

## HYPERPROLACTINEMIA IN NEWLY DIAGNOSED BREAST CANCER IN YOUNGER (UNDER 50 YEARS) WOMEN

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**ABSTRACT**

Breast cancer is a common malignancy among women. There are a number of established risk factors for breast cancer in younger population. Hyperprolactinemia is observed to be higher in breast cancer patients. However its presentation in younger (<50 years) women is not well understood. This study was conducted to describe serum prolactin level in newly diagnosed breast cancer patients presented with nipple discharge without any apparent other cause of hyperprolactinemia. The results showed high serum prolactin levels in all these patients. There was no significant correlation observed between serum prolactin and the age of the patients.

It was concluded that breast cancer patients presenting with nipple discharge show varying degree of hyperprolactinemia. It requires further studies to explore if it has a causal relationship or it is a feature of breast cancer.

**Key Words:** Breast cancer, Prolactin, Hyperprolactinemia

### INTRODUCTION.

Prolactin is an important hormone released from the pituitary gland and responsible for breast development, milk production and lactation. The hormone plays an important role in the breast development even in utero(1). On the other hand, breast cancer is the leading cancer in women and the rate is expected to rise more in future(2). Pakistan has a rising trend of breast cancer in the younger population and associated with high mortality.

The primary site of prolactin production is pituitary gland but breast tissue has also capability to produce prolactin locally. Normal/ physiological rise in prolactin is seen in pregnant women and during lactation, advancing age also showed higher prolactin levels.

Hyperprolactinemia is reported to occur more commonly in females with a reported rate of 1% of population(3). Most common cause of hyperprolactinemia is pituitary adenoma, additionally certain drugs and systemic diseases can also cause hyperprolactinemia(4). Since, breast tissue has capability of local production of prolactin, thus rise in breast cancer could be local production with normal pituitary gland. There is an evidence of rise in prolactin levels in patients taking anti-psychotic drugs, which in turn causes rise in the rate of pre-cancerous lesions(5). On the other hand there is an evidence that prolactin signaling pathway plays a role in breast cancer, thus paved a way for development of anti-prolactin anti-body(6). The prolactin receptor is reported to be over-expressed in breast cancers(7). However, prolactin pathway blockers couldn't show promising results in controlling disease progression in metastatic breast cancers. Previously reported studies

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have shown association of raised serum prolactin level with advanced and metastatic breast cancer(8).

Given the rise in breast cancer incidence in Pakistan and higher rate in younger patients it can be suspected that there are risk factors which need to be explored. From the available literature serum prolactin level in breast cancer in pre-menopausal women is least studied. Thus this study was conducted to describe range of serum prolactin in newly diagnosed breast cancer patients presenting with nipple discharge.

## **METHODS**

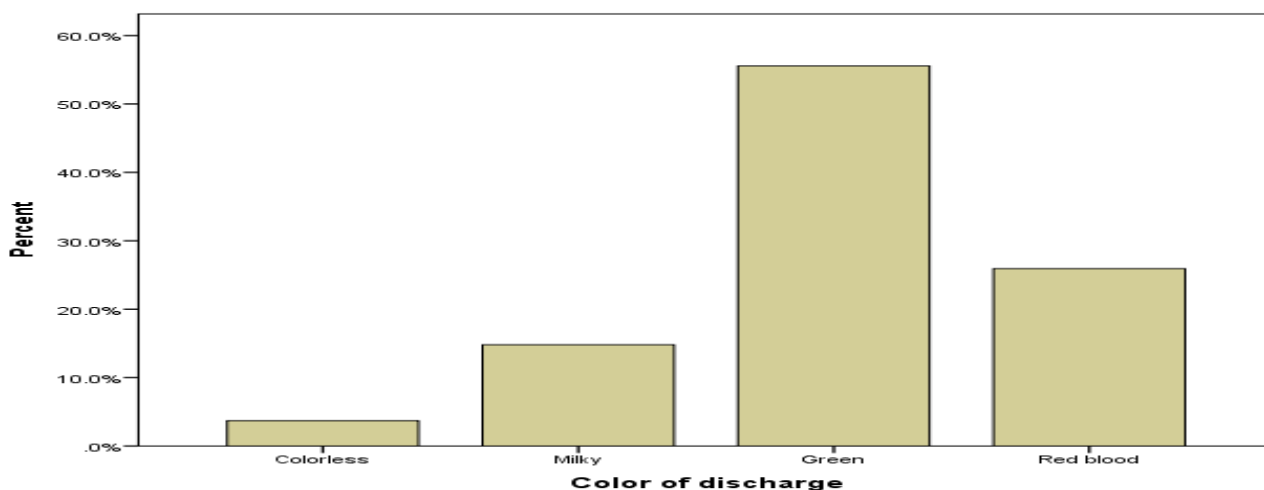
This was a descriptive cross-sectional study conducted from 20<sup>th</sup> July 2016 to 30<sup>th</sup> March 2022. During this period women under 50 years of age, diagnosed with breast cancer at the Department of Surgery, Indus Medical College, Tando Mohammad Khan, Pakistan were included. The study includes the women who presented with breast discharge with and without a clinically palpable lump in the breast. All these women had triple assessment for their discharge and serum prolactin levels were also assessed as a routine practice due to nipple discharge. These all patients were found to have a suspicious lump on ultrasound or mammogram and underwent biopsy to confirm the diagnosis of breast cancer. They all had MRI done to rule out Pituitary adenoma. Pregnant and lactating mothers were excluded. Women who were on any kind of medication were excluded. Women with pituitary adenoma on MRI were also excluded (n=3). The serum prolactin level was assessed from venous blood, within 4 hours of waking up by using Immunoassay. The reference range of the laboratory was followed and females having serum prolactin level >30 ng/ml were considered as having hyperprolactinemia. They all had normal liver function test, urea and creatinine.

Data was collected and analysed by using Statistical Package for Social Sciences version 28.0. Mean and standard deviation of the continuous variables were given. Categorical data has been presented as frequency distribution. Spearman correlation was applied to analyze association between age and serum prolactin levels.

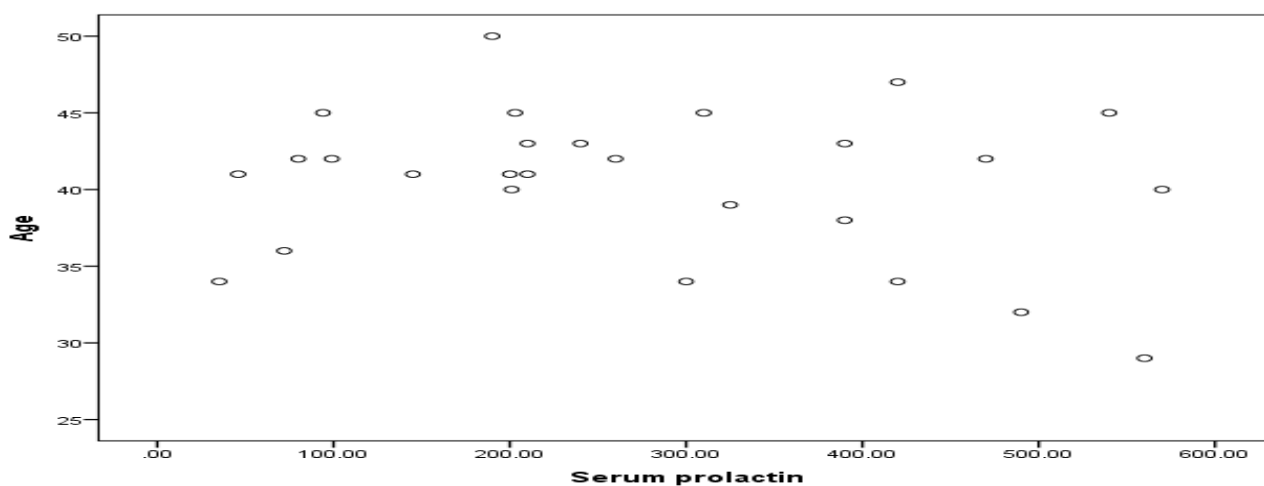
## **RESULTS**

A total of 27 women presented with nipple discharge and normal brain MRI and underwent triple assessment to have a diagnosis of breast cancer. Mean age of the patients was 40 years (range 29 to 50 years  $\pm$ SD 4.81). Five patients had a complaint of pain, 10 had discomfort and remaining (n=12) had no pain or discomfort. Great majority (n=22) had green or red blood discharge from nipple (Figure 1). Underlying breast lump was present in all patients. Nine patients did not complaint of any irregularity in their menstrual cycle and 15 patients reported delayed cycle.

Serum prolactin level was above normal reference range in all of these patients with mean levels at 276.67 (range 35.2- 570ng/ml,  $\pm$ SD 163.93) ng/ml. There was no significant association of age and serum prolactin level found (p-value=0.57) (Figure 2).



*Figure 1. Pattern of color of discharge in women having hyperprolactinemia*



*Figure 2. Scatter plot presenting correlation of age and serum prolactin levels*

## DISCUSSION

The study has shown raised serum prolactin level in women presenting with nipple discharge without having any obvious reason of hyperprolactinemia in pre-manopausal women.

This is a complex pathway to understand as the raised prolactin is a cause of breast cancer or it's a feature. Both are equally possible. As there is evidence of local production of prolactin in breast tissue thus breast cancer might start producing more prolactin which in turn causes more progression thus a vicious circle of cancer cells and prolactin starts. However there is no evidence till date to comment on this theory. Though there is evidence available suggesting association of raised serum prolactin levels in women with advanced breast cancer(8).

On the other hand when it was reported to be associated with disease progression but the drugs (i.e. Raloxifene) which controlled other hormones did not affect prolactin in pre-manopausal women(9). Similar other studies have reported that prolactin is raised but not associated with disease specific clinical outcome neither it is associated with basic prognostic factors in breast cancer i.e. Oestrogen and progesteron. These findings were interestingly reported after 10 years long term in Naples

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Adjuvant (GUN) study(10). Another study was conducted to see the predictive significance of prolactin in breast cancer and Bromocriptin was given but did not show any significant influence on disease outcome(11).

The high serum level of prolactin has been reported to be linked with resistance to chemotherapy in advanced breast cancer(12). With the same reference, it was thought that the use of a combination of chemotherapy with anti-prolactin therapy will be beneficial and improves response. But the studies have shown contradicting results. Some reported benefits of adding anti-prolactanemic therapy and others have shown no added benefit(11,13,14).

The study has a small sample size is considered as a limitation. However study from a single centre is the strength of the study.

## CONCLUSION

The study concludes that the younger women presenting with breast cancer has shown high serum prolactin level. The serum prolactin is an important novel factor can be added to breast cancer risk assessment and early detection system. Further large scale cohort studies are required to confirm these findings and established a role of serum prolactin in breast cancer.

## ETHICAL CONSIDERATION

The data was collected as part of the routine departmental data collection. Confidentiality of the patients was maintained.

## FUNDING

The study was conducted was part of routine data collection within the department, no additional funds required.

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