

Research article

Significance of Bcl-2 expression in breast cancer

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ABSTRACT

Introduction and Aim: The most prevalent and lethal form of cancer in women, breast carcinoma is thought to account for 2,088, 849 (11.6%) of all new cases each year. Protooncogene Bcl-2 is primarily present in the perinuclear membrane. Examining the significance of Bcl-2 expression as a predictive factor in breast cancer is the goal of the current investigation.

Materials and Methods: From December 2019 to January 2021, a tertiary care hospital in Chennai conducted this investigation on 42 cases of mastectomy specimens. Using tools from Path Insitu, Bcl-2 marker immunohistochemistry was carried out. Scores were taken after observing Bcl-2 expression in the cytoplasm of tumor cells.

Results: Total 42 cases were studied, and the age of patient ranged from 33-80 years. Out of 42 cases of IDC-NST (Invasive ductal carcinoma- No special type) 19 cases (45%) showed positive expression and 23 cases (54%) showed lack of staining for Bcl-2. Tumor size and grade of IDC-NST has significant relationship with Bcl-2 expression with p value of 0.05. No correlation has been found between lymph nodes harboring malignant cells and Bcl2expression with p value >0.05.

Conclusion: The staging and prognosis of breast cancer depend heavily on the size, grading based on histopathology, and lymph node harboring tumor cells. Hormonal receptor tests are frequently used in the process of treating breast cancer. The goal of the current investigation was to assess Bcl2's value as an additional marker for prognosis. Significant Bcl-2 expression was seen in tumors of modest histologic grade and size.

Keywords: IDC NST; Bcl-2; AJCC TNM staging.

INTRODUCTION

According to GLOBOCAN 2018, the most prevalent and lethal form of cancer in women, breast carcinoma is predicted to account for nearly two million, eighty-eight thousand eight fifty (around 11%) of all new cases and 6,26,679 (around 6%) of all deaths every year (1). The incidence is 1,62,468 (27.7%), and the mortality rate is 87,090 (11.1%) in India (2). Early menarche age, later menopause age, nulliparity, late first-birth age, oral contraceptive use, hormone replacement therapy use, and alcohol use are possible causes for breast cancer (3).

In 1984, a protooncogene called Bcl-2 was discovered. The protein is mostly present in the endoplasmic reticulum, on the perinuclear membrane, and in the mitochondrial periphery (4). Bcl-2 antisense treatment has been advocated for several tumors in an *in vitro* environment (5-7). The goal of current study is to evaluate Bcl-2 expression's worth as a breast cancer predictive marker.

MATERIALS AND METHODS

Forty-two mastectomy specimens that were obtained between December 2019 and January 2021 at a tertiary care hospital in Chennai, India, served as the

subject of this investigation. Using the convenience sampling method, representative blocks were chosen depending on inclusion and exclusion criteria. All samples underwent a second evaluation by a skilled pathologist for histological confirmation of Invasive Ductal Carcinoma-No Special Type prior to IHC labelling. Using PathInSitu tools Bcl-2 marker immunohistochemistry was carried out. Tumor cells' cytoplasm were found to express Bcl-2, and those cells were scored as shown in Table 1.

Table 1: The scores for cytoplasmic Bcl-2 expression

Bcl-2 expression score	Percentage of cells
NEGATIVE SCORE 0	No Staining
POSITIVE SCORE 1+	Less than 10% of tumor cells
POSITIVE SCORE 2+	10-50% of tumor cells
POSITIVE SCORE 3+	More than 50% of tumor cells

Age group distribution of breast carcinoma

A total of 42 cases were studied, and the age of patients ranged from 33-80 years. The most common age group affected was between 51-60 years (19 cases -45.2%) followed by 41-50 years (11 cases- 25.2%), >60 years (7 cases- 16.7%) and between 31-40 years (5 cases- 11.9%).

Statistical analysis

IBM SPSS version 23 was used for the statistical analysis and correlation. P values of 0.05 or less were regarded as significant.

RESULTS

Bcl2 expression in IDC-NST of breast carcinoma

Out of 42 cases of IDC-NST 19 cases (45%) showed positive expression and 23 cases (54%) showed lack of staining.

Association of tumor size with Bcl2 expression in IDC-NST

Bcl2 expression and IDC-NST tumor size were significantly correlated, with a p value of 0.05. (Table 2)

Table 2: Bcl2 expression and tumor size are related in IDC-NST

Tumour size	Bcl-2 Expression		P value
	Negative	Positive	
T1 < 2cm	4 (33.3%)	8 (66.7%)	0.05
T2 2-5 cm	10 (62.5%)	6 (37.5%)	
T3 > 5cm	9 (64.3%)	5 (35.7%)	

Association of histological grade with Bcl-2 expression in IDC-NST

With a p-value of 0.05, there was a significant correlation between grade and Bcl-2 expression in IDC-NST (Table 3; Figs. 1 and 2).

Table 3: Bcl-2 expression and histology grade are related in IDC-NST

Histopathological grade	Bcl-2 expression		P value
	Negative	Positive	
I	3 (13%)	3(13%)	0.043
II	18(78.3%)	16(84.2%)	
III	2 (8.7%)	0(0.0%)	

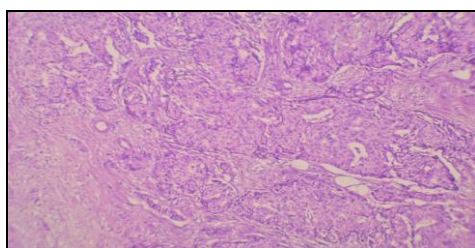


Fig. 1: H&E staining of IDC-NST grade II [10x view]

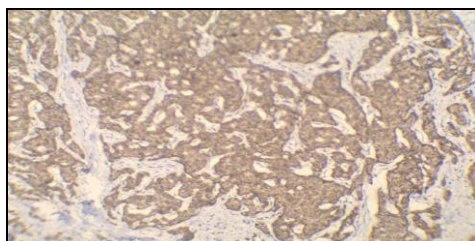


Fig. 2: Bcl-2 expression in IDC-NST grade II [10x view]

Bcl-2 expression and lymph node harboring malignant tumor cells are related in IDC-NST. With a p value greater than 0.05, no correlation between lymph node status and Bcl-2 expression was found (Table 4)

Table 4: Bcl-2 expression in IDC-NST is correlated with lymph node status

Lymph node status	Bcl- 2 Expression		P value
	Negative	Positive	
N0	6 (30%)	7 (53.8%)	0.06
N1	5(25%)	3(23.1%)	
N2	3(15%)	2(15.4%)	
N3	6(30%)	1(7.7%)	

DISCUSSION

Carcinoma breast constitutes a significant case load in a tertiary care centre. In addition to histopathological examination, routine Immunohistochemical assays like ER, PR, and Her2neu are done for prognostic evaluation and therapeutic purpose The goal of the current study was to assess Bcl2 expression's potential as an additional prognostic indicator.

With a mean age of around 51.5 years and an age range of 33 to 80 years, our study's age distribution was comparable to that of Hwang *et al.*, (9). In our study 45% (19 out of 42) cases expressed Bcl2 positivity which were like the study of Zaha *et al.*, in which 54.1% of cases showed Bcl-2 expression (10). In a study by Balakrishnan *et al.*, 57.3% of cases expressed Bcl-2 positivity (11). In the current investigation, Grade III cancer had no immunoreactivity, while Bcl-2 expression was found in 13% of Grade I ductal carcinoma and 84.2% of Grade II carcinoma. This finding was consistent with research by Bhargava *et al.*, (12), Dema *et al.*, (13), Martinez-Arribas *et al.*, (14), Zaha *et al.*, (10) Sierra *et al.*, (15), and Barbareschi *et al.*, (16) that also shown a relationship between Bcl2 and the lower grade IDC.

Tumors are divided into three categories by AJCC TNM (American Joint committee on Cancer-Tumor, Lymph node, Metastasis) Staging: T1<2cm, T2<5cm, and T3>5cm. We observed that Bcl-2 expression was inversely correlated with tumour growth, with 66.7% of T1 cells expressing Bcl-2. Our results are found to be similar to the studies by Dema *et al.*, (13), Martinez-Arribas *et al.*, (14), Zaha *et al.*, (10), Kobayashi *et al.*, (17) and Barbareschi *et al.*, (16). The lymph node status was categorised as: Absence of metastases (N0); 1 to 3 involved nodes (N1); 4-9 nodes positive (N2) and >10 nodes positive (N3) according to AJCC TNM Staging.

In our analysis, there was no discernible correlation between lymph node status and Bcl-2 expression. The studies by Balakrishnan *et al.*, (11), Zaha *et al.*, (10) and Kobayashi *et al.*, (17) revealed similar results. In this study we found a significant positive correlation

between Bcl-2 expression and low histologic grade, as well as tumour size. The presence or absence of lymph nodes harbouring tumor cells had no correlation.

CONCLUSION

Breast cancer staging and prognosis are highly influenced by tumor size, histological grade, and lymph node harboring tumor cell status. Breast cancer therapy involves, hormonal receptor assays like ER, PR, and Her2neu are frequently performed. Bcl-2 can therefore be utilized in addition to standard staging and hormonal testing to evaluate the risk of disease-free survival. Use of this could contribute to the management of breast cancer with a successful result.

CONFLICT OF INTEREST

Authors declare that there is no conflict of interest.

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