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Original Research Article

A Clinico-Epidemiological Study of Tumour PD-LI Status in Breast Cancer

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Abstract

Introduction: Breast cancer continues to be the most common malignancy among women globally and represents a significant cause of cancer-related mortality. Its heterogeneity, encompassing diverse molecular subtypes and clinical behaviors, poses considerable challenges in diagnosis, prognostication, and treatment selection.

Aims: To investigate the expression of PD-L1 and its association, if any, with the prognosis of breast carcinoma of a patient.

Materials and Methods: The present study was an institution based descriptive, cross-sectional and observational study. This Study was conducted fromJanuary 2020 to June 2021 at Medical College & Hospital, Kolkata. Total 52 patients were included in this study.

Result: In our study of 52 breast carcinoma patients, PD-L1 expression was not significantly associated with age, socioeconomic status, pain, ulceration, or tumor size. Invasive ductal carcinoma was the predominant subtype (78.8%), followed by lobular (17.3%) and medullary carcinoma (3.8%). A strong association was observed between PD-L1 positivity and HER2 expression, as 75% of HER2-positive cases were PD-L1 positive. Importantly, PD-L1 positivity was linked to more aggressive disease features, including significantly higher nodal involvement (mean 10.88 vs. 4.75, $p < 0.0001$) and increased distant metastasis, particularly to the lung (31.3%) and bone (12.5%).

Conclusion: In conclusion, our study demonstrated that PD-L1 expression in breast carcinoma was not significantly influenced by age, socioeconomic status, tumor size, pain, or ulceration. However, important clinicopathological correlations were noted. PD-L1 expression showed a strong association with HER2 positivity, suggesting a potential link between these biomarkers.

Keywords: Breast cancer. PD-L1, HER2, Metastasis, Prognosis, Biomarker.

Introduction

Breast cancer continues to be the most common malignancy among women globally and represents a significant cause of cancer-related mortality [1]. Its heterogeneity, encompassing diverse molecular subtypes and clinical behaviors, poses considerable challenges in diagnosis, prognostication, and treatment selection [2]. Recent advances in immuno-oncology have highlighted the pivotal role of immune checkpoint pathways, particularly the programmed cell death protein 1 (PD-1) and its ligand PD-L1, in modulating the tumor microenvironment and influencing disease progression [3]. The interaction between PD-1 on T cells and PD-L1 on tumor cells allows tumors to evade immune surveillance, thereby promoting tumor growth and metastasis [4]. Evaluating PD-L1 expression in breast cancer is therefore essential to identify potential therapeutic targets and predict clinical outcomes [5]. PD-L1 expression has been found to correlate with several clinicopathological parameters. Higher PD-L1 expression is frequently associated with aggressive tumor features, including larger tumor size, higher histological grade, and the presence of lymph node metastases [6]. Furthermore, PD-L1 positivity is more prevalent in hormone receptor-negative subtypes, particularly triple-negative breast cancer (TNBC), which is characterized by a poor prognosis and limited therapeutic options [7]. For instance, Zhang et al. [1] reported that PD-L1 overexpression in

breast tumors was significantly associated with lymph node metastasis, larger tumor size, and estrogen receptor negativity. Similarly, Sobral-Leite et al. [5] observed that PD-L1 expression varied among breast cancer subtypes, highlighting its potential as a biomarker for aggressive disease phenotypes. The prognostic significance of PD-L1 expression in breast cancer remains an area of ongoing research. Some studies suggest that high PD-L1 expression correlates with poor overall survival (OS) and disease-free survival (DFS), whereas others find no significant association [2,8]. For example, Cirqueira et al. [2] conducted a meta-analysis and demonstrated that PD-L1 expression was associated with age ≥50 years, lymph node-negative status, progesterone receptor negativity, elevated Ki-67, and HER2-negative status. The inconsistency in these findings reflects the complexity of PD-L1 biology and underscores the need for further population-specific studies [3,9]. Therapeutically, PD-L1 has emerged as a promising target for immune checkpoint inhibition. Immune checkpoint inhibitors, such as pembrolizumab and atezolizumab, have shown efficacy in PD-L1-positive TNBC, improving progression-free survival when combined with chemotherapy [4,10]. This development emphasizes the dual role of PD-L1 as both a predictive biomarker for patient selection and a therapeutic target in breast cancer management [7,10].

In the Indian context, breast cancer incidence is rising, and it remains the leading malignancy among women [6]. Despite the increasing clinical relevance of PD-L1-targeted therapies, studies evaluating PD-L1 expression in Indian breast cancer populations are limited. Understanding the prevalence of PD-L1 expression and its association with clinicopathological features is crucial for optimizing treatment strategies and guiding therapeutic decision-making [8, 9]. Population-specific data could also inform the applicability of immunotherapy and help predict treatment response in this demographic [5, 10]. Considering these factors, this study aims to conduct a clinico-epidemiological analysis of PD-L1 expression in breast cancer, focusing on its prevalence, association with clinicopathological parameters, and potential prognostic significance. By elucidating these aspects, the study intends to contribute to the growing body of knowledge on PD-L1 biology in breast cancer and support the rational implementation of PD-L1-targeted therapies, particularly in the Indian population [1–10].

Materials and Methods

Study Area: Medical College & Hospital, Kolkata.

Study Population: All patients of Breast Cancer presenting to OPD, ER & indoor patients of General Surgery, Medical College & Hospital, and Kolkata.

Study Period: From January 2020 to June 2021.

Sample Size: Based on previous year's data they expect to recruit about 50 patients during the study period.

Sample Design: All patients fulfilling the inclusion and exclusion criteria was included.

Study Design: Institution based descriptive, cross-sectional and observational study.

Inclusion Criteria: Any female patient suffering from breast carcinoma.

Exclusion Criteria: Patients not consenting to take part in the study.

Study Tools

- Informed Consent Form
- Family History- if any 1st degree or 2nd degree family member is suffering from breast carcinoma or not
- Personal History- parity, breast feeding, menstrual history
- Clinical examination of breast
- Routine blood investigations
- USG of breast
- Mammography/MRI/Bone scan
- Clinical proforma for tabulation of data
- Tables & Diagrams for statistical analysis

Statistical Analysis: Data from the study were analyzed using SPSS software, with continuous variables (e.g., age, liver enzyme levels) expressed as mean ± SD and compared using t-tests or Mann–Whitney U tests. Categorical variables (e.g., gender, CBD stones, and complications) were presented as frequencies and percentages, and compared using Chi-square or Fisher’s exact tests.

Diagnostic accuracy (sensitivity, specificity, PPV, NPV, and accuracy) was calculated for MRCP-first and EUS-first strategies, using ERCP/intraoperative findings as the reference. Kaplan-Meier analysis may be used for time-to-intervention comparisons. A p-value < 0.05 was considered significant.

Result

Table 1: Distribution of PD-L1 Expression According to Age and Socioeconomic Status in Breast Cancer Patients

PD L1					
Age in Group		**Negative**	**Positive**	**Total**	**P Value**
	21-30	5(13.9%)	0(0%)	5(9.6%)	0.4419
	31-40	5(13.9%)	1(6.3%)	6(11.5%)	
	41-50	17(47.2%)	10(62.5%)	27(51.9%)	
	51-60	3(8.3%)	1(6.3%)	4(7.7%)	
	≥61	6(16.7%)	4(25%)	10(19.2%)	
	Total	36(100%)	16(100%)	52(100%)	
Sex	Lower Class	12(33.3%)	7(43.8%)	19(36.5%)	0.7699
	Lower Middle Class	13(36.1%)	5(31.3%)	18(34.6%)	
	Middle Class	11(30.6%)	4(25%)	15(28.8%)	
	Total	36(100%)	16(100%)	52(100%)	

Table 2: Association of PD-L1 Expression with Pain and Ulceration in Breast Cancer Patients

		Negative	**Positive**	**Total**	**P Value**
Pain	No	9(25%)	1(6.3%)	10(19.2%)	0.1133
	Yes	27(75%)	15(93.8%)	42(80.8%)	
	Total	36(100%)	16(100%)	52(100%)	
Ulceration	No	29(80.6%)	16(100%)	45(86.5%)	0.0579
	Yes	7(19.4%)	0(0%)	7(13.5%)	
	Total	36(100%)	16(100%)	52(100%)	

Table 3: Correlation of PD-L1 Expression with Histopathological Type and HER2 Status in Breast Cancer Patients

PD L1				
HPE		**Negative**	**Positive**	**Total**
	IDC	28(77.8%)	13(81.3%)	41(78.8%)
	LC	7(19.4%)	2(12.5%)	9(17.3%)
	MC	1(2.8%)	1(6.3%)	2(3.8%)
	Total	36(100%)	16(100%)	52(100%)
HER	Negative	32(88.9%)	4(25%)	36(69.2%)
	Positive	4(11.1%)	12(75%)	16(30.8%)
	Total	36(100%)	16(100%)	52(100%)

Table 4: Association between Metastasis: PD L1

Pd L1			
Metastasis	**Negative**	**Positive**	**Total**
Bone	0(0%)	2(12.5%)	2(3.8%)
Lung	0(0%)	5(31.3%)	5(9.6%)
No	36(100%)	9(56.3%)	45(86.5%)
Total	36(100%)	16(100%)	52(100%)

Table 5: Comparison of Tumor Size and Nodal Status between Negative and Positive Groups

		Number	**Mean**	**SD**	**Minimum**	**Maximum**	**Median**	**P-Value**
T-Size	Negative	36	4.4611	1.6354	1.3	8.3	4.4	0.165
	Positive	16	5.125	1.3988	2.5	8.1	4.9	
Nodal Status	Negative	36	4.75	3.3155	0	13	5	<0.0001
	Positive	16	10.875	1.5438	9	14	10.5	

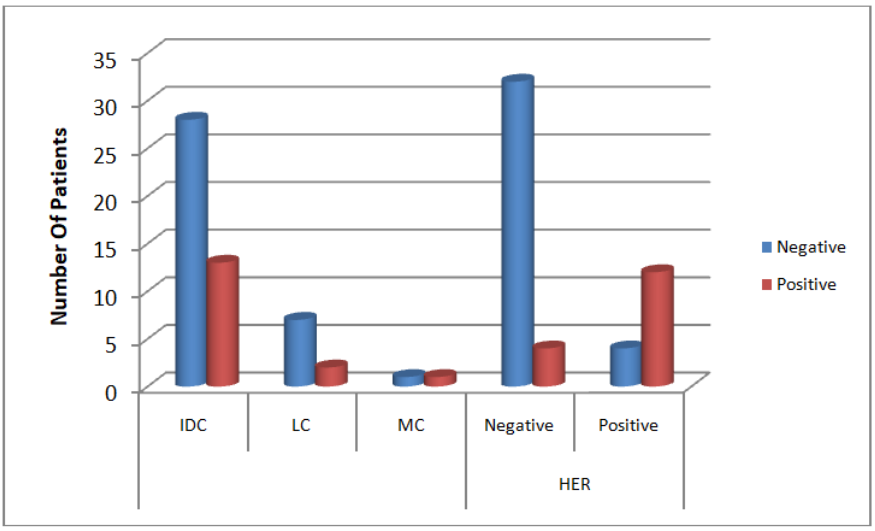

Figure 1: Correlation of PD-L1 Expression with Histopathological Type and HER2 Status in Breast Cancer Patients

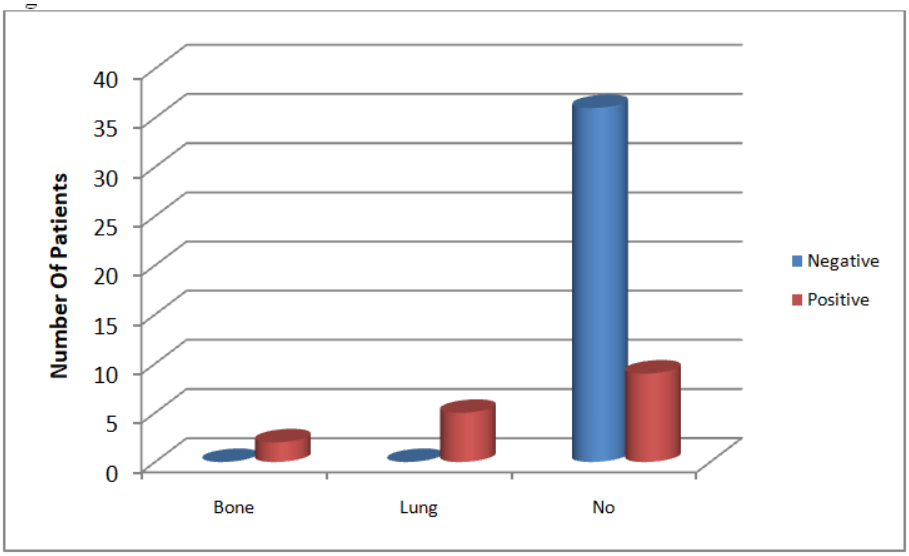

Figure 2: Association between Metastasis: PD L1

In our study of 52 patients, PD-L1 expression was observed to vary across different age groups and socioeconomic strata. Among the negative group (n=36), the majority belonged to the 41–50 years age group (17, 47.2%), followed by ≥61 years (6, 16.7%), whereas in the positive group (n=16), the highest proportion was also in the 41–50 years age group (10, 62.5%), followed by ≥61 years (4, 25%). However, the association between age and PD-L1 status was not statistically significant (p=0.4419). Regarding socioeconomic status, 33.3% of PD-L1 negative and 43.8% of positive patients were from the lower class, 36.1% and 31.3% respectively from the lower middle class, and 30.6% and 25% respectively from the middle class. The distribution across socioeconomic categories also showed no statistically significant association with PD-L1 status (p=0.7699). In our study of 52 patients, pain was reported by 42 (80.8%) individuals, of whom 27 (75%) were PD-L1 negative and 15 (93.8%) were PD-L1 positive, while 10 patients (19.2%) had no pain. Although pain was more frequent among PD-L1 positive cases, the association was not statistically significant (p=0.1133). Ulceration was present in 7 patients (13.5%), all of whom were PD-L1 negative (19.4%), while none of the PD-L1 positive cases had ulceration. The absence of ulceration in PD-L1 positive cases suggested a possible trend, but the association did not reach statistical significance (p=0.0579). In our study of 52 patients, histopathological examination (HPE) revealed that invasive ductal carcinoma (IDC) was the most common subtype, observed in 41 cases (78.8%), comprising 28 (77.8%) PD-L1 negative and 13 (81.3%) PD-L1 positive cases. Lobular carcinoma (LC) accounted for 9 cases (17.3%), with 7 (19.4%) PD-L1 negative and 2 (12.5%) PD-L1 positive, while medullary carcinoma (MC) was seen in only 2 cases (3.8%), one each in the negative (2.8%) and positive (6.3%) groups.

Regarding HER2 status, 36 patients (69.2%) were HER2 negative, of which 32 (88.9%) were PD-L1 negative and 4 (25%) were PD-L1 positive, while 16 patients (30.8%) were HER2 positive, comprising 4 (11.1%) PD-L1 negative and 12 (75%) PD-L1 positive cases, suggesting a strong association between HER2 positivity and PD-L1 expression.

In our study, metastasis was present in 7 out of 52 patients (13.5%), while the remaining 45 patients (86.5%) showed no evidence of metastatic spread. Among PD-L1 positive patients, metastasis was more frequent, with 2 cases (12.5%) involving bone and 5 cases (31.3%) involving the lung. In contrast, none of the PD-L1 negative patients had bone or lung metastasis, as all 36 (100%) were metastasis-free. This indicates that PD-L1 expression was strongly associated with the presence of distant metastasis, particularly to the lung (31.3%) and bone (12.5%).

In our study, the mean tumor size among PD-L1 negative patients was 4.46 ± 1.63 cm (range: 1.3–8.3 cm; median: 4.4 cm), while among PD-L1 positive patients it was slightly higher at 5.13 ± 1.40 cm (range: 2.5–8.1 cm; median: 4.9 cm). However, this difference was not statistically significant ($p = 0.165$). In terms of nodal status, PD-L1 negative patients had a mean nodal involvement of 4.75 ± 3.32 (range: 0–13; median: 5), whereas PD-L1 positive patients showed significantly higher nodal involvement with a mean of 10.88 ± 1.54 (range: 9–14; median: 10.5), and this difference was highly significant ($p < 0.0001$).

Discussion

Our findings in a 52-patient breast cancer cohort show that PD-L1 positivity clustered with adverse clinicopathological features—most notably higher nodal burden, HER2 positivity, and presence of distant metastasis—while age and socioeconomic status were not associated with PD-L1 status, aligning with much of the contemporary literature.

Meta-analyses consistently link tumoural PD-L1 expression to aggressive biology, including higher histological grade and lymph-node involvement, and to poorer survival endpoints in several settings [11–13, 20]. The strong co-occurrence we observed between PD-L1 positivity and HER2 positivity mirrors reports that describe biological and therapeutic crosstalk between HER2 signalling and the PD-1/PD-L1 axis, as well as cohort data in HER2-positive disease showing meaningful associations with response and prognosis [14, 15, 19].

Our demonstration of substantially greater nodal involvement in PD-L1–positive cases is concordant with pooled estimates indicating enriched PD-L1 expression in node-positive tumours [11–13,20]. The signal we noted for metastatic spread among PD-L1–positive cases, particularly to lung and bone, fits with evidence that PD-L1 marks more aggressive disease, although studies also highlight discordance of PD-L1 status between primary and metastatic sites and heterogeneity across compartments, underscoring assay and sampling considerations in advanced disease [16,17]. Histology in our series was dominated by invasive ductal carcinoma across PD-L1 strata, a distribution typical of published cohorts [11–13]. Finally, the lack of association with age (and with socioeconomic status, which is rarely reported) is in line with multiple analyses that have not shown consistent relationships between PD-L1 and demographic variables once tumour biology is accounted for [11–13,20]. Collectively, these data support incorporating PD-L1 testing—particularly alongside HER2 status and nodal assessment—into risk stratification frameworks, while recognizing the need for standardized assays and attention to intra-tumour and temporal heterogeneity when PD-L1 guides therapy selection [15–17,20].

Conclusion

In conclusion, our study demonstrated that PD-L1 expression in breast carcinoma was not significantly influenced by age, socioeconomic status, tumor size, pain, or ulceration. However, important clinicopathological correlations were noted. PD-L1 expression showed a strong association with HER2 positivity, suggesting a potential link between these biomarkers. Furthermore, PD-L1 positivity was significantly correlated with higher nodal involvement and the presence of distant metastasis, particularly to the lung and bone, highlighting its potential role as an indicator of aggressive disease behavior and poor prognosis. These findings suggest that PD-L1 may serve as a valuable prognostic marker in breast cancer, warranting further exploration in larger cohorts.

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