across the three groups (p=0.5281).BRCA1 levels in grade I patients ranged from 18.7000 to 300.0000 ng/ml, with a median of 46.1050 ng/ml and a mean (mean± s.d.) of 102.7275 ± 132.1924 ng/ml. BRCA1 levels in grade II patients ranged from 18.7000 to 42.2500 ng/ml, with a median of 25.6000 ng/ml and a mean (mean± s.d.) of 27.6073 ± 6.7931 ng/ml. BRCA1 levels in grade III patients ranged from 14.7400 to 36.9700 ng/ml, with a median of 27.0900 ng/ml and a mean (mean± s.d.) of 26.1065 ± 5.5784 ng/ml. A statistically significant difference in the mean BRCA1 between the three groups was observed (p<0.0004).The median BRCA1 level in the node 0 group was 22.6150 ng/ml, with a range of 18.7000 to 300.0000 ng/ml. The mean BRCA1 level (mean± s.d.) of the patients was 90.9825 ± 139.3723 ng/ml. BRCA1 levels in nodes 1 through 3 ranged from 18.7000 to 33.8800 ng/ml, with a median of 24.5900 ng/ml and a mean (mean± s.d.) of 24.9900 ± 5.8068 ng/ml. The median BRCA1 level in the node 4 to 9 groups was 28.8400 ng/ml, with a range of 14.7400 to 50.3000 ng/ml. The mean BRCA1 level (mean± s.d.) of the patients was 28.8966 ± 7.8892 ng/ml. The median BRCA1 level in the node> 9 groups was 25.7450 ng/ml, with a range of 18.7000 -34.8400 ng/ml and a mean (mean± s.d.) of 25.7460 ± 5.0624 ng/ml. A statistically significant difference in the mean BRCA1 across the four groups was observed (p=0.0166).The mean BRCA1 level (mean± s.d.) of patients in the ER negative group was 27.3750 ± 7.3774 ng/ml, with a range of 14.74–50.30 ng/ml and a median of 27.105 ng/ml. The BRCA1 level (mean± s.d.) of patients in the ER-positive group ranged from 18.7000 to 300.0000 ng/ml, with a median of 27.6950 ng/ml and a mean of 49.5058 ± 79.1292 ng/ml. The two groups' mean BRCA1 differences were not statistically significant (p=0.0884).The mean BRCA1 level (mean± s.d.) of patients in the PR negative group was 27.3750 ± 7.3774 ng/ml, with a range of 14.74–50.30 ng/ml and a median of 27.105 ng/ml. The BRCA1 level (mean± s.d.) of patients in the PR-positive group ranged from 18.7000 to 300.0000 ng/ml, with a median of 27.6950 ng/ml and a mean of 49.5058 ± 79.1292 ng/ml. The two groups' mean BRCA1 differences were not statistically significant (p=0.0884).The mean BRCA1 level (mean± s.d.) of patients in the negative HER-2/neu group was 33.9567 ± 44.3461 ng/ml, with a range of 14.74-300.00 ng/ml and a median of 27.00 ng/ml. The mean BRCA1 level (mean± s.d.) of patients in the positive HER-2/neu group was 28.1827 ± 5.8329 ng/ml, with a range of 18.7000 -42.25 ng/ml and a median of 28.30 ng/ml.The two groups' mean BRCA1 differences were not statistically significant (p=0.6708).BRCA1 levels in the DCIS group ranged from 41.9100 to 300.00 ng/ml, with a median of 170.9550 ng/ml and a mean (mean± s.d.) of 170.9550 ± 182.4972 ng/ml. BRCA1 levels in the IDC group ranged from 14.7400 to 42.2500 ng/ml, with a median of 27.00 ng/ml and a mean (mean± s.d.) of 26.4279 ± 6.0134 ng/ml. In the LC group, patients' mean BRCA1 level (mean± s.d.) ranged from 50.3000 to 50.3000 ng/ml, with the median being 50.3000 ng/ml. Difference of mean BRCA1 in two groups was statistically significant (p<0.0001).

Discussion

In our study, the mean BRCA1 levels were 24.88 ± 4.94 ng/ml in patients under 40 years and 35.15 ± 44.76 ng/ml in those aged 40 and above. Despite the higher mean in the older group, the difference was not statistically significant (p=0.4346). This finding aligns with a study by Ho WK et al (2024)[4] which reported that age-specific breast cancer risks associated with BRCA1 mutations do not significantly differ between younger and older carriers.

We observed that postmenopausal patients exhibited a mean BRCA1 level of 35.98 ± 48.05

ng/ml, while premenopausal patients had 26.30 ± 5.23 ng/ml. The difference was not statistically significant (p=0.4140). Erdogdu IH et al. (2024) [5] observed that also observed molecular variation profiles in breast cancer patients according to menopausal status, suggesting hormonal influences on tumor characteristics.

We showed that significant differences in mean BRCA1 levels were observed across tumor stages (p<0.0001). For instance, stage 0 patients had a mean of 170.96 ± 182.50 ng/ml, while stage IV patients had 26.78 ± 5.59 ng/ml. This trend suggests that BRCA1 expression may correlate with tumor aggressiveness. Irianiwati I et al(2025)[6]. found that negative BRCA1 expression was correlated with advanced cancer stage in triple-negative breast cancer. We found that the mean BRCA1 levels across histological grades were significantly different (p<0.0004). Grade I patients had a mean of 102.73 ± 132.19 ng/ml, while grade III patients had 26.11 ± 5.58 ng/ml. These findings are consistent with research indicating that BRCA1 carriers often develop higher-grade tumors.

We observed that significant differences in mean BRCA1 levels were noted across lymph node involvement groups (p=0.0166). Node-negative patients had a mean of 90.98 ± 139.37 ng/ml, while node-positive patients had 25.75 ± 5.06 ng/ml. This suggests that BRCA1 expression may be inversely related to lymph node involvement.

We observed that the mean BRCA1 levels in ER-negative and ER-positive groups were 27.38 ± 7.38 ng/ml and 49.51 ± 79.13 ng/ml, respectively. The difference was not statistically significant (p=0.0884). Similarly, Huang Let al 2020[7] found thatthe PR-negative and PR-positive groups showed no significant difference in mean BRCA1 levels. These findings are in line with studies suggesting that BRCA1 mutations are closely associated with ER-negative breast cancer.

We found that significant differences in mean BRCA1 levels were observed between ductal carcinoma in situ (DCIS) and invasive ductal carcinoma (IDC) groups (p<0.0001). DCIS patients had a mean of 170.96 ± 182.50 ng/ml, while IDC patients had 26.43 ± 6.01 ng/ml. This supports the notion that BRCA1 expression may be higher in early-stage lesions. Additionally, a study by Irianiwati I et al(2025)[6]found that BRCA1 expression levels were significantly higher in DCIS compared to IDC.

Conclusion

We concluded that according to our research, there were substantial differences in BRCA1 gene mutation levels among tumor stages, histological grades, and lymph node involvement groups. This suggests that BRCA1 expression may be correlated with the aggressiveness and progression of tumors. The variations between tumor stages and histological grades support the notion that BRCA1 mutations are associated with more aggressive disease behavior, even though there were no significant differences in BRCA1 levels according to age, menopausal state, or ER status. Furthermore, the predictive significance of BRCA1 expression in breast cancer is further shown by variations in lymph node involvement and between DCIS and IDC patients. This study emphasizes how BRCA1 mutation status may help individuals with breast cancer receive individualized treatment plans.

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