



## Original Research Article

## Correlation of ER &amp; PR with proto-oncogene &amp; with proliferative marker Ki-67

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## ABSTRACT

**Background & Methods:** This study was prospective and retrospective. Prospective cases were selected from the patients admitted for surgery of invasive ductal carcinoma breast in Medical College Hospital. As regards retrospective cases, they were obtained from the histopathological records obtained from Pathology department of SRMS-IMS, Bareilly.

**Result:** There was a significant relationship between the grades & Ki-67 status. As the grade increases the proliferative index increases. Here the value of ( $p < .0001$ ) which is significant. In the study as observed, in maximum cases (69.64%) tumour size was 20-50mm followed by more than 50mm was in 13 cases (23.21%) and in only 4 cases (7.14%) size was less than 20mm.

**Study Designed:** Observational Study.

**Conclusion:** Out of 56 cases, 40 cases (71.42%) clinically presented with painless lump in breast followed by painful lump in 9 cases (16.7%). 7 cases (12.50%) presented with axillary mass. Out of 40 cases presented with lump, 48.21% were with lump localized on right side while 23.21% were on left side. Among 56 cases, in 39 cases (69.64%) tumor size varied between 20-50mm followed by 13 cases (23.21%) with size greater than 50mm and in only 4 cases (7.14%) size was less than 20mm. The proliferative index Ki-67 was highest in grade 3 and lowest in grade 1 tumours.

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## 1. Introduction

Ki-67 is a mouse mono clonal antibody to nuclear component of a cell line derived from Hodgkin's lymphoma. The antibody react with a nuclear antigen expressed in proliferating cells throughout the cell cycle but which is absent from quiescent cell.<sup>1</sup> It has been so that there is the close correlation in breast carcinomas between the Ki-67 growth fraction and S-Phase Fraction (SPF) determined by flow cytometry,<sup>2</sup> the TL1 and mitotic counts. The Ki-67 labelling occurs throughout the cell cycle, the percentage of the cell is consistently higher and generally about twice the proportion in S-phase. However, Ki-67 positivity may not accurately reflect proliferative activity under some circumstances. Ki-67 expression may be so low as to be undetectable at the

outset of DNA replication, particularly in cell with a long G1-Phase. Cell with proliferation impaired or arrested by immunohistochemically demonstrable Ki-67 antigen.

A statistically significant positive correlation between Ki-67 positivity and the number of nucleolar organizer regions in mammary carcinoma nuclei has been reported.

The mean value of Ki-67- positive cells (3% to 4%) in benign breast lesions is substantially lower than the mean value (16% to 17%) in mammary carcinoma.<sup>3</sup> The Ki-67 growth fraction is significantly related to grade in most tumors, being highest in poorly differentiated carcinoma & invasive duct carcinomas with comedo feature. Ki-67 detection represent a valuable tool & is a good objective substitute for mitotic counts when used in grading system. Invasive lobular & mucinous carcinomas have a low to moderate growth fraction, whereas medullary carcinomas have more than 50% Ki-67 positive cells.<sup>4</sup> Estrogen & progesterone receptor negative tumors tend to have a high

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Ki-67 positive fraction.<sup>5</sup> Several studies have reported a significant inverse association between Ki-67 staining & disease free & overall survival.<sup>6</sup> A comparison of screen-detected & interval carcinoma revealed that interval carcinoma had higher Ki-67 labelling & higher mitotic rates than tumor detected by screening.

**2. Materials and Methods**

The present study entitled “Correlation of ER & PR with proto-oncogene & with proliferative marker Ki-67” was conducted in Dept. of Pathology, at SRMSIMS, Bareilly.

This case study was prospective and retrospective. Prospective cases were selected from the patients admitted for surgery of invasive ductal carcinoma breast in Medical College Hospital. As regards retrospective cases, they were obtained from the histopathological records obtained from Pathology department of SRMS-IMS, Bareilly.

1. Biopsies and mastectomy specimens were fixed in 10% formalin.
2. Detailed history about age, family history, clinical diagnosis and chief complaints was enquired.
3. Tissue was fixed in buffered formalin for about 6 hour after adequate slicing.
4. Gross appearance of mastectomy specimen/biopsy was noted.
5. Paraffin blocks after thorough tissue processing were prepared.
6. Sections were cut 3-4 micron thick and subjected to following:
7. Routine haematoxylin and eosin staining was done for histological typing and grading of all cases.
8. Immunohistochemistry was done using labelled antibodies for hormone receptor status (Oestrogen receptor & Progesterone status), Her2/neu & proliferative index Ki-67.

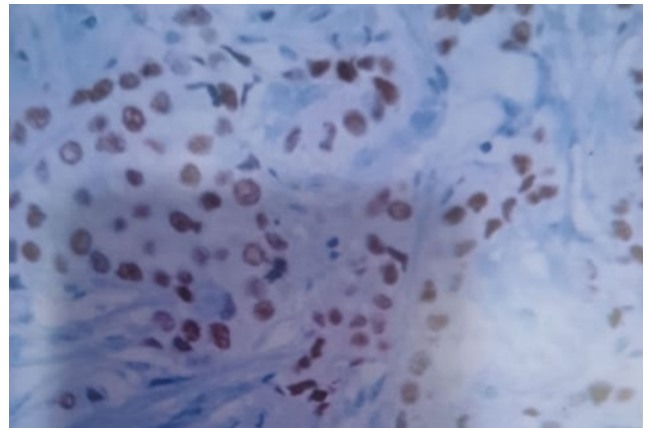
Invasive ductal carcinomas and all other invasive tumours were graded based on an assessment of tubule/gland formations, nuclear pleomorphism, and mitotic counts as per criteria of Nottingham’s grading.

**3. Results**

**Table 1:**

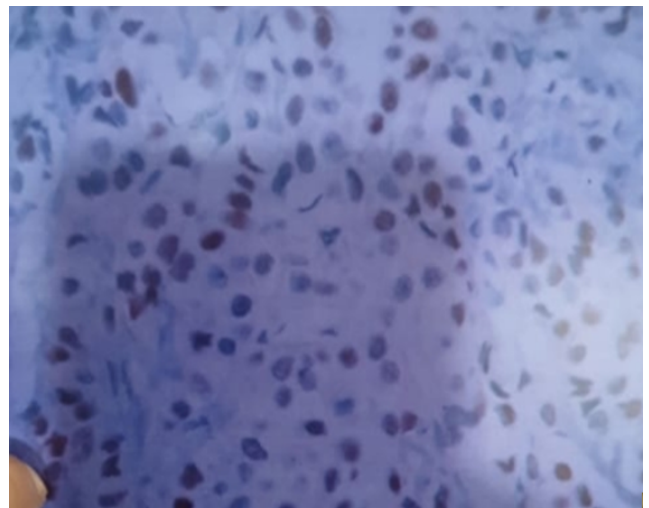
Presenting Feature	No. of cases	Percentage
Right breast lump	27	48.21%
Left breast lump	13	23.21%
Painful lump	09	16.07%
Axillary mass	07	12.50%

As most common clinical presentation of breast carcinoma is palpable lump. Maximum 40 cases (71.42%) presented with lump in breast followed by 9 cases (16.7%)



7-ER Positive Case

**Fig. 1: ER Positive Case**



8-PR Positive case

**Fig. 2: PR Positive Case**

presented with painful lump. 7 cases (12.50%) presented with only axillary mass. No case with nipple discharge was seen. In 27 cases lump involved right breast and 13 case lump was present in left breast.

**Table 2: Relation of Ki-67 with grading of tumour**

Grade	No. of cases	Ki-67
Grade 1	07	25.42%
Grade 2	39	45.69%
Grade 3	10	69%

There was a significant relationship between the grades & Ki-67 status. As the grade increases the proliferative index increases. Here the value of (p<.0001) which is significant.

In the study as observed, in maximum cases (69.64%) tumour size was 20-50mm followed by more than 50mm was in 13 cases (23.21%) and in only 4 cases (7.14%) size

**Table 3:** Tumour size wise distribution of cases

Tumour size	No. of cases	Percentage
<20mm	04	7.14%
20-50mm	39	69.64%
>50mm	13	23.21%

was less than 20mm.

#### 4. Discussion

Out of the 56 cases studied, maximum patients were in age group 41-50 years (53.5%) followed by 21.4% patients were from 51-60 years of age group. (14.28%) patients were from above 60 years and (10.7%) patients were from 31-40 years of age group. This is in accordance with study of Hussain et al, who found peak incidence between ages of 41-50 years.<sup>7</sup> Among the 56 patients studied, all the patients were female. No single case in male was found. Similar findings were found by Hussain.<sup>7</sup>

Out of 56 cases maximum cases (71.42%) clinically presented with lump in breast followed by painful lump in 9 cases (16.07%). 7 cases (12.50%) presented with axillary mass. These findings are in accordance with the study of Blamey, who noticed frequency of symptoms of women presenting in a breast clinic with lump 60-70% followed by pain 14-18%, nipple problems 7-9%, deformity 1% and inflammation 1%.<sup>8,9</sup>

In our study, out of 40 cases presented with breast lump, 27(48.21%) cases with lump were localized on right side while in 13 (23.21%) cases were localized on left side. This was in accordance with the study of Haagensen<sup>9</sup> who showed that there is slight higher frequency of invasive breast cancer in the right breast with a reported right to left ratio of approximately 2.07:191.

#### 5. Conclusion

Out of 56 cases, 40 cases (71.42%) clinically presented with painless lump in breast followed by painful lump in 9 cases (16.7%). 7 cases (12.50%) presented with axillary mass. Out of 40 cases presented with lump, 48.21% were with lump localized on right side while 23.21% were on left side. Among 56 cases, in 39 cases (69.64%) tumor size varied between 20-50mm followed by 13 cases (23.21%) with size greater than 50mm and in only 4 cases (7.14%) size was less than 20mm. The proliferative index Ki-67 was highest in grade 3 and lowest in grade 1 tumours.

#### 6. Source of Funding

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#### 7. Conflict of Interest

The authors declare they have no conflict of interest.

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