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Research Article

A Study of Ki-67 Expression in Breast Cancer, Its Correlation with ER/PR, Her-2 Neu and Histological Grading of Breast Cancer

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ABSTRACT

Objectives: The assessment of neoplastic cell proliferation through immunohistochemical analysis of the proliferative index (Ki-67) can provide insights into the aggressiveness of breast malignant tumors. This study aims to investigate the expression of Ki-67 in individuals with primary breast cancer and establish correlations with estrogen and progesterone receptors, as well as her-2 neu. ***Methods:*** This series investigation included 48 cases of primary breast cancers with histological evidence. Tissue specimens fixed in paraffin wax underwent immunohistochemical staining for the markers Ki-67, ER, PR, and her-2 neu. The evaluation of Ki-67 involved selecting the area with the highest proliferation, categorizing cases with more than 20% positive nuclei as high Ki-67 expression, and considering cases with less than 20% positive nuclei as having low Ki-67 expression. The study examined the association between Ki-67 results and the patients age, histological type, tumor grade, as well as estrogen, progesterone, and her2 neu receptors. ***Results:*** High expression of Ki-67 immune reactivity was observed in 45% of the patients. Progesterone and estrogen receptors were present in 77.5% and 67.5% of the cases, respectively. The Ki-67 showed strong correlations with tumor grade, estrogen receptor, and progesterone receptor, with corresponding p-values of 0.0057, 0.037, and 0.006. However, no statistically significant correlation was found between patient age and histological types. ***Conclusion:*** The expression of Ki-67 demonstrates a noteworthy negative association with established predictive variables such as estrogen and progesterone receptors, while showing a significant positive correlation with tumor grade.

INTRODUCTION

Breast cancer (BC) constitutes a significant global health challenge, with more than 2.1 million new cases reported annually. This alarming figure is anticipated to escalate, potentially reaching 3.2 million diagnoses per year by 2030. The sheer prevalence of BC underscores its prominence as the most common malignant tumor affecting women worldwide. The rising trend raises concerns about the global burden of the disease and the imperative need for proactive healthcare measures [1-3]. However, the landscape of cancer incidence exhibits intriguing regional disparities. In India, breast cancer assumes the second position in terms of frequency among malignancies in women. The primary position is occupied by cervical carcinoma, indicating a distinctive pattern of cancer prevalence in this region. This variance highlights the necessity of tailoring healthcare strategies to the specific epidemiological characteristics of each region. Understanding the regional nua-nces in cancer incidence is crucial for effective healthcare planning and interventions. It emphasizes the need for targeted screening programs, awareness campaigns, and treatment resources that align with the prevailing cancer landscape. By acknowledging and addressi-ng these regional variations, healthcare systems can optimize their efforts to combat breast cancer and other prevalent malignancies, contr-ibuting to more targeted and efficient public health initiatives [4-6].

The presence of estrogen receptors (ER) and progesterone receptors (PR) in breast cancer patients has been established as a significant factor influencing clinical outcomes. This correlation holds profound implications for the prognosis and treatment strategies in the realm of breast cancer. ER and PR receptors, being key biomarkers, are indicative of the responsiveness of breast cancer cells to hormonal treatments, particularly anti-estrogen therapies. When these receptors are expressed in the tumor tissue, it suggests that the cancer is dependent on hormonal signals for its growth. Consequently, such hormone receptor-positive tumors are generally more responsive to tre-

-atments that target and block estrogen signaling, leading to improved outcomes and increased chances of successful management [7-10].

Hormonal therapies, including anti-estrogen treatments like tamoxifen or aromatase inhibitors, have become pivotal in breast cancer management. They function by interfering with the hormonal pathways that fuel the growth of cancer cells [11, 12]. The presence of ER and PR receptors provides a roadmap for clinicians to tailor treatment plans, ensuring that patients with hormone receptor-positive tumors receive the most effective and targeted interventions. Beyond their role in predicting treatment response, ER and PR status also offers valuable insights into the aggressiveness of breast can-

-cer [13, 14]. Tumors that lack these receptors, termed hormone receptor-negative, often exhibit a more aggressive behavior and may necessitate different therapeutic approaches. Understanding the hormone receptor status becomes a critical aspect of evaluating the disease and tailoring an individualized treatment approach. Figure 1 represents that the basal-like subtype of breast cancer, known as triple-negative breast cancer (TNBC), represents the most aggressive molecular form, occurring in approximately 15–20% of breast cancer diagnoses. TNBC typically exhibits elevated cellular proliferation rates, increasing the likelihood of metastasis and recurrence. Furthermore, TNBC lacks a targeted treatment strategy [15-17].

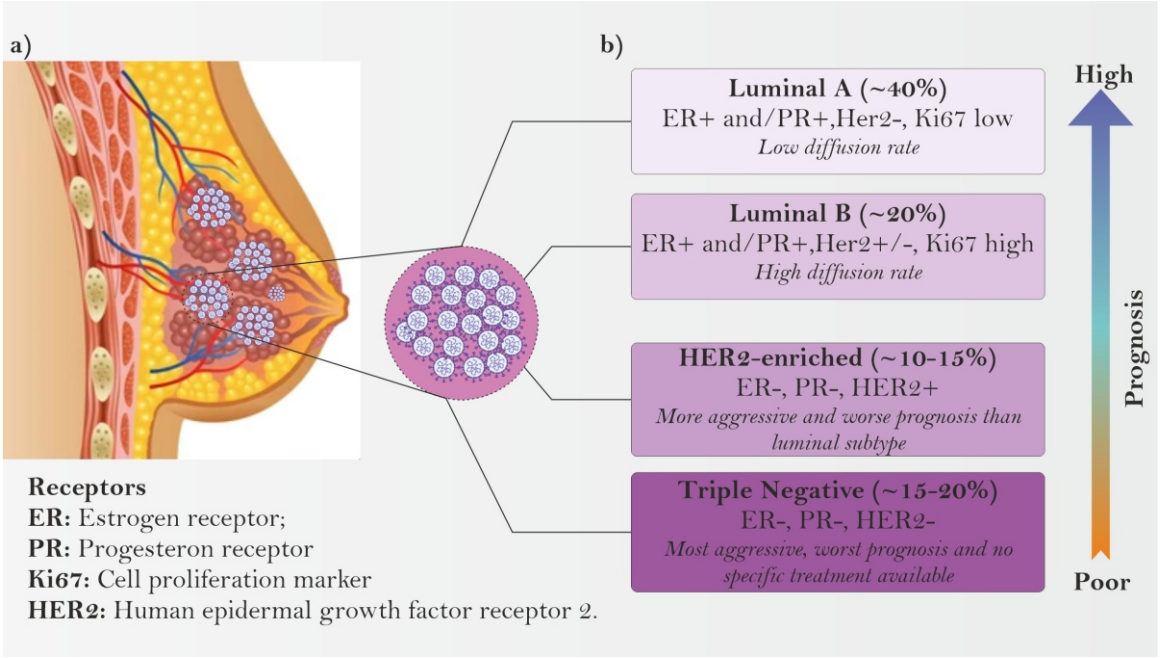

Figure 1: Molecular classification of breast cancer (Image courtesy: D.D. Singh & D.K. Yadav, 2021 [18])

Proliferation rates, another crucial aspect of breast cancer assessment, further contribute to understanding the disease's dynamics. High proliferation rates indicate a more rapid and aggressive growth of cancer cells, potentially leading to a poorer prognosis. Integrating proliferation rates into the comprehensive evaluation of breast cancer helps clinicians gauge the severity of the disease and make informed decisions about the appropriate course of treatment [2, 19]. In the realm of clinical practice, the knowledge of ER and PR status, coupled with proliferation rates, becomes a fundamental reference point for formulating personalized treatment plans. The intricate interplay between these factors allows healthcare professionals to stratify patients into different risk categories, guiding the selection of therapies tailored to the specific characteristics of the tumor. This personalized approach to breast cancer treatment enhances the precision and efficacy of interventions, ultimately optim-

-mizing patient outcomes [20-23].

The Ki-67 protein has emerged as a widely utilized, rapid, and cost-effective marker for assessing the proliferation rate of cells. Unlike histones, Ki-67 is a nuclear cortical protein involved in the initial stages of ribosomal RNA production, dependent on polymerase I activity. Its discovery dates back to 1983 when it was first identified in Hodgkin lymphoma. One distinctive feature of Ki-67 is its expression pattern throughout the cell cycle. Notably, it is not expressed during the G0 and early G1 phases, signifying its absence in cells that are in a resting state or just entering the cell cycle. However, its presence becomes prominent in cells actively progressing through the mid G1, S, and G2 phases, as well as during mitosis [24-27].

The absence of Ki-67 in G0 and early G1 is particularly noteworthy, as it provides a valuable contrast between quiescent and proliferating cells. This attribute makes Ki-67

an effective marker for identifying and quantifying actively dividing cells within a given tissue or sample. Its specificity to actively cycling cells during the phases of DNA synthesis (S phase), cell growth (G2 phase), and cell division (mitosis) positions Ki-67 as a reliable indicator of cellular proliferation. The utility of Ki-67 as a proliferation marker extends beyond its role in research and pathology. In clinical settings, Ki-67 immunohistochemical staining is commonly employed to assess the proliferative activity of tumors, aiding in the determination of their aggressiveness and potential response to treatment [28-30].

The simplicity and efficiency of Ki-67 staining make it a practical tool for pathologists and clinicians seeking valuable information about the growth characteristics of cancer cells. The dynamic expression of Ki-67 across various phases of the cell cycle underscores its versatility as a marker. Its presence in actively dividing cells makes it a valuable asset for not only understanding basic cellular processes but also f--or evaluating the proliferative potential of tumors. The accessibility and cost-effectiveness of Ki-67 staining contribute to its widespread adoption in both research and clinical settings, further solidifying its status as a key player in the assessment of cellular proliferation. Although Ki-67 is crucial for cell growth, its exact purpose is unclear, remained a mystery. Therefore, in order to evaluate Ki-67 expression and correlate changes in the current results as compared with those of earlier studies, this research is conducted on the paraffin embedded blocks of patients with primary breast cancer. Figure 2 shows that Ki-67 expression is closely linked to the proliferation and growth of tumor cells, making it a commonly employed marker in routine pathology for both assessing proliferation and aiding in diagnosis. The nuclear protein Ki-67 (also known as pKi-67) serves as a well-established prognostic and predictive factor, particularly valuable for evaluating cell proliferation in cancer patient biopsies [31-33].

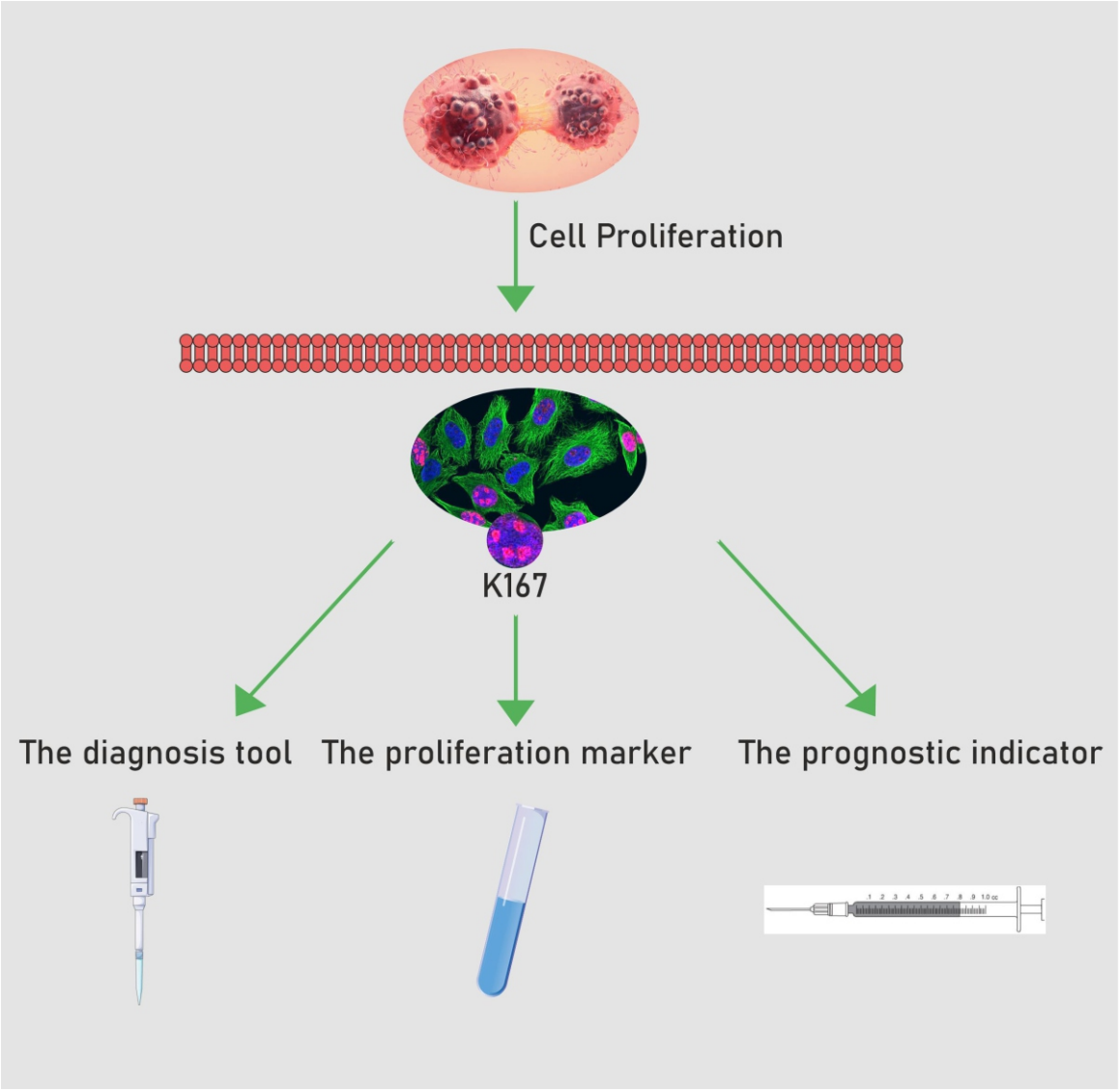

Figure 2: Diagram illustrating Ki67 as a potent molecular target for cancer diagnosis (Image courtesy: Li LT et al., 2014 [31]).

MATERIAL AND METHODS

Following the acquisition of informed consent, the research comprised females of various age groups diagnosed with breast malignancy at the Department of Pathology, in a tertiary care center, undergoing histopathological examination. The prospective cases considered for the study spanned from October 2022 to November 2023. In situ lesions of female breasts were included in the study. Exclusions from the study encompassed patients with metaplastic carcinoma, metastatic tumors and patients on radiotherapy or chemotherapy and already treated cases for contralateral breast cancer.

Procedure

The specimens, upon arrival at the pathology department, were immersed in 10% formalin for 6-8 hours. A consistent procedure for surgical grossing of the specimens was adhered to in each case. Following a comprehensive description of the specimens, multiple sections were obtained through conventional processing. Paraffin sections, with a thickness of 5 micrometers, were prepared and subsequently stained with hematoxylin and eosin (H & E) for histopathological examination. The histological types were evaluated in accordance with the WHO classification of breast tumors and graded using the Modified Bloom-Richardson grading method.

3-micrometer sections were sliced from a paraffin block of tumor tissue and mounted on four glass slides coated with poly-L-lysine for immunohistochemistry (IHC) targeting the detection of Ki-67, estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor-2 (HER-2/neu) markers in breast malignancy expression. The slides underwent dewaxing on a hot plate for one hour. Once the dewaxing process was completed, the slides were directly immersed in xylene from the hot plate. They were kept in xylene for 10 minutes and subsequently transferred to a second xylene solution for an additional 10 minutes.

Subsequently, the slides were sequentially immersed in decreasing concentrations of alcohol, progressing through 100%, 70%, and 50%, with each concentration maintained for 5 minutes. Following this, the slides underwent a thorough wash with distilled water for 5-10 minutes. The next phase involved antigen retrieval (for Ki-67, ER, PR, HER-2-NEU) using citrate buffer (pH-6) under high temperature and pressure conditions. Upon completion of the retrieval process, the slides were placed in a moist chamber, allowing them to cool down to room temperature over approximately 30 minutes.

The slides underwent multiple washes with TRISS buffer (pH-7.5) (2-3 times), followed by the addition of peroxidase blocker to each section for a 15-minute duration. After another set of 3 washes with TRISS buffer, the slides were labeled as Ki-67, ER, PR, and HER-2 NEU. Subsequently, t-he slides were incubated with the respective primary antibodies for 1 hour, followed by 3 additional washes with TRISS buffer. The next step involved incubation with the secondary antibody HRP (horse radish peroxidase) for 30 minutes, followed by another set of 3 washes with TRISS buffer.

To visualize the reaction, the DAB chromogen was prepared by mixing it with a DAB buffer in a ratio of 1:50, and this mixture was applied to the slides for 30 minutes. After 3 washes with distilled water, the slides were counterstained with hematoxylin for an appropriate duration (3-5 minutes). Finally, after another set of 3 washes with distilled water, the slides were dried, mounted with DPX, and subjected to microscopy.

Statistical Analysis

The Fisher Exact test and the Chi-square test were employed to examine the association between Ki-67 and variable categories. Regarding statistical analysis, a P value of 0.05 or lower was considered statistically significant.

RESULTS

Our study encompassed 48 cases, with patients ranging in age from 24 to 74 years (mean = 50.4). Among the patients, 26 cases (53.75%) were under the age of 50. Examining the histological types, the majority were invasive ductal carcinoma, not otherwise specified (IDC-NOS), constituting 42 out of 48 cases (86.25%), while four cases were invasive lobular carcinoma (ILC) (10% of all cases), and two cases were ductal carcinoma in situ (DCIS) (3.75% of cases).

There were 8 cases (17.4%) categorized as IDC -NOS grade I, 18 cases (36.2%) as grade II, and 22 cases (46.4%) as grade III. 37 cases (77.5%) were ER-positive, 33 cases (67.5%) were PR-positive, and 22 cases (45.8%) were HER2/neu-positive. Ki-67 immunohistochemical analysis indicated strong expression (20% of nuclei positive) in 22 patients (45%) and low expression in 26 cases (55%). Detailed patient characteristics are presented in **Table 1.** Figure 3, 4, 5 and 6 shows the histopathological slides of breast cancer positive for hormone receptors.

Ki-67 expression did not exhibit a statistically significant correlation with patient age or histological type and HER2/neu (P values of 0.333, 0.682, and 0.961, respectively). However, an inverse relationship between Ki-67 expression and ER positivity was observed, indicating that higher Ki-67 expression was associated with decreased ER positivity, and this association was found to be statistically significant (P=0.037). Additionally, there was a significant direct association between Ki-67 expression and grade (P=0.0057). Similar patterns were noted when examining PR positivity, and the correlation (P=0.006) was found to be statistically significant.

31 cases (66.25%) of patients were positive for both ER and

Table 1: Distribution of cases on the basis of baseline characteristics

VARIABLES		NUMBER	PERCENTAGE
Age group (in years)	<50	26	53.75%
	≥50	22	46.25%
Histological type	IDC-NOS	42	86.25%
	ILC	4	10%
	DCIS	2	3.75%
Grade of IDC-NOS	I	8	17.4%
	II	18	36.2%
	III	22	46.4%
Estrogen receptor	Positive	37	77.5%
	Negative	11	22.5%
Progesterone receptor	Positive	33	67.5%
	Negative	15	32.5%
HER2-neu	Positive	22	45.8%
	Negative	26	54.2%
Hormonal receptors status	ER+PR+	31	66.25%
	ER+PR-	6	11.25%
	ER-PR+	1	1.25%
	ER-PR-	10	21.25%
Ki-67 expression	High	22	45%
	Low	26	55%
Total no. of the cases		48	100%

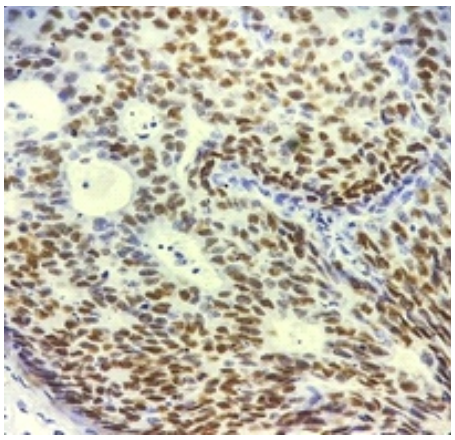

Figure 3: Positive for ER (X400).

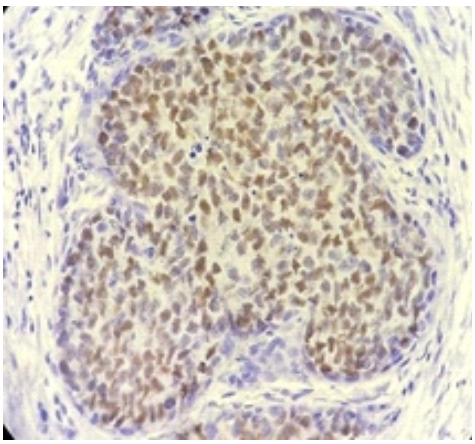

Figure 4: Positive for PR (X400).

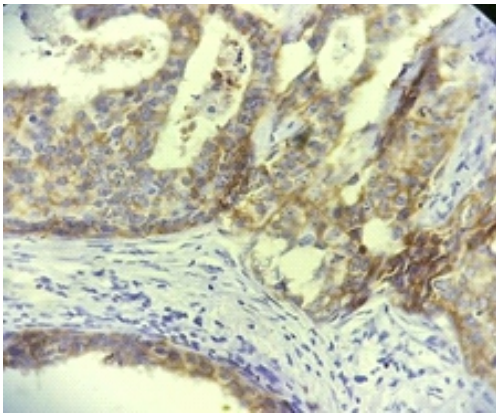

Figure 5: Positive Her 2-neu in breast cancer

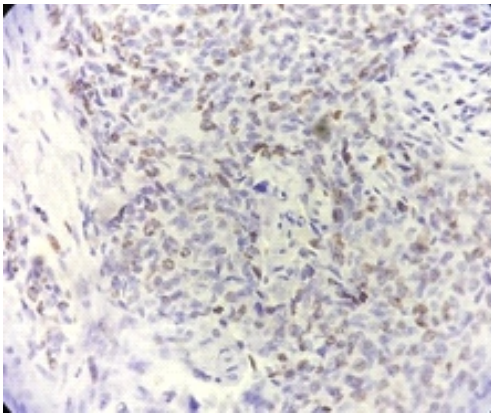

Figure 6: High Ki-67 expression in breast cancer

PR (ER+PR+). Among them, 22 cases (45%) displayed low Ki-67 expression. Additionaamong them displayed high Ki-67 expression. Only one case (1.25%) was ER-PR+ and exhibited high Ki-67 expression, while 10 cases (21.25%) were ER-PR- and 6 of them displayed high Ki-67 expression. The relationship between Ki-67 and hormonal status demon-

-strated a statistically significant unfavorable association (P=0.0054). Further details regarding the relationship between Ki-67 and other factors, as well as distinct histological types, are summarized in **tables 2 and 3**.lly, 5 cases (11.25%) were ER+PR-, and 4 cases

Table 2: Relation of Ki-67 expression with the different parameters.

Parameters		**Ki-67**		**Total**	**P-value**
		High expression	**Low expression**		
Age of patients	<50 year	13(27.5%)	13(26.25%)	26(53.75%)	0.333
	≥50 year	8(17.5%)	14(28.75%)	22(46.25%)	
Grade of tumor	Grade I	1(2. 9%)	7(14.5%)	8(17.4%)	0.0057
	Grade II	12(26.1%)	5(10.1%)	17(36.2%)	
	Grade III	11(23.2%)	11(23.2%)	22(46.4%)	
ER	Positive	14(28.75%)	23(47.5%)	37(76.25%)	0.037
	Negative	8(16.25%)	4(7.5%)	12 (23.75%)	
PR	Positive	11(22.5%)	21(45%)	32(67.5%)	0.006
	Negative	11(22.5%)	5(10%)	15(32.5%)	
HER2-neu	Positive	12(25%)	10(20.8%)	22(45.8%)	0.961
	Negative	14(29.1%)	12(25%)	26(54.1%)	
Hormonal receptors (ER and PR) status	ER+PR+	10(21.25%)	22(45%)	32(66.25%)	0.0054
	ER+PR-	4(8.75%)	1(2.5%)	5(11.25%)	
	ER-PR+	1(1.25%)	0(0%)	1(1.25%)	
	ER-PR-	6(13.75%)	4(7.5%)	10(21.25%)	

Table 3: Relation of Ki-67 with histological type of tumors.

Histological types	Ki-67 expression		Total	P value
	High	Low		
IDC-NOS	19(37.5%)	23(48.75%)	42 (86.25%)	0.682
ILC	2(5%)	2(5%)	4(10%)	
DCIS	1(2.5%)	1(1.25%)	2 (3.75%)	
Total	22(45%)	26(55%)	48(100%)	

Breast cancer positive for hormone receptors.

Ki-67, an immunohistochemical marker, assesses the proliferative activity of a tumor, offering insights into its aggressiveness and the patient's prognosis. Ki-67 can be utilized to subclassify patients and, when combined with other immunohistochemistry markers such as ER and PR, enables more accurate classification. This precise categorization aids in tailoring appropriate treatment plans, potentially preventing patients from undergoing ineffective treatments. To validate this hypothesis, additional research involving the follow-up of breast cancer patients with varying Ki-67 expression and diverse ER/PR cancer phenotypes is imperative. Such studies would contribute to demonstrating the predictive and prognostic value of Ki-67, thereby guiding more personalized and effective approaches to breast cancer treatment.

DISCUSSION

Immunohistochemistry has gained global acceptance as a crucial approach in the management of endocrine therapy for detecting Estrogen and Progesterone receptors in breast cancer. This study reinforces the understanding of breast cancer as a multifaceted disease, consisting of distinct biological subtypes with diverse natural histories. These subtypes are increasingly acknowledged for presenting a varied spectrum of clinical, pathological, and molecular features, each carrying different prognostic and therapeutic implications. This investigation contributes to the ongoing effort to unravel the complexities of breast cancer and refine therapeutic strategies based on a more nuanced understanding of its diverse subtypes [34-36].

The findings of present study closely align with those of a similar investigation conducted in Nineveh Province by Hatem Abd-AlMajeed Al-Nuaimi in 2020 (mean age: 50; range: 27-74), as well as a 2015 study in the same province by Al-Nuaimy (mean age: 50.4). However, our results are also consistent with broader trends recorded in other countries, w-hich indicate that 53.75% of the cases in our study were younger than 50 years old, contrasting with the notion of breast cancer incidence typically increasing with age. This pattern was noted in studies by Al-Nuaimy and Mahmoud, where 46.25% of cases were 50 years or older. In our study, invasive ductal carcinoma, not otherwise specified (IDC-NOS), emerged as the predominant histological type, constituting 86.25% of cases. This result is comparable to the findings of Neelakanth, who reported IDC-NOS accounting for 90.7% of cases, and Mahmoud, who observed it as the most prevalent type in his study, making up 93.5% of cases. The convergence of our results with these studies highlights the consistent prevalence of IDC-NOS in breast cancer across various regions and populations [37-39].

Concerning the histological grade of the tumors, the majority of IDC-NOS cases (82.6%) in our study exhibited high grades (grade II and III), with grade III constituting 46.4% of them. This outcome mirrors the findings of a study conducted in Kirkuk, Iraq, in 2014 by Mahmoud, where grade III was the most prevalent, forming 46.4% of the cases. A similar prevalence of grade III was also observed in a study by Soliman in Egypt, where it accounted for 53% of the cases. These variations could be attributed to differences in demographic traits, racial origins, or the inherent heterogeneity of tumor cells. Notably, studies in cases conducted by different researchers observed grade II as the most common grade. These findings contrast with those of a research study conducted in Morocco in 2016 by Mahir W et al., where ER and PR were positive in 73.1% and 69.1% of cases, respectively. The variations in these results further emphasize the complex and multifaceted nature of breast cancer, influenced by diverse factors across different populations [40, 41].

In our study, positive immunohistochemistry for ER and PR was identified in 76.25% and 67.5% of cases, respectively. These results are notably consistent with findings from a stu-

-dy conducted in Baghdad in 2015 by Al-Sarraf, where 75% and 72.5% of cases exhibited positivity for ER and PR, respectively. Similarly, our outcomes align with another study conducted in Baghdad in 2012 by Elyass, reporting positive rates of 72% for ER and 68% for PR. It's worth noting that these findings may deviate from those reported by other researchers, underlining the variability in breast cancer characteristics across different populations and geographical regions. The overall pattern, however, supports a recurring theme of hormone receptor positivity being a significant aspect of breast cancer in these studied populations [42, 43].

The Ki-67 antigen has been identified in the initial stages of polymerase I-dependent ribosomal RNA synthesis. Despite its prominent role in cell proliferation, the specific function of the Ki-67 protein remains unclear, and there is a scarcity of published studies on this topic. Numerous studies have explored the predictive value of Ki-67 in breast cancer, but such research has not been conducted in the province of Nineveh. In light of this gap, the current study aimed to assess the prognostic significance of Ki-67 in primary breast cancer [44]. This assessment involved comparing Ki-67 with well-established traditional clinicopathological prognostic parameters, including patient age, histological type, tumor grade, and its correlation with ER and PR. ER and PR are considered the most useful markers in predicting the response to hormonal therapy [45].

Despite numerous studies yielding significant results on Ki-67, there remains ongoing debate over the cut-point to differentiate breast cancer (BC) patients with low Ki-67 expression from those with high expression, with reported ranges from 1 to 29%. This uncertainty has limited its clinical applicability. The 2009 St. Gallen Consensus initially categorized Ki-67 expression into three groups: low (≤15%), intermediate (16–30%), and high (>30%). In 2011, St. Gallen proposed a Ki-67 cut-point of 14% to distinguish ER+ tumors into luminal A (Ki-67≤14%) and luminal B (Ki-67>14%). In 2013, this was updated to 20%, with an option for locally specified cut-points. The 2015 St. Gallen Breast Cancer Conference suggested a median cut-off value between 20 and 29% for classifying "luminal B-like" tumors. Bustreo et al. (2016) conducted a study with 1,577 HER2-/ER+ breast cancer patients, using Ki-67 cut-offs of 14% and 20%. They found no differences in disease-free interval (DFI) and disease-specific survival (DSS) between tumors with Ki-67 values below 14% and those between 14 and 20%, while tumors with Ki-67 levels above 20% had the worst prognosis. The 20% cut-off was employed in the current investigation, consistent with prior studies [46-48].

In this study, approximately 45% of patients had elevated Ki-67 expression, aligning with findings from studies in Iran and Finland. However, variations in outcomes between studies may be attributed to the use of different antibodies, demographic subgroups, Ki-67 detection techniques, and sc-oring methods. Immunohistochemical staining with the MIB-1 antibody is a common method for examining Ki-67 expression, with variations in antibodies used across studies contributing to discrepancies. Additionally, differences in Ki-67 scoring methods, such as the proportion of stained nuclei or counting nuclei in various tumor locations, may contribute to the observed variations in reported results [49].

The correlation between Ki-67 expression and patient age did not reach statistical significance (P=0.333), consistent with previous findings. Liu et al., reported a significant correlation between Ki-67 and age, indicating that patients with higher Ki-67 expression tended to be younger. However, in this study, no significant association was observed between Ki-67 and the histological type of the tumor, aligning with the findings of Soleman and Ermiah et al. It is worth noting that the limited inclusion of non-ductal types in this study may have influenced this outcome [50]. In contrast, a substantial and consistent association between Ki-67 expression and tumor grade was observed. The mitotic index, a component of the Modified Bloom-Richardson grading system for breast cancer, contributed to this association. This finding aligns with several prior studies that also highlighted the correlation between Ki-67 expression and tumor grade. A low histologic grade is generally indicative of a poorer prognosis, and the current study supports the notion that Ki-67 expression increases with higher tumor grades. This underscores the common understanding that rapidly dividing cells often exhibit increased Ki-67 expression, reinforcing the link between cell proliferation and tumor aggressiveness [38].

The majority of breast cancer patients in the current study (66.25% of cases) had positive hormonal receptors (ER+PR+), aligning with the findings of Al Sarraf and Al-Rawaq. Hormonal receptors, notably estrogen receptor (ER) and progesterone receptor (PR), are widely recognized as crucial predictive and prognostic indicators in breast cancer. Consistent with findings from other researchers, a significant negative relationship between Ki-67 expression and both ER and PR was observed in this study. According to Liu et al., breast cancer with high Ki-67 expression is associated with a poor prognosis but shows a favorable response to neoadjuvant treatment. This could be attributed to the heightened sensitivity of dividing cells to cytotoxic medications, making them more responsive to neoadjuvant therapies. Following chemotherapy, studies such as the one conducted by Faneyte et al. have demonstrated a significant decrease in Ki-67 expression. Additionally, it was noted that patients with breast cancer who have a negative ER status and high Ki-67 expression tend to exhibit better responses to treatment. These insights highlight the intricate relationship between hormonal receptors, Ki-67 expression, and treatment response, providing valuable information for the development and refinement of therapeutic strategies in bre-

-ast cancer management[9, 51-53]. In table 1, data from our study suggests a need for further research in our region to identify risk factors that predispose individuals to developing breast cancer at younger ages.

CONCLUSION

In the present study, 45% of female patients with breast cancer exhibited a high Ki-67 expression. The age of patients and the histological types of breast cancer did not show a significant correlation with Ki-67. However, there was a clear correlation between Ki-67 expression and tumor grade, and Ki-67 demonstrated a negative correlation with two well-established predictive variables, namely estrogen receptor (ER) and progesterone receptor (PR). To enhance the prognostic and predictive significance of Ki-67 in breast cancer, further research involving the follow-up of breast cancer patients with diverse Ki-67 expressions and various ER/PR cancer phenotypes is deemed necessary. This continued investigation would contribute to a more comprehensive understanding of the relationship between Ki-67 expression, tumor characteristics, and the predictive value of hormonal receptors in breast cancer, ultimately refining its clinical applicability.

ETHICS APPROVAL

All necessary approval including ethical approval has been taken before conducting this study.

AVAILABILITY OF DATA AND MATERIAL

Data is available with the author and can be shared on request.

CONFLICT OF INTERESTS

Authors declared that there is no conflict of interest.

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