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Original Research

Expression of p53 in Triple-Negative Breast Carcinoma: A Diagnostic Insight

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ABSTRACT

Background: Triple-negative breast cancer (TNBC) represents a highly aggressive form of breast carcinoma. This research aimed to examine the expression of p53 in TNBC cases and analyze its correlation with various clinical and pathological parameters, including age, tumor size, grade, lymph node involvement, and others.

Materials and Methods: The study included 65 cases of histologically and immunohistochemically confirmed TNBC. A detailed clinical data collection was performed for each patient, and the data was recorded systematically using a pre-designed proforma to ensure consistency and accuracy in documenting patient demographics, clinical presentation, and relevant histopathological findings. After histopathological analysis, all the cases were subjected to immunohistochemical (IHC) staining to evaluate the expression of p53.

Results:65 female TNBC patients, aged 30-80 years (most commonly 41-50), were analyzed. The left breast was affected in 58.8%, and the upper outer quadrant in 64.6%. Tumor sizes ranged from 1 to 8 cm, with 79.9% between 2-5 cm. Most cases (93.4%) were IDC-NOS, with 60.1% grade III and 83.8% showing lymphovascular invasion (LVI), linked to higher tumor grade ($p<0.05$). Lymph node involvement was present in 95.1%, more prevalent in premenopausal women ($p<0.05$). p53 expression was observed in 62.3%, correlating with LVI ($p<0.05$). No associations were found with tumor size or perineural invasion.

Conclusion: This study demonstrated that overexpression of p53 was predominantly associated with high-grade tumors and an increased likelihood of metastasis. Therefore, p53 may serve as a valuable prognostic marker and could be considered a potential target for therapy.

Key Words:p53, Breast Cancer, Immunohistochemistry

INTRODUCTION

Breast carcinoma is the most prevalent cancer among women globally. In 2020, approximately 2.3 million new cases were diagnosed, and 685,000 deaths occurred, making it the second leading cause of cancer-related mortality in women. The development of breast tumors generally begins with ductal hyperproliferation, which may progress to benign, malignant, or metastatic carcinomas, influenced by various oncogenic factors. Several risk factors, including gender, age, estrogen exposure, family history, genetic mutations, and lifestyle choices, contribute to the increased likelihood of breast cancer development [1].

The prognosis of breast carcinoma is influenced by multiple factors, with age, tumor size, lymph node involvement, tumor type, hormone receptor status, molecular subtype, grade, local invasion (such as skin or muscle), and distant metastasis being the most significant. Diagnostic tools such as mammography, fine-needle aspiration cytology (FNAC), histopathology, and immunohistochemistry (IHC) play a crucial role in determining prognosis and guiding treatment decisions. Histopathology remains the gold standard for diagnosing breast cancer, while IHC has become essential for assessing breast carcinoma subtypes [2, 3].

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Immunohistochemistry aids in tumor classification based on the presence of specific receptors, including Estrogen Receptor (ER), Progesterone Receptor (PR), Her2neu, p53, and Cytokeratins. The ER, PR, and Her2neu receptors are commonly evaluated in newly diagnosed cases of breast cancer. Depending on the receptor status, tumors can be classified into subtypes such as luminal A/B, Her2-enriched, basal-like, or triple-negative. This classification is crucial for determining the appropriate treatment approach, as each subtype has distinct therapeutic options. For example, luminal subtypes typically respond well to hormonal therapies, whereas triple-negative tumors are often treated with chemotherapy [4].

Triple-negative breast cancer (TNBC) is characterized by the absence of all three major receptors—ER, PR, and Her2neu. This subtype is known for its aggressive nature, high recurrence rate, and accounts for approximately 15% of all breast cancers. Due to the lack of conventional receptors, p53 is often considered a critical marker for TNBC [5].

The p53 gene is often referred to as the "guardian of the genome" due to its crucial role in regulating cellular stress and preventing the development of tumors. It is one of the most commonly mutated genes in breast cancer, particularly in TNBC. Approximately 80% of TNBC cases exhibit abnormal expression of p53. Elevated levels of p53 expression are generally associated with a poor prognosis, reflecting the aggressive nature of this cancer subtype. Given the high frequency of p53 mutations and the lack of other key receptors in TNBC, p53 has emerged as a potential therapeutic target. Additionally, p53 expression serves as a significant biomarker for predicting the prognosis of TNBC, providing valuable insight for clinical management and treatment decisions [6, 7].

MATERIAL AND METHODS

The present study was conducted on 65 cases of TNBC. As part of the routine diagnostic protocol for breast cancer, estrogen receptor (ER), progesterone receptor (PR), and Her-2neu receptor status were assessed in all breast cancer cases. From this cohort, the TNBC cases were selected for further investigation.

A detailed clinical data collection was performed for each patient, and the data was recorded systematically using a pre-designed proforma to ensure consistency and accuracy in documenting patient demographics, clinical presentation, and relevant histopathological findings.

The tissue samples obtained from the patients were preserved using formalin fixation, followed by paraffin embedding to maintain the integrity of the tissue architecture and cellular details. Hematoxylin and eosin (H&E) staining was performed on the paraffin-embedded tissue sections for histopathological evaluation. This step allowed for the classification and grading of the tumors based on established histological criteria, providing important insights into the morphological characteristics of the tumors, including tumor grade and type.

After histopathological analysis, all the cases were subjected to immunohistochemical (IHC) staining to evaluate the expression of p53, a tumor suppressor protein. The IHC procedure facilitated the detection of p53 expression at the protein level, aiding in the determination of its potential role in the tumor biology of TNBC and its correlation with clinicopathological factors, such as tumor grade, size, and lymph node involvement.

RESULTS

The age of the patients in our study ranged from 30 to 80 years. The largest proportion of patients was in the 41-50 years age group, accounting for 48% of the total cohort, with a mean age of 51.45 years. The majority of the patients (n=41) were in the premenopausal age category.

The left breast was affected in 58.8%, and the upper outer quadrant in 64.6%. Tumor sizes ranged from 1 to 8 cm, with 79.9% between 2-5 cm. Most cases (93.4%) were IDC-NOS, with 60.1% grade III and 83.8% showing lymphovascular invasion (LVI), linked to higher tumor grade ($p<0.05$). Lymph node involvement was present in 95.1%, more prevalent in premenopausal women ($p<0.05$). p53 expression was observed in 62.3%, correlating with LVI ($p<0.05$). No associations were found with tumor size or perineural invasion.

The relationship between tumor grade and the presence of lymphovascular invasion (LVI) was statistically significant (Table 1, $p<0.05$). Notably, no cases of LVI were observed among patients with grade I tumors. In grade II tumors, 24.62% of cases exhibited LVI, while the proportion increased markedly in grade III tumors, with 50.77% of cases showing LVI. Interestingly, among grade IV tumors, 4.62% of cases presented with LVI, which is relatively lower than observed in grade III tumors.

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Table 1: Correlation between Tumour Grade and LVI in BC patients

Tumour Grade	LVI Absent		LVI Present		P Value
	n	%	n	%	
I	0	0.00	0	0.00	<0.05
II	6	9.23	16	24.62	
III	3	4.62	33	50.77	
IV	4	6.15	3	4.62	

Age demonstrated a significant correlation with the presence of metastasis (Table 2, $p<0.05$). Among patients younger than 50 years, metastasis was observed in 32.31% of cases, whereas a smaller percentage (23.08%) of patients aged 50 years and above exhibited metastasis. This trend suggests a higher likelihood of metastatic involvement in younger patients compared to older ones .

Table 2: Correlation between age and metastasis in BC patients

Age in Years	Metastasis Absent		Metastasis Present		P Value
	n	%	n	%	
<50	8	12.31	21	32.31	<0.05
≥50	21	32.31	15	23.08	

The association between tumor stage and vascular metastasis was also statistically significant (Table 3, $p<0.05$). Among patients with stage 0 tumors, vascular invasion was identified in 32.31% of cases. A lower frequency of vascular invasion was seen in patients with stage 2 tumors (13.85%), while stages 3 through 6 displayed varying frequencies, ranging from 4.62% to 10.77%. These findings highlight an increasing trend of vascular invasion with advancing tumor stages .

Table 3: Correlation between Stage and vascular metastasis in BC patients

TumourStage	Vascular Invasion Absent		Vascular Invasion Present		P Value
	n	%	n	%	
0	2	3.08	21	32.31	<0.05
2	1	1.54	9	13.85	
3	3	4.62	3	4.62	
4	4	6.15	4	6.15	
5	4	6.15	6	9.23	
6	1	1.54	7	10.77	

DISCUSSION

The age range of patients in our study was primarily from 30 to 81 years. The age group of 41-50 years had the highest number of patients. Most patients were from the premenopausal age group. A similar study conducted by Sood et al. [8] on 36 patients with TNBC reported a mean age of 45.18 years. Rao et al. [9] in their study of 50 TNBC cases found the mean age to be 46.8 years, with the largest number of patients in the 41-50 years age group. The increased incidence in the premenopausal population may be attributed to improved screening techniques and advancements in imaging modalities.

In our study, the left breast was more frequently involved compared to the right breast. The upper outer quadrant was the most commonly affected area. Tumor size is one of the most significant prognostic factors in breast cancer. Tumor sizes in our study ranged from 1 cm to 8 cm, with the majority of tumors falling within the 2-5 cm range. In a similar study by Rao et al. [9] on 50 TNBC cases, 68% of tumors were in the 2-5 cm size range. Saleh and Abdeen's study on 166 cases also showed that 53.6% of tumors fell within this size range [10].

In our study, majority of the cases were classified as Infiltrating Ductal Carcinoma (IDC), and only about 2% were of special types, including carcinosarcoma, lobular carcinoma, and mucinous carcinoma. A similar pattern was observed in Rao et al.'s study, where IDC was identified in 88% of the 50 cases [9].

The Nottingham modification of the Bloom-Richardson grading system was applied in our study. Among 65 TNBC cases, majority were classified as grade III. Shet et al., in their study of 11,780 cases, reported that 70% of cases were grade III [11]. Sood et al. [8] found that grade II tumors comprised 47%, while grade III tumors accounted for 38% of the 36 TNBC cases. In our study, axillary lymph node metastasis was observed in more than half of cases, aligning with findings by Suhani et al. [12], who reported lymph node involvement in 59.2% of TNBC cases. A similar result was seen in Jindal B's study, where 55.56% of the 50 cases had lymph node involvement [13].

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In our study, lymph node metastasis was observed in more than 70% of premenopausal patients, compared to 41% in postmenopausal patients, with a statistically significant correlation. Similarly, Saghir N S et al. [14] found that premenopausal patients had a higher incidence of lymph node involvement. Lymphovascular invasion (LVI) was observed in more than 80% of the TNBC cases in this study. A correlation between LVI and tumor grade was noted, with majority of Grade II and III tumors showing LVI. The incidence of LVI increased with tumor grade, and a statistically significant correlation was found. This finding is consistent with a study by EmadA R et al., who reported a direct correlation between LVI and tumor grade in 3,812 breast carcinoma cases [15].

The expression of p53 was found in more than 60% of TNBC cases in our study. The frequency of positive p53 expression ranged from <10%, 10%-50%, and >50%, with varying intensities of staining. In our study, the highest expression of p53 was observed in patients aged 41-50 years. Pan Y et al., in their study on 115 TNBC cases, also reported higher p53 expression in patients under 60 years of age [16]. In our study, all patients with tumors smaller than 2 cm expressed p53. This suggested a reverse relationship between tumor size and p53 expression, although this correlation was not statistically significant. Pan Y et al. [16] reported that most patients (55.7%) had tumors in the 2-5 cm range. A study by Hashmi AA also indicated that larger tumor sizes were associated with higher p53 expression [7]. In our study, the p53 expression in Grade II and Grade III tumors was found to be more than 60%, with no significant correlation between tumor grade and p53 expression. Conversely, studies by Hashmi AA et al. [7] and Jing-Ping Li et al. [17] reported a significant positive association between tumor grade and p53 expression. Among the cases with LVI, more than 50% exhibited p53 expression. LVI was more common in p53-positive cases compared to p53-negative cases. A statistically significant correlation was observed between p53 expression and LVI. These findings align with studies by Hashmi AA et al. [7] and Jing-Ping Li et al. [17].

CONCLUSION

The cases exhibiting overexpression of p53 were predominantly high-grade tumors and showed a stronger association with lymphovascular invasion (LVI). These findings suggest that tumors with p53 overexpression are more aggressive and are linked to a poorer prognosis. The detection of p53 expression serves as a valuable prognostic marker, offering insight into the tumor's behavior and aiding in the refinement of treatment strategies for patients diagnosed with TNBC. Unlike ER, PR, or Her-2neu positive breast cancers, TNBC lacks targeted therapies such as hormonal treatments or Herceptin, and patients are consequently subjected to more aggressive chemotherapy regimens. Therefore, it is crucial to assess p53 expression in all TNBC cases, as it may help in identifying potential therapeutic targets. Furthermore, p53 has the potential to emerge as a novel biomarker for targeted therapies, contributing to the more precise evaluation and treatment of TNBC.

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