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Original Research Article

# Evaluation of role of serum prolactin & ki-67 in different stages of breast cancer

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ABSTRACT

Breast cancer is the most frequent cancer among women. Prolactin (PRL) is a hormone secreted from anterior pituitary gland which stimulates cell proliferation, survival of cancer cells, its migration, invasion and angiogenesis. Breast cancer is strongly associated with raised plasma Prolactin level (PRL). The Prolactin behaves like Growth Hormone and its actions by the growth-promoting JAK/STAT pathway suggests its tumor-promoting effects.
Ki-67 a Nuclear Protein is highest in Luminal B, Ki67 are not related to age but is correlated with tumor size. Fraction of Ki-67 positive tumor cells correlates with the clinical course of cancer cells. Hence, Ki-67 can be an effective target in cancer therapy. Ki-67% and Serum Prolactin level may be considered a valuable biomarker in breast cancer patients and be used in treatment, follow-up and Prognosis.



## 1. Introduction

Breast cancer is the most frequent cancer among women, Breast cancer (BC) has a major impact on women's health worldwide. It is considered the most common malignancy embodying the second leading cause of cancer deaths after lung cancer impacting 2.1 million women each year, and also causes the greatest number of cancer-related deaths among women. In 2018, it is estimated that 627,000 women died from breast cancer – that is approximately 15% of all cancer deaths among women. While breast cancer rates are higher among women in more developed regions, rates are increasing in nearly every region Globally (WHO Data).

Incidence rates vary from 27 per lac women in Eastern Africa to 98 per lac in Western Europe. The range of mortality rate is similar, approximately 6-20per lac, because of the more favourable survival of BC cases in developed country.[1]

So far India is concerned, incidence rate varies across the country due to demographic differences (education), adipocity, menarche, menopause, awareness, limited access to cost effective early diagnosis and treatment. Diet, endocrine, genetics all have a major role in Breast Cancer. Breast cancer has ranked number one cancer among Indian females with age adjusted rate as high as 25.8 per1,00,000 and mortality 12.7 per 1,00,000 women.[1] Better health awareness and availability of breast cancer screening and advanced therapeutic applications would cause a favourable and positive clinical picture in the country. Women living in less developed regions have a greater number of cases in comparison to more developed regions. With a lot of advancement in early diagnosis and treatment, outcome has changed, mortality rate has declined. In case of treatment failure, survival of patients

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and quality of life is severely affected. Hence it is important to evaluate all etiological, prognostic factors for taking more reliable decision during treatment of breast cancer and to improve survival rate of patients. Prognostic factors are clinicopathological parameters which include tumor size, staging, hormone receptor status.

Breast cancer is a group of diseases in which cells in breast tissue change and divide uncontrolled, typically resulting in a lump or mass. Most breast cancers begin in the lobules (milk glands) or in the ducts There are many types of breast cancer, Ductal carcinoma in situ, Lobular carcinoma in situ, Invasive (or infiltrating) ductal carcinoma, Invasive (or infiltrating) lobular. A new lump or mass is the most common sign, mostly painless, hard mass with irregular edges. X-rays, MRI, Ultrasound waves, or radioactive substances are used to make a picture of the inside of breast.[2,3] Diagnostic mammograms is the most common testing that is used for screening the breast tissue. A biopsy is the only way to tell if cancer is really present and what type it is. Molecular classification is necessary to predict prognosis and outcome. Breast cancer has been classified as four molecular subtypes. Molecular subtypes classified as Luminal A (ER+ and/orPR+, HER2-) Luminal B (ER+ and/or PR+, HER2+), HER2 positive (ER- and PR-, HER2+) and triple negative (ER- andPR-, HER2-).[4]

Serum Prolactin and Ki67 % have a positive upward trend in Breast Cancer patients and their higher values are significant in clinical staging, predictive of prognosis with favourable outcome and have positive clinical picture.

Prolactin (PRL) a hormone from Anterior Pituitary gland stimulates cell proliferation, survival of cancer cells, its migration, invasion and angiogenesis.[5] Administration of exogenous prolactin increases rates of mammary tumor formation and suppression of prolactin levels decreases tumor formation.[3,6] PRL receptor (PRLR) are expressed in normal and cancerous breast epithelium so it appears, PRL may act as an autocrine /paracrine factor in mammary tissue independent of circulating levels.[7] There is a functional autocrine/paracrine loop in the breast stimulating cancer cell growth and there is more survival in the presence of PRL blocking antibodies and antagonists.[7,8] Breast cancer is strongly associated with raised plasma Prolactin level(PRL)[9] andProlactin receptors(PRLR) The Prolactin behaves like Growth Hormone and its actions by the growth-promoting JAK/STAT pathway suggest its tumor-promoting effects.[10,11]

Ki-67 is a Nuclear Protein encoded by MKi-67 gene and is identified by monoclonal antibody.[12] p53, Ki-67, BRCA1 are expressed differently in molecular subtypes of Breast Cancer. p53 and Ki-67 is lowest in Luminal A and BRCA1 is lowest in Luminal B subtype of breast cancer. However, Ki-67 is highest in Luminal B and BRCA1 is highest in Luminal A subtype of breast cancer. p53 and Ki67 are not related to age but is correlated with tumor size.[13] Fraction of Ki-67 positive tumor cells correlates with the clinical course of cancer cells. Hence, Ki- 67 can be an effective target in cancer therapy. This study assesses Ki-67 a promising molecular prognostic factor in diagnosis of Breast cancer Clinical staging.

## 2. Materials and Methods

### 2.1. Patient selection

Between $1^{st}$ September 2019 and $30^{th}$ September 2020 patients with diagnosed Breast cancer were included in this study. Totally, the data of 102 women with breast cancer were evaluated. Patients having any medical problem like Diabetes, dyslipidemia, hypothyroidism, alcoholism, polycystic ovarian disease, Cushing's syndrome, acute or chronic renal insufficiency were excluded. The inclusion criteria's were women between age of 30-70 years receiving screening, mammography or diagnosed with metastatic breast cancer.

Serum Prolactin was analyzed in chemiluminescence immunoassay (CLIA). The calibration and quality control and control were done daily before analyzing the sample. Normal Serum Prolactin level –2.64 to 26.72ng/dl. After the patient's consent, blood sample was collected and serum prolactin was assessed by one step immuno- enzymatic assay procedure done at IGIMS Biochemistry lab.

### 2.2. Immunohistochemistry (IHC) evaluation

After the patient's consent, fresh or frozen breast cancer tissue were collected. Ki-67% was assessed in frozen breast cancer tissue taken from operated patients of Breast Cancer, examined by Immunohistochemistry.

### 2.3. Statistical analysis

There were 100 normal individuals as control (for Prolactin estimation) and102 breast cancer patients as case (for Prolactin) Among the total 100 subjects in the control group there were 75 pre-menopausal and 25post menopausal subjects while among breast cancer cases there were53pre menopausal and 49 post-menopausal, (Mean ±S.D.) age of the control group is 42.50 ± 1.09and that of case group is 49.40 ± 1.08. There is a significant age difference between the two groups.

Range, mean, S.D, SEM and p Value of serum prolactin concentration in control group and its comparison with case group there is highly significant increase ($p < 0.001$) in mean serum prolactin level in case group I (age less than 35 yrs), group II age between 35-39 yrs mean value of Prolactin were significantly raised (45.02ng/dl) and (45.02ng/dl) respectively as compared to the control group.

Range, mean, S.D., SEM and p Value of serum prolactin in different clinical stages among cases of Breast Cancer, there is significant difference between the level of serum

prolactin among different clinical stages in breast cancer patients (p =0.017), more marked in stage IV (mean 70.33ng/dl).

There were 124 operated cases of Breast Cancer for KI67% estimation. 124 operated cases included 57 cases common for both (Prolactin and Ki67%.) In the study, range, mean, S.D, SEM and p Value of KI 67 % in different age groups among cases of Breast Cancer, there is significant difference between the abundance of KI67 among different age groups in breast cancer patients (p =0.034).

In this study molecular marker with luminal classification of subjects among different clinical stages of breast cancer patients there were ER+ mostly in 1A,1B (few cases in III B), PR+ mostly in 1A,1B (few cases in III B), HER-2 positive mostly in IIA, IIB, III C. In Luminal classification triple negative mostly in IIA, IIB, III C.

In TNM classification KI67% were 62.16 in T4, 45.68 in T3, in N2 65, N1 54.34, Ki 67% were higher in Trip N (55.94), Luminal B(45.02), HER-2 (41.57)There is also significant difference between the level KI 67% among different clinical stages in breast cancer patients (p =0.001).

There is significant difference between the distribution of KI67% among different prognostic stages in breast cancer patients (p <0.05).

## 3. Results

This study was carried out on 102 women with breast cancer. The mean age of patient was between 30-70 years, receiving screening, mammography or diagnosed with metastatic breast cancer. The different features of cases are shown as below:

## 4. Conclusion

In this present study there is highly significant increase (p <0.001) in mean serum prolactin level in case group as compared to the control group. In breast cancer patients group I (age less than 35 yrs), II age between 35-39 yrs mean value of Prolactin were significantly raised (45.02ng/dl) and (45.02ng/dl) respectively. There is significant difference between the level of serum prolactin among different clinical stages in breast cancer patients (p =0.017), more marked in stage IV (mean 70.33ng/dl). Follow up study, a study at large target population are needed to determine whether Prolactin can be a good marker for diagnostic and clinical as well as prognostic staging of breast cancer.

KI 67% in different age groups among cases of Breast Cancer, there is significant difference between the abundance of KI67 among different age groups in breast cancer patients (p =0.034). (*Kruskal Wallis test) molecular marker with luminal classification of subjects among different clinical stages of breast cancer patients there were ER+ mostly in 1A,1B (few cases in III B), PR+ mostly in 1A,1B (few cases in III B), HER-2 positive mostly in IIA, IIB, III C. In Luminal classification triple negative mostly in IIA, IIB, III C. Chi Square test

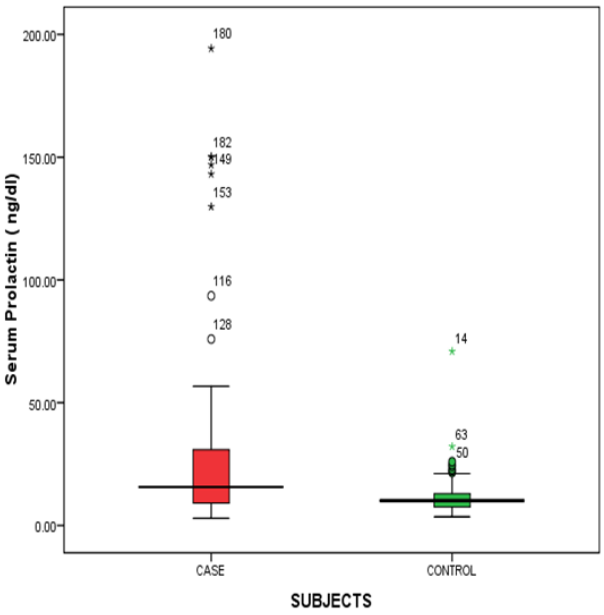


**Fig. 1:** Showing serum prolactin levels among the two groups

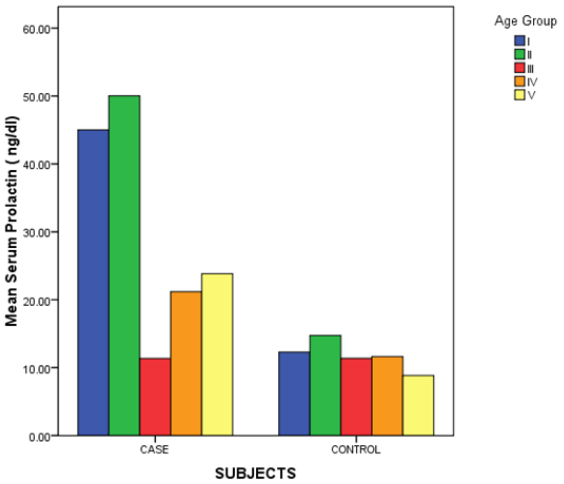


**Fig. 2:** Showing Ki 67 percentage indifferent age groups of cases of breast cancer

In TNM classification KI67% were 62.16 in T4, 45.68 in T3, in N2 65, N1 54.34, Ki 67% were higher in Trip N (55.94), Luminal B (45.02), HER-2 (41.57)There is also significant difference between the level KI 67% among different clinical stages in breast cancer patients (p =0.001)., *Kruskal Wallis test

There is significant difference between the distribution of KI67% among different prognostic stages in breast cancer

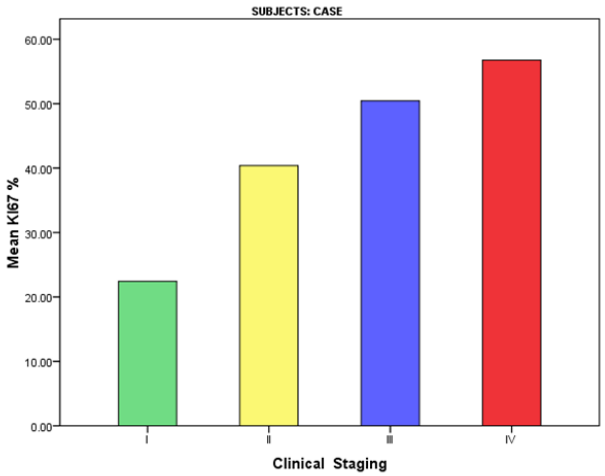


**Fig. 5:** Showing mean KI67% in different clinical stages of breast cancer

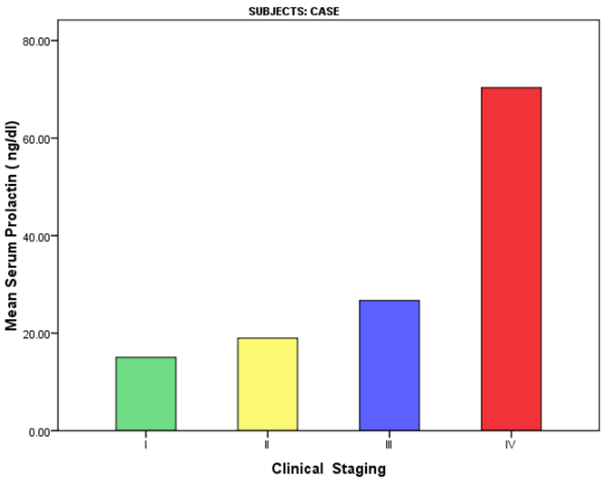


**Fig. 4:** Showing mean serum prolactin levels in different clinical stages of breast cancer

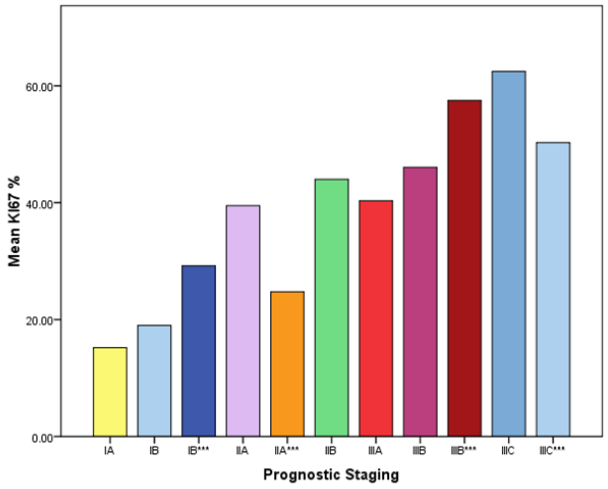


**Fig. 6:** Showing mean KI67% in different prognostic stages of breast cancer

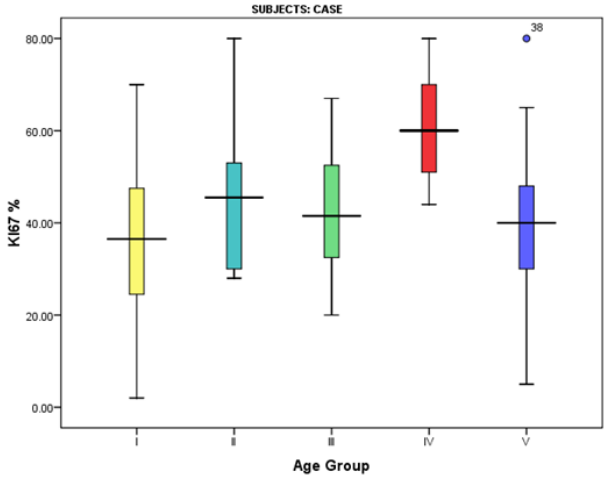


**Fig. 3:** Showing Ki 67 percentage indifferent age groups of cases of breast cancer

patients ($p < 0.05$).

The present results indicated that Ki-67% and Serum Prolactin level may be considered a valuable biomarker in breast cancer patients and be used in treatment, follow-up and Prognosis. Future work should focus on standardization of Ki-67 assessment and specification of its role in making treatment decisions.

## 5. Source of Funding

None.

## 6. Conflict of Interest

None

## References

1. Malvia S, Bagadi SA, Dubey US, Saxena S. Epidemiology of breast cancer in Indian women. *Asia Pac J Clin Oncol*. 2017;13(4):289–95.
2. Welsch CW, Nagasawa H. Prolactin and murine mammary tumorigenesis: a review. *Cancer Res*. 1977;37(4):951–63.
3. Bernstein L, Ross RK. Endogenous hormones and breast cancer risk. In: Kelsey JL, editor. Epidemiologic reviews. Baltimore: The Johns Hopkins University School of Hygiene and Public Health; 1993. p. 48–65.
4. Chuthapisith S, Permsapaya W, Warnnissorn M, Akewanlop C, Sirivatanauksorn V, Prasarttongosoth P. Breast cancer subtypes identified by the ER, PR and HER-2 status in Thai women. *Asian Pac J Cancer Prev*. 2012;13(2):459–62.
5. Clevenger CV, Furth PA, Hankinson SE, Schuler LA. The role of prolactin in mammary carcinoma. *Endocr Rev*. 2003;24(1):1–27.
6. Welsch CW, Nagasawa H. Prolactin and murine mammary tumorigenesis: a review. *Cancer Res*. 1977;37(4):951–63.

7. Fields K, Kulig E, Lloyd RV. Detection of prolactin messenger RNA in mammary and other normal and neoplastic tissues by polymerase chain reaction. *Lab Invest*. 1993;68(3):354–60.
8. Clevenger CV, Chang WP, Ngo W, Pasha TL, Montone KT, Tomaszewski JE. Expression of prolactin and prolactin receptor in human breast carcinoma. Evidence for an autocrine/paracrine loop. *Am J Pathol*. 1995;146(3):695–705.
9. Ginsburg E, Vonderhaar BK. Prolactin synthesis and secretion by human breast cancer cells. *Cancer Res*. 1995;55(12):2591–5.
10. Ingram DM, Nottage E, Roberts A. Prolactin and breast cancer risk. *Med J Aust*. 1990;153(8):469–73.
11. Sophie B, Touraine P, Goffin V. New concepts in prolactin biology. *J Endocrinol*. 2010;206(1):1–11.
12. Li L, Jiang G, Chen Q, Zheng JN. Ki67 is a promising molecular target in the diagnosis of cancer (review). *Mol Med Rep*. 2015;11(3):1566–72.
13. Li Y, Zhang X, Qiu J, Pang T, Huang L, Zeng Q. Comparisons of p53, KI67 and BRCA1 expressions in patients with different molecular subtypes of breast cancer and their relationships with pathology and prognosis. *J BUON*. 2019;24(6):2361–8.

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