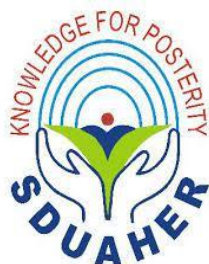


**“CORRELATION OF PROGNOSTIC FACTORS OF
CARCINOMA BREAST WITH Ki 67 PROLIFERATION ASSAY”**

By

Dr. YADAMREDDY ROHIT KUMAR



**DISSERTATION SUBMITTED TO SRI DEVARAJ URS ACADEMY OF
HIGHER EDUCATION AND RESEARCH CENTER, KOLAR, KARNATAKA**

In partial fulfillment of the requirements for the degree of

**MASTER OF SURGERY
IN
GENERAL SURGERY**

**Under the Guidance of
Dr. P.N SREERAMULU
PROFESSOR**



**DEPARTMENT OF GENERAL SURGERY,
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ACKNOWLEDGEMENT

I am highly indebted to my guide **Dr. P.N SREERAMULU, Professor, Dept. of General Surgery**, Sri Devaraj Urs Medical College, Tamaka, Kolar, and my co-guides **DR.HEMALATHA.A, Professor, Dept. Of Pathology** and **Dr. MANJUNATH.G.N, Associate professor, Dept. of Radiotherapy** who guided me in carrying out my thesis work with their thought-provoking ideas and constant encouragement.

It gives me immense pleasure to express my gratitude and sincere thanks to **Dr. K. KRISHNA PRASAD , Professor and H.O.D., Department of General Surgery**, Sri Devaraj Urs Medical College, Tamaka, Kolar, who gave constant support by encouraging in moulding this work.

I would also like to acknowledge **Dr. SRINIVASAN D, Dr. MOHAN KUMAR K, Dr. PRAKASH DAVE, Dr. SHASHIREKHA C.A**, Department of General Surgery, Sri Devaraj Urs Medical College, Tamaka, Kolar, who gave me moral support and guidance by correcting me at every step.

I am much indebted and sincerely thankful to my parents Mr. Siva Sankar Rao & Mrs. Bharathi and my brother Mr. Rakesh for their unconditional love and constant support in all my endeavors.

I express my sincere thanks to **DR. RAADHIKA RAJA** for helping me all through my post graduation and for the support and encouragement.

I express my sincere thanks to **DR. DEEPTHI** for moral support and encouragement.

I express my sincere thanks to all my assistant professors and lecturers, of Department of General Surgery, Sri Devaraj Urs Medical College, Tamaka, Kolar, for their support and encouragement.

I am also thankful to my colleagues, seniors, juniors, nursing staff and operation theatre staff of Sri Devaraj Urs Medical College, Tamaka, Kolar for their support during this work.

My sincere thanks to the faculty and staff of Department of Pathology of Sri Devaraj Urs Medical College, Tamaka, Kolar for their support during the study.

My heartfelt gratitude to all my patients who submitted themselves most gracefully and wholeheartedly to participate in this study.

Last, but not the least, I would like to express my gratitude to the **Almighty** for all his blessings.

Signature of the candidate

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ABSTRACT

Background: Prognostic factors are important for the diagnosis of breast cancer as it helps in identification of high risk patients. The objective of the study is to assess the proliferation index, Ki-67 and correlate it with other markers.

Methods: This study is conducted at Department of General Surgery, R.L. Jalappa Hospital, Kolar on a cohort of patients admitted with biopsy-proven diagnosis of carcinoma of breast from the period of Dec 2019 to June 2021. All the patients meeting the inclusion and exclusion criteria are recruited sequentially by convenient sampling until the sample size is attained, with the agreement of the institutional ethics committee.

Results: A total of 98 patients with a mean age of 53.61 ± 12.48 years were studied in the final analysis. The mean duration of lump was 4.62 ± 2.18 months and only 6.12% had the complaint of pain. Majority of them had stage IIIB carcinoma at 43.88%, followed by stage IIA at 27.55%, 15.31% stage IIB, 13.27% stage IIIA. At cut off 20, 69(70.40%) had ki67 proliferation index ≥ 20 and 29(29.59%) had < 20 . Correlation of Ki-67 Index with expression of estrogen receptor status had a p value of 0.019 and with progesterone receptor status, p 0.003 which was significant.

Conclusions: In the age group of 31 to 60 years, majority of them had ≥ 20 Ki-67 but age showed no significant association with Ki-67. Duration of lump, menstrual history, physical characteristics of the effected breast, physical characteristics of the lump, size of the lump, stage and lymph node status had no significant association with the Ki-67 expression. While the estrogen receptor expression had significant association with Ki-67 with p value 0.019, the expression of progesterone receptor showed a significant correlation with Ki-67 with p 0.003.

Based on Chi square test, our study demonstrated a significant association between expression of estrogen and progesterone receptor and Ki-67.

Keywords: Ki-67, Breast carcinoma, Cell proliferation, Immunohistochemistry, Hormone receptor status

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ABBREVIATIONS

Glossary	Abbreviations
FNAC	Fine Needle Aspiration Cytology
IHC	Immunohistochemistry
ASCO	American Society Of Clinical Oncology
ER	Estrogen Receptor
PR	Progesterone Receptor
LMIC	Low Middle Income Countries
HIC	High Income Countries
BC	Breast Cancer
MRI	Magnetic Resonance Imaging
PET	Positron Emission Tomography
SPECT	Single-Photon Emission Computed Tomography
CT	Computed Tomography
EGTM	European Group On Tumor Markers
DCIS	Ductal Carcinoma In Situ
NACT	Neoadjuvant Chemotherapy
HER 2 Neu	Human Epidermal Growth Factor Receptor 2
IMPACT	Immediate Preoperative Anastrozole, Tamoxifen, Or Combination With Tamoxifen
POETIC	Perioperative Endocrine Therapy For Individualizing Care
IUCC	International Union Cancer Committee
DALY	Disability-Adjusted Life Years

INTRODUCTION



INTRODUCTION:

The most frequent form of cancer in women is cancer of the breast and is responsible for most of the deaths.¹ It is a multifactorial ailment and several factors contribute to its incidence. Breast cancer is prevalent across the world but its frequency, death rate, and survival rates differ noticeably among various parts of the world. This can be attributed to the type of population, genetic factors and location.² Variations in risk factors have led to an upsurge in the frequency of carcinoma breast, which is growing every day. Even though screening people can decrease the burden of breast cancer, over - diagnosis, side effects and expensive costs are the drawbacks of this method. Classification of women depending on the susceptibility of risk factors predisposing them to breast cancer can be effective in improving risk-free methods and designing targeted programs for screening of breast cancer.³

According to the World Health Organization (WHO) the prevalence of BC in women, globally is 2.3 million in 2020 and mortality was found in 6,85,000. The death rate in breast cancer is mainly due to extensive metastasis. From the last 5-year data up to 2020, there has been nearly 7.8 Mn w newly diagnosed cases of BC. Therefore, making BC as the most dominant cancer globally. Breast cancer can occur at any age post puberty however, the incidence is greater at older age.⁴

Breast cancer represents numerous entities ranging from carcinoma-insitu to metastatic carcinoma. Breast cancer is often diagnosed through clinical evaluation and special investigations such as fine needle aspiration (FNAC) or core needle biopsy and mammography.⁵ Nevertheless, histopathology is the gold standard investigation for breast cancer. Further, the immunohistochemical (IHC) markers help in classifying the type of pathology and directs therapeutic indications.⁶

Prognostic variables are critical in the evaluation of BC as it helps in the identification of high-risk patients.⁷ The currently used traditional prognostic factors are successful in identifying approximately 30% of the BC patients.

Hence, there is an utmost need for new prognostic markers.⁸ Because radiotherapy and various medical hormonal manipulations might cause adverse effects, risk-based refined procedures are necessary to minimise these unwanted effects. Over the last few years, certain additional prognostic factors have been identified.⁹ However, clinical confirmation is still required for majority of them.¹⁰ Tumor markers have received a lot of attention in the search for potential breast cancer prognostic indicators. Invasive breast cancers clinical behavior is heavily influenced by cell proliferation. Cellular Proliferation is associated with a negative prognosis. As actively proliferating cells can be identified by Ki 67 labelling, it is more sensitive than other techniques. As obtaining a consistent mitotic index requires particular training in counting with the fraction assessed method, mitotic count and Ki 67 proliferation index are regarded as practicable approaches.^{11,12} Ki 67 index has lately sparked renewed interest as a possible marker for predicting chemotherapy response.¹³ Ki 67 immuno-staining is more convenient for determining the proliferation index when compared to other markers. Ki 67 immunostaining is a simple and economical technique that is utilized in practically all pathology laboratories. It just takes a little tissue sample, which can be obtained by fine-needle aspirations. In most studies, high Ki 67 levels are linked to a favourable prognosis.^{14,15}

NEED OF THE STUDY

Biomarkers currently play an indispensable role in the treatment of patients with breast cancer, especially in deciding the type of systemic therapy to be administered. In 2005, the European Group on Tumor Markers (EGTM) published guidelines on the use of biomarkers in BC.¹⁶ However, since then, a number of important new developments have been reported, especially with tissue-based biomarkers. These include the use of multiparameter signatures for predicting patient outcome and the use of HER2 for the upfront identification of likely response to several different forms of anti-HER2 therapy. In addition, new recommendations have been published for performing a number of breast cancer biomarker assays such as oestrogen receptors (ER), progesterone receptors (PR) and HER2.¹⁷

The presence of hormone receptors and Her2neu has a predictive and prognostic impact on the treatment of BC. As a result, according to “American Society of Clinical Oncology” (ASCO) guidelines, completing oestrogen receptor (ER), progesterone receptor (PR), and her2neu biomarker testing has become standard of care in breast cancer management.¹⁸ Proliferation markers that are high in any malignancy imply a poor prognosis. The performance and interpretation of proliferative index markers such as thymidine labelling index, S-phase fraction assessed by flow cytometry, and immunohistochemistry have been the subject of considerable dispute in recent years (IHC). Overall, IHC-determined proliferative index correlates well with flow cytometry-measured S phase fraction.¹⁹ Although there is a debate on the best cutoff value for deciding on treatment, multiple studies have revealed that a high ki67 index is linked to a higher likelihood of relapse and a worse prognosis for BC survivors.²⁰ Although it is widely understood that cancer management is based on a loco-regional profile, and therapeutic guidelines should be developed accordingly, there is no large-scale cancer registry in this region. Furthermore, the proliferative activity of

cancer cells may influence the response to chemotherapy, so ki67 could be a valuable marker in customising treatment regimens.²¹ Hence this study is aimed at assessing the proliferation Index, Ki-67, in women with carcinoma of the breast.

AIMS & OBJECTIVES



AIMS AND OBJECTIVES:

1. To asses all the prognostic factors of carcinoma breast.
2. To assess the proliferation index (ki67) of each of the patient with carcinoma breast
3. To compare the prognostic factors with the ki67

REVIEW OF LITERATURE



REVIEW OF LITERATURE:

1. BREAST CARCINOMA - DEFINITION

BC is a disease in which cells replicate uncontrolled. There are different types of BC. The type of BC depends on which cell undergoes malignant change. Breast is made up of 3 main components: ducts, lobules and fibrofatty connective tissue. The lobules are the milk producing glands. The ducts carry milk to the nipple. The fibrofatty connective tissue forms parenchyma. Most breast cancers arise from the ducts or lobules and can spread outside the breast through blood vessels and lymph vessels.

2. ANATOMY OF BREAST

Milk secreting glands for nourishing offspring are present only in mammals and are a defining feature of the class Mammalia. In humans, mammary glands are present in both females and males, but typically are functional only in the postpartum female. In rare circumstances, men have been reported to lactate. In humans, the breasts are rounded eminences that contain the mammary glands as well as an abundance of adipose tissue (the main determinant of size) and dense connective tissue. The glands are located in the subcutaneous layer of the anterior and a portion of the lateral thoracic wall. Each breast contains 15–20 lobes that each consist of many lobules. At the apex of the breast is a pigmented area, the areola; surrounding a central elevation, the nipple. The course of the nerves and vessels to the nipple runs along a suspensory apparatus consisting of a horizontal fibrous septum that originates from pectoral fascia overlying the 5th rib, and 2 vertical septae, one along the sternum and the other at the lateral border of the pectoralis minor muscle.

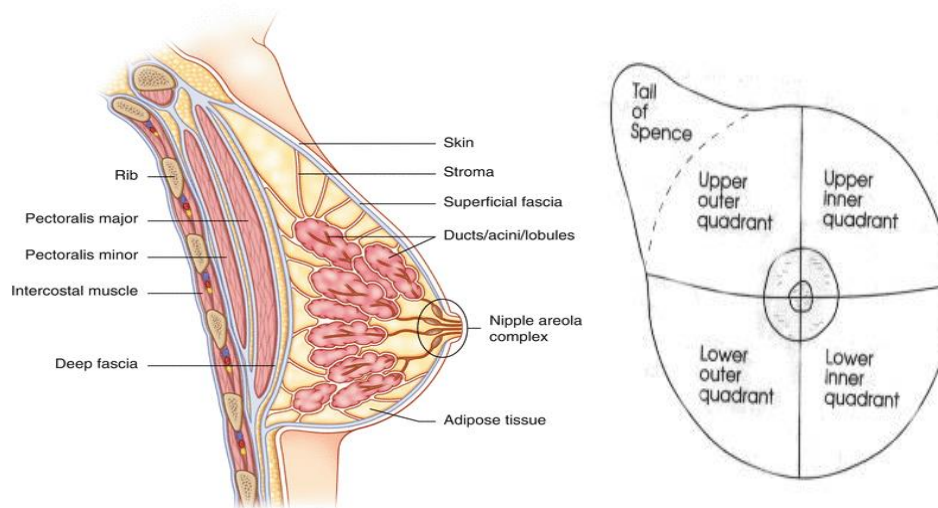


Figure 1: Sagittal Section Through Lactating Breast.

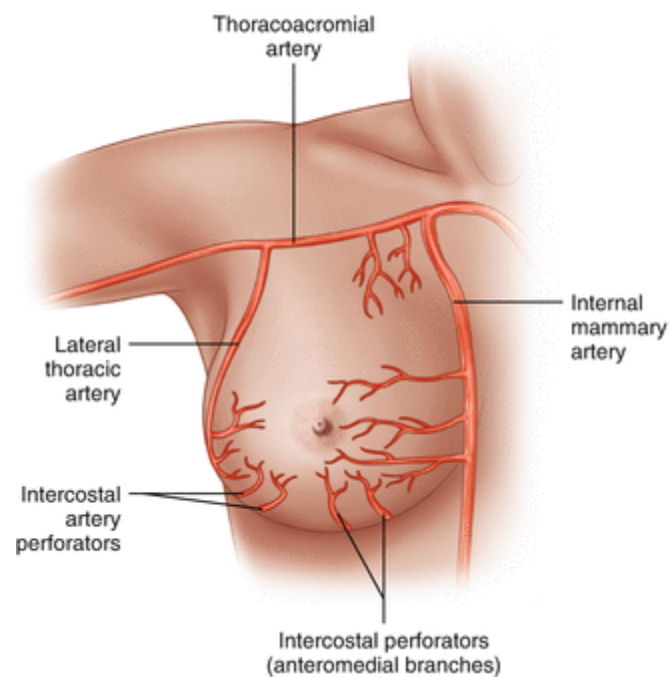


Figure 2: Vascular supply of the breast

Vascular Supply Of The Breast:

Arterial blood is supplied by branches of the axillary artery (lateral thoracic and pectoral branch of the thoracoacromial trunk). Additional blood supply is from medial mammary branches of the internal thoracic (internal mammary) artery and from lateral branches of the posterior intercostal arteries. Venous drainage is via veins that parallel the arteries with the addition of a superficial plexus.

Nerve Supply:

Innervation of the breast is derived from anterior and lateral cutaneous branches of 4th- 6th intercostal nerves, with the 4th branch nerve being the primary supply to the nipple. The lateral and anterior cutaneous branches of the second, third and 6th intercostal nerves, as the supraclavicular nerves (from C3 and C4), can also contribute to breast innervation. Most of the cutaneous nerves extend into a plexus deep up to the areola.

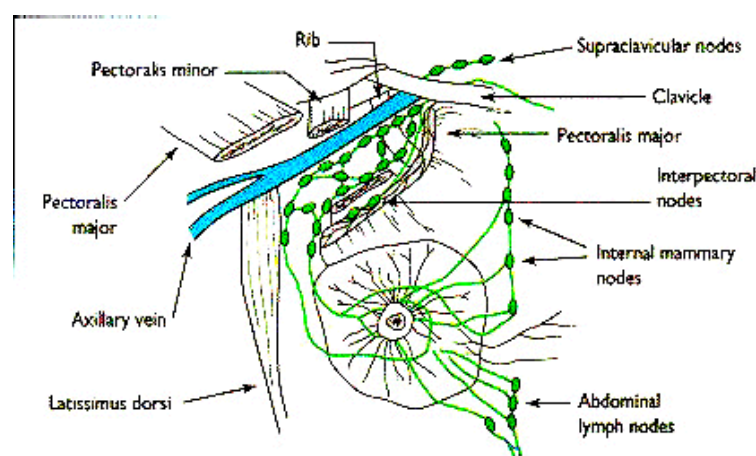


Figure 3: Lymphatic Drainage of The Breast.

Lymphatic Drainage Of The Breast-

Most drainage is into the axillary nodes indicated as level I, level II and level III based on their relationship to the pectoralis minor muscle. Level I nodes are lateral to the muscle, level

II are behind it and level III are medial to it. Also, note the internal mammary nodes located just lateral to the edge of the sternum and deep to the thoracic wall musculature.

Histology Of Breast :

The breast is a modified sweat gland consisting of 15-25 secretory lobes. These lobes are compound tubular acinar structures. These acini drain into ducts, that are lined by cuboidal epithelium surrounded by myoepithelial cells. These ducts are surrounded by smooth muscle in the region of the nipple, contraction of which makes the nipple become erect.²⁴

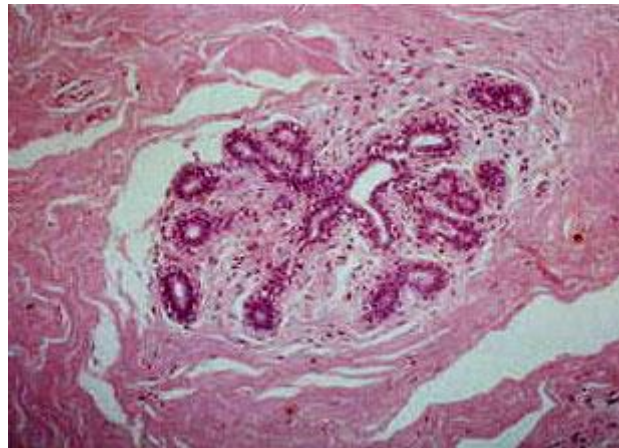


Figure 4: Histopathological Image Of The Secretory Lobe Breast Tissue At Low Power.

3. EPIDEMIOLOGY

A. Global Burden Of Breast Cancer

According to the Global Burden of Disease Cancer Collaboration²⁵, BC incidence has increased with variability in the burden of disease across countries of different income order. In low-income nations, around 69% of total DALY were lost due to breast cancer.²⁶ Even though the total incidence rate of BC is lower in LMIC compared to HICs, there is a spike in the incidence rate in the LMICs. The mortality rates of breast cancer since 1990 in few HICs have shown to be decreasing, but in other HICs and LMICs have been witnessing increasing

mortality rates. For instance, even though the HIC such as the USA had shown a sturdy decline in age-standardized breast cancer mortality rates between 1990 and 2013 (22.3 per 100,000 in 1990 to 13.4 per 100,000 in 2013), Japan being the HIC in the same years has witnessed an increase mortality rate from 6.3 per 100,000 to 9.1.²⁷ The reasons for such spike in the burden and mortality are due to obnoxious habits unhealthy lifestyle and sedentary life.

However, other factors for increasing numbers even in HICs and LMIs include universal unacceptance of initiating screening programmes or cancer prevention strategies. For instance, controversies about the age of start and the frequency of mammography screening thrive and have led to varied country-specific screening policies, even among HIC countries. The economic cost of mammography has been in question due to the expenditure required to sustain one to two-year screening programs are greater than its profits of screening in a few HICs. However, in LMICS due to restricted resources, imposing population-based mammographic screening program as recommended by WHO necessitates added infrastructure.²⁸

In addition to disparities in secondary prevention ingenuities worldwide, tertiary prevention in the form of chemotherapy and radiation therapy can be effective, but then the accessibility and uptake may be limited in LMICs and low-economic settings.²⁹

B. Indian Burden Of Breast Cancer

According to “Globocan 2012”, India, along with the USA and China collectively accounts for almost one third of the global breast cancer burden. India is facing challenging situation due to 11.54% increases in incidence and 13.82% increase in mortality due to breast cancer

during 2008–2012.³⁹ The main reasons for this observed hike in mortality is due to lack of inadequate breast cancer screening, diagnosis of disease at advanced stage and unavailability of appropriate medical facilities. Breast cancer attains top rank even in individual registries (Mumbai, Bangalore, Chennai, New Delhi and Dibrugarh) in females during the period of 2012–2014. The relative proportion of BC in different registries varied from 30.7% in Chennai to 19% in Dibrugarh. A total district wise minimum age-adjusted incidence rate per 100 000 for India. AAR more than 20 per 100 000 has been noted for districts Chandigarh (39.5), Panchkula (34.6), Aizwal (36.2) and Goa (36.8).³² Mortality/incidence ratio (MIR) is another novel measure to evaluate cancer mortality in relation to incidence.

According to a survey conducted by the "Indian Council of Medical Research" (ICMR) in metropolitan cities from 1982 to 2005, the incidence of BC nearly doubled.³³ Breast cancer occurs at a younger premenopausal age in Indian women than in western women, implying that breast cancer occurs at a younger premenopausal age in India. Young people's cancers are more aggressive. The APC ranged from 0.53 percent to 2.64 percent in the oldest age group, which included individuals over 64 years old.³⁴ According to studies, the disease peaks in Indian women between the ages of 40 and 50.³⁵ Many of these malignancies are HER2 positive but ER/PR negative, or HER2/ER/PR negative, and have a terrible prognosis. Except in the north eastern registries, where the peak is seen in even 10-year younger age groups, trends for 5-year age distribution among different registries showed a peak relative proportion between 45 and 49 years.³⁶ Most of the patients diagnosed in India are locally progressed or metastatic when diagnosed first.

4. ETIOPATHOGENESIS OF BREAST CANCER

A. Etiology And Risk Factors Of Breast Cancer

Geography: Breast cancer is estimated to affect 1Mn people every year worldwide, with more than half of these occurring in Western world: 200,000 cases in USA and 320,000 cases in Europe. In addition, it was responsible for 3-5 percent of deaths in the Western world, 1-3 percent in poorer countries, and is thought to be uncommon in Japan. However, Dumitrescu and Cotarla recently reported a death rate of 2.3 percent per year in the United States, citing improved screening techniques as well as new and better treatment options as reasons for the drop.

Age: Breast cancer is exceedingly uncommon before the age of 20 years, but the incidence rises with age, and by the age of 90 years, one-fifth of women had been diagnosed. It's also thought that the age at which a woman reaches menarche and the age at which she reaches menopause play a role in the length of time she is exposed to the carcinogenic effects of gonadal (sex) hormones.

Gender: Males account for less than 1% of BC . The differences are assumed to be hormonal because even male BC has been shown to express oestrogen, progesterone, and androgen receptors (ARs), and men with Klinefelter's syndrome have higher risk of breast cancer.

Genetic factors: In comparison to the general population, women with positive family history of BC are more likely to develop the disease. Only around 5% of breast tumours are linked to a specific mutation, according to Russell et al.³⁸ In addition, a meta-analysis of 52 different epidemiological studies found that 13% of women with BC had one or more

relatives who are affected, and 12% of patients have one or more relatives who are affected. According to the findings, women who have one or more first-degree relatives with BC are more predisposed than those who do not.³⁷

Diet and alcohol: These are thought to play a role in the aetiology of breast cancer, and there is a link between diets low in phyto-oestrogens and high intake of alcohol. The risk increases progressively in a dose-dependent manner to an alcohol intake of 60 g (2-5 drinks) per day, depending on the strength of the drink and for every 10 g increment (approximately 0.75-1 L drink) in daily alcohol consumption, the risk increases with 9%.

Lifestyle and physical activity: Exercise, like food, can affect hormone levels in the blood, which can influence the development of breast cancer. These two factors influence body weight independently or in combination, and obesity raises the risk of BC in postmenopausal women.

Hormonal factors: Infertile women and mothers who do not breastfeed their children are more likely to get breast cancer. Early full-term pregnancy, especially when combined with late menarche and early menopause (both of which reduce a woman's oestrogen exposure), has been demonstrated to be protective. This is because oestrogen levels are lower during pregnancy and in women who have had a lot of children.

Exogenous factors: Long-term HRT, according to a major meta-analysis, is responsible with a cumulative excess of breast tumours in women between the ages of 50 and 70. HRT is also linked to an elevated risk of BC (with a relative risk of 1.21-1.40), particularly among women who have been using oestrogen + progestin for 5 years or more.

Mammographic density: It is seen that women with >75% increased breast density on mammography have up to a 5-fold increased risk over those with <5% increased breast density.³⁷

B. Pathogenesis Of Breast Cancer:

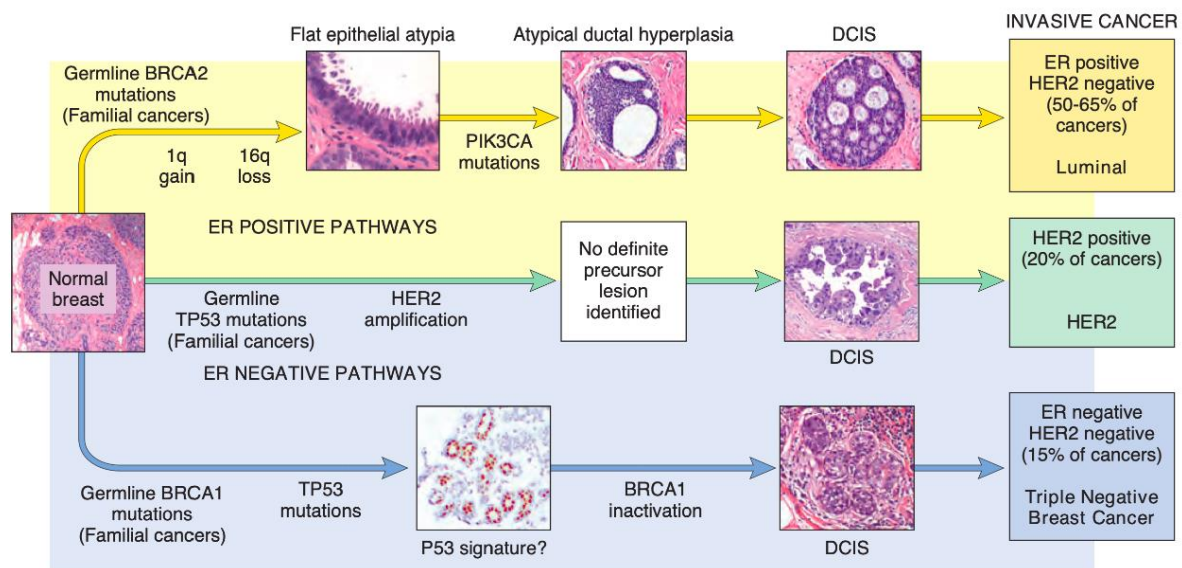


Figure 5 : Major pathways of breast cancer development.

Three main pathways have been identified. The most common pathway (*yellow arrow*) leads to luminal (ER-positive) carcinomas. Recognizable non-obligate precursor lesions include flat epithelial atypia and atypical hyperplasia. A less common pathway (*blue arrow*) leads to triple-negative breast cancer (ER-negative/HER2-negative). A possible precursor lesion consisting of morphologically normal cells that overexpress p53 has been identified (analogous to the “p53 signature lesions” for ovarian carcinoma). The third pathway (*green arrow*) consists of HER2-positive cancers. Amplification of HER2 can occur in either ER-positive or ER-negative lesions.²²

5. CLASSIFICATION OF BREAST CARCINOMAS

Table 1: Histopathological WHO classification of breast tumour 2020.

<ul style="list-style-type: none"> • Epithelial tumors
<ul style="list-style-type: none"> • Benign epithelial proliferation and precursors <ul style="list-style-type: none"> ○ Usual ductal hyperplasia ○ Columnar cell lesions including flat epithelial atypia ○ Atypical ductal hyperplasia
<ul style="list-style-type: none"> • Adenosis and benign sclerosing lesions <ul style="list-style-type: none"> ○ Sclerosing adenosis ○ Apocrine adenoma ○ Micro glandular adenosis ○ Radial scar / complex sclerosing lesion
<ul style="list-style-type: none"> • Adenomas <ul style="list-style-type: none"> ○ Tubular adenoma NOS ○ Lactating adenoma ○ Duct adenoma NOS
<ul style="list-style-type: none"> • Epithelial - myoepithelial tumors <ul style="list-style-type: none"> ○ Pleomorphic adenoma ○ Adenomyoepithelioma NOS ○ Adenomyoepithelioma with carcinoma ○ Epithelial-myoepithelial carcinoma
<ul style="list-style-type: none"> • Papillary neoplasms <ul style="list-style-type: none"> ○ Intraductal papilloma, ○ Ductal carcinoma in situ, papillary, ○ Encapsulated papillary carcinoma ○ Encapsulated papillary carcinoma with invasion ○ Solid papillary carcinoma in situ ○ Solid papillary carcinoma with invasion ○ Intraductal papillary adenocarcinoma with invasion
<ul style="list-style-type: none"> • Non-invasive lobular neoplasia <ul style="list-style-type: none"> ○ Atypical lobular hyperplasia ○ Lobular carcinoma in situ NOS, 8520/2 ○ Classic lobular carcinoma in situ ○ Florid lobular carcinoma in situ ○ Lobular carcinoma in situ, pleomorphic
<ul style="list-style-type: none"> • Ductal carcinoma in situ (DCIS) <ul style="list-style-type: none"> ○ Intraductal carcinoma, non -infiltrating, NOS ○ DCIS of low nuclear grade ○ DCIS of intermediate nuclear grade ○ DCIS of high nuclear grade
<ul style="list-style-type: none"> • Invasive breast carcinoma <ul style="list-style-type: none"> ○ Infiltrating duct carcinoma (NOS), ○ Oncocytic carcinoma, ○ Lipid rich carcinoma, ○ Glycogen rich carcinoma, ○ Sebaceous carcinoma,

<ul style="list-style-type: none"> ○ Lobular carcinoma NOS, ○ Tubular carcinoma, ○ Cribriform carcinoma NOS, ○ Mucinous adenocarcinoma, ○ Mucinous cystadenocarcinoma NOS, ○ Invasive micropapillary carcinoma of the breast, ○ Metaplastic carcinoma NOS
<ul style="list-style-type: none"> ● Rare and salivary gland type tumors <ul style="list-style-type: none"> ○ Secretory carcinoma ○ Acinar cell carcinoma ○ Mucoepidermoid carcinoma ○ Polymorphous adenocarcinoma, ○ Adenoid cystic carcinoma, ○ Classic adenoid cystic carcinoma ○ Solid basaloid adenoid cystic carcinoma ○ Adenoid cystic carcinoma with high-grade transformation ○ Tall cell carcinoma with reversed polarity
<ul style="list-style-type: none"> ● Neuroendocrine neoplasms <ul style="list-style-type: none"> ○ Neuroendocrine tumor, NOS, ○ Neuroendocrine tumor, grade 1, ○ Neuroendocrine tumor, grade 2, ○ Neuroendocrine carcinoma NOS, ○ Neuroendocrine carcinoma, small cell, ○ Neuroendocrine carcinoma, large cell,

TNM staging:

Five decades ago, Pierre Denoix, from the institute Gustav – Roussy, France, devised the TNM staging system, and its application to breast cancer was published 24 years later in 1968. At the introduction of this system, the International Union Cancer Committee (IUCC) defined the aims of cancer staging as:

- i. To provide some indication of prognosis.
- ii. To aid the clinician in planning cancer treatment.
- iii. To assist in evaluating the results of treatment.
- iv. To facilitate the exchange of information between treatment and centres.
- v. To contribute to the continuing investigation of human malignancies.

Breast cancer is staged based on:

- The size of the breast tumour (T)
- Whether cancer has spread to lymph nodes (N)
- Whether cancer has metastasized (M)

Table 2: TNM staging system.

Tumour size (T)	
TX	Primary tumour cannot be assessed
T0	There is no primary tumour
Tis (DCIS)	Ductal carcinoma in situ
Tis (Paget)	Paget disease not linked to invasive cancer or DCIS.
T1	Tumour size ≤ 20 mm
T1mi	Tumour size ≤ 1 mm
T1a	Tumour size > 1 mm but ≤ 5 mm
T1b	Tumour size > 5 mm but ≤ 10 mm
T1c	Tumour size > 10 mm but ≤ 20 mm
T2	Tumour size > 20 mm but ≤ 50 mm
T3	Tumour size > 50 mm
T4	Tumor that has spread to the chest wall and/or the skin, causing macroscopic alterations
T4a	Tumor with invasion of the chest wall
T4b	Tumor having macroscopic skin alterations, such as ulceration, satellite skin nodules, and edoema
T4c	Tumor that meets both T4a and T4b criteria
T4d	Inflammatory carcinoma
pN Category	pN Criteria
– pNX:	The lymph nodes in the region cannot be examined (e.g., not removed for pathological study or previously removed)
pN0	There was no evidence of regional lymph node metastases or ITCs alone [#]
pN0 (i+):	In regional lymph nodes, only ITCs (malignant cell clusters no larger than 0.2 mm) were seen

pN0 (mol+):	Positive molecular findings by reverse transcriptase-polymerase chain reaction (RT-PCR); no ITCs detected
pN1mi:	Micro metastases (approximately 200 cells, larger than 0.2 mm, but none larger than 2.0 mm)
pN1a: ##	At least one metastasis greater than 2.0 mm in with metastases in 1 to 3 axillary lymph nodes
pN1b:	Metastases in ipsilateral internal mammary sentinel nodes, excluding ITCs
pN1c:	pN1a and pN1b combined
pN2a:	4–9 axillary lymph nodes metastatic (at least 1 tumour deposit greater than 2.0 mm)##
pN2b:	With pathologically negative axillary nodes, metastases in clinically identified in internal mammary lymph nodes with or without microscopic confirmation.
pN3a:	Metastases to ten or more axillary lymph nodes (at least one tumour deposit greater than 2.0 mm) or infraclavicular (Level III axillary lymph) nodes ##
pN3b:	pN1a or pN2a in the presence of cN2b (positive internal mammary nodes by imaging); or pN2a in the presence of pN1b
pN3c:	Metastases in the lymph nodes of the ipsilateral supraclavicular artery
M Category	M Criteria
M0	No clinical or radiographic evidence of distant metastases
pM1	Any histologically proven metastases in distant organs or if in non-regional nodes, metastases greater than 0.2mm

Table 3: Modified AJCC Staging Of Breast Carcinoma.

Stage 0	Tis	N0	M0
1A	T1	N0	M0
IB	T0	N1mi	M0
	T1	N1mi	M0
IIA	T0	N1	M0
	T1	N1	M0
	T2	N0	M0
IIB	T2	N1	M0
	T3	N0	M0
IIIA	T0	N2	M0
	T1	N2	M0
	T2	N2	M0
	T3	N1	M0
	T3	N2	M0
IIIB	T4	N0	M0
	T4	N1	M0
	T4	N2	M0
IIIC	Any T	N3	M0
IV	Any T	Any N	M1

6. CLINICAL FEATURES:

Predominant symptoms and signs of carcinoma of breast cancer are nipple discharge, “lumpiness,” or a palpable mass and inflammatory changes. However, few symptoms are so severe as to require treatment, and the key reason for investigating their cause is to assess the possibility of malignancy. Most symptomatic breast lesions (>90%) are benign. Of females with cancer, about 45% have symptoms, however the remainder comes to attention through screening tests.²²

- Palpable masses can arise from the proliferation of stromal cells or epithelial cells and are generally detected when they are 2 to 3 cm in size. Most (~95%) are benign; these tend to be round to oval and to have circumscribed borders. In contrast, malignant tumors usually invade across tissue planes and have irregular borders.

-
- “Lumpiness or diffuse nodularity” throughout the breast is usually a result of normal glandular tissue. When pronounced, imaging studies may help to determine whether a discrete mass is present.
 - Nipple discharge - Discharges that are spontaneous, unilateral and bloody are of greatest concern for malignancy.
 - Inflammation - An important mimic of inflammation is “inflammatory” breast carcinoma.

7. DIAGNOSTIC MODALITIES OF BREAST CARCINOMA

A) Imaging Techniques:

Various imaging techniques such as mammography, magnetic resonance imaging (MRI), positron emission tomography (PET), Computed tomography (CT), and single-photon emission computed tomography (SPECT) could be used in identifying and monitoring patients with BC in various stages.⁴²

Mammography:

A mammogram is an X-ray picture of the breast. Digital mammography (DM) has replaced conventional (film screen) mammography in some breast screening services. Potential advantages of DM include the use of computer-aided detection, algorithm-based computer programs that alert the radiologist to possible abnormalities on the mammogram and allowing centralized film reading. Moreover, false-positive calls lead to additional imaging or histopathological assessment, mainly percutaneous breast biopsy.⁴³

B) Cyto-Histopathology:

Fine-needle aspiration cytology (FNAC) and core needle biopsy (CNB) are used in the diagnosis of BC.⁴³ FNAC is least invasive, easy to perform, and quick smears can be used to assess the adequacy of the tissue sample. CNB removes a core of tissue that can be analyzed for malignant cells.⁴⁴ Core biopsy specimen can be subjected to IHC analysis and ki67 immunostaining. Breast biopsy is the definitive diagnostic modality for BC

IHC: IHC uses antibodies to detect protein expression. Antibodies complementary to the antigen of interest are labelled with a marker (either visible by light microscopy or fluorescence), allowing detection of the antibodies bound to regions of protein expression in a tissue sample. Diagnostic IHC is widely used, for example, to detect tissue markers associated with specific cancer. The most common immunohistochemical breast carcinoma prognostic and therapeutic markers used include ER, HER2, Ki-67, PR, and p53. In addition markers of angiogenesis and apoptosis are used.⁴⁶

8. DIFFERENT TREATMENT MODALITIES:

The main types of treatment for breast cancer are surgery, radiation therapy (RT), chemotherapy (CT), endocrine (hormone) therapy (ET), and targeted therapy. Breast conservation surgery is the trending approach in the treatment of localized breast cancer. The surgery is preceded by neoadjuvant therapy to shrink tumour bulk. Surgery is usually followed by neoadjuvant therapy to ensure full recovery and minimize the risk of metastases.

Neoadjuvant Therapy:

Neoadjuvant therapy is the pre-operative treatment of tumors with radiotherapy, chemotherapy and endocrine therapy. The aim of NACT was to down stage the tumors and permitting breast-conserving surgery instead of mastectomy.⁴⁷

Indication:

- Tumor size small to improve the overall prognosis of patients.
- To facilitate complete surgical resection, especially when breast cancer presents in a large, bulky fashion.
- Breast tumors close to or involving the axilla can be particularly challenging if they are large and abutting critical neurovascular structures such as the thoracodorsal vessels and nerve.

The advantages of neoadjuvant therapy include:

- Aids in response prediction.
- Offers quick assessment of the drug development and endorsement in breast cancer by monitoring advantage from the intercession at initial stages of the disease.
- Down stages the tumor and helps in preserving breast during surgery instead of mastectomy.⁴⁷

Neoadjuvant chemotherapy and endocrine therapy are widely used and studied in breast cancer.⁴⁷ The neoadjuvant chemotherapy is been effective in breast cancer since the 1970s.

The insight of presurgical chemotherapy was familiar beforehand 50 years ago in the conduct of subjects with unfeasible breast cancer, locally progressive.⁴⁸ Later, in a few decades, the role of this chemotherapy changed to neoadjuvant chemotherapy (NACT) which is now considered as the principle treatment before surgery. Neoadjuvant therapy was defined as "the optimal treatment option for stage II/III triple-negative and HER2-positive breast cancer" at the 2017 "St. Gallen International Breast Cancer Conference".⁴⁹ Importantly, presurgical treatment allows the breast cancer to be downstaged and increases the likelihood of breast preservation; pathologic full remission is achieved (pCR). As a result, until now, NACT has been regarded as the most appropriate endpoint.⁵⁰

The “National Surgical Breast and Bowel Project”'s (NSABP) trial B-27 looked at pCR by combining four cycles of pre- and post-operative docetaxel (AC) with four cycles of NACT docetaxel, and found a significant pCR. NACT showed an increase from 12.9 percent (AC) to 26.1 percent (NACT), with a significant connection between pCR and overall survival.⁵¹

This finding sparked a slew of studies aimed at improving pCR rates by incorporating more chemotherapeutic agents, switching to new medications instead of existing ones, or incorporating physiologically targeted agents like antibodies or small molecules into routine treatment. In this context, the definition of pCR is important, and today, pCR usually refers to a complete remission of invasive disease in the breast and axilla (with or without the presence of ductal carcinoma in situ), as this definition best distinguishes between patients with a favourable and unfavourable prognosis.⁵²

9. PROGNOSTIC FACTORS DETERMINING OUTCOME IN BREAST CARCINOMA

Prognostic indicators of breast cancer:

- 1. Age at diagnosis:** Age is an independent prognostic factor among women with more than 35 years to show poor 10-year distant recurrence-free survival.⁵³
- 2. Size of the tumor:** Tumor size is a good prognostic marker for distant relapse among node-negative patients, although patients with small tumor having a size less than 1cm if not treated have 12% chance of relapse of the disease.⁵⁴ Size of tumor correlates with the presence and number of involved axillary lymph nodes. It is also an independent prognostic factor for distant recurrence rates, especially among node-negative cases.
- 3. Spread to lymph nodes:** Nodal status, including the number of positive lymph nodes, affects the disease prognosis in terms of disease-free and overall survival. Still, 30%

of node-negative cases may develop recurrence by 10 years. Lymphatic invasion is especially useful prognostic factor among patients with borderline tumor size.

4. **Tumor grade:** Low-grade tumors are likely to have less aggressive behavior, while high-grade tumors progress aggressively. Tumor grade is a strong prognostic factor which itself act as a molecular signature, and if analyzed properly, it could add information superior to currently existing commercial molecular methods.⁵⁵
5. **The initial stage at diagnosis:** When diagnosed at an early-stage, breast cancer has a favorable prognosis as compared to late-stage diagnosis. If diagnosed at a late stage with distant metastasis, obviously there are more chances of recurrences resulting in a poor outcome. Bone marrow micro metastasis has also been proposed as a prognostic factor associated with tumor size, nodal status and grade of the tumor.⁵⁵
6. **Hormone receptor (HR) status:** Hormone receptor-positive tumors (Estrogen receptor- ER, Progesterone receptor PR) are often less aggressive, low grade and have a low risk of metastasis and recurrence. So, they have a good prognosis and respond well to the treatment. ER and PR are dimeric, gene regulatory proteins. Recently the role of ER as a negative and HER2 as a positive indicator for chemotherapy has been recognized. Female sex steroid hormones often regulate the growth of breast cancer. Hence, determination of both ER and PR in the tumor continues to be used as prognostic markers for potential benefits anti-hormonal therapy.⁵⁵
7. **Tumor proliferation rate:** It is a very important prognostic factor in breast cancer. It is estimated by various methods like S-phase fraction by flow cytometry, cell cycle-related antigens by immunohistochemistry and expression of nuclear phosphoprotein mitocin. Ki67 is a non-histone protein antigen in the nucleus which is expressed only in the cells in the proliferative phase of the cell cycle (G1, S, G2 and M phases). If

more than 50% of the cells show overexpression of Ki67, they are at high risk of developing the recurrent disease.⁵⁶

8. **Period of disease-free interval:** If recurrence is after 5 years of initial diagnosis, the prognosis is favorable. But recurrence in <2 years results in the poor outcome.⁵⁵
9. **Special histologic types:** Some histologic types of cancer are strongly correlated with very favorable survival (e.g., tubular, adenoid cystic).
10. **Gene expression profiling:** The most important clinical value of these assays is to identify patients with antiestrogen-responsive cancers who do not need chemotherapy.

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10. KI67 INDEX:

Gerdes et al. discovered the Ki-67 antigen, a non-histone protein, when they raised mouse monoclonal antibodies to the nucleus of a Hodgkin's disease cell line. The "Ki" refers to Kiel University in Germany. In a 96-well plate, the "67" refers to the clone number.⁶⁰

Immunohistochemistry with a monoclonal antibody may detect the Ki-67 antigen in all stages of cell proliferation. It is not present in the resting (G0) phase, but appears in the S, G1, and G2 phases. It appears on the surface of the chromosomes in mitosis.

The percentage of cells positively stained is the Ki-67 score or index. The original anti-Ki-67 monoclonal antibody could only be used on fresh frozen tissue, but a different anti-human monoclonal antibody, N1B-1 (clone 42), is used to assess Ki-67 in formalin-fixed, paraffin-embedded sections that have been archived for decades.⁶¹

In a retrospective research of 3658 cases of invasive BC entered in the Regensburg clinical cancer registry in Bavaria, Germany, from 2005 to 2011, the significance of Ki-67 index as a predictive marker was investigated.³ Ki-67 percentage was part of the regular workup

for these individuals, along with the receptor status and commonly noted histological characteristics. In a univariate analysis, a Ki-67 of more than 25%, together with unfavourable clinical and histological characteristics, had a poor prognosis in the study population. Patients with low Ki-67 (15%) had 87 percent disease-free survival and 89 percent overall survival after five years, respectively, whereas those with high Ki-67 (>45%) had 76 percent disease-free survival and 83 percent overall survival. These findings back up De Azambuja's earlier meta-analysis, found that a high Ki-67 % was associated with lower survival rate in node-negative, node-positive, and untreated BC patients in a univariate model.⁴

Despite the fact that aggressive clinical and histopathological features (receptor negativity, high grade cancer, positive nodal status, young age, and lymphovascular invasion) are significantly associated with worse outcomes, a multivariate analysis of the Regensburg data revealed that a high Ki-67 percentage (> 25%) remained an independent prognostic parameter for disease-free and overall survival, regardless of the clinical and histopathological features of the cancer.³

Ki-67 And The Molecular Subtyping Of Breast Cancer

Ki 67 has been utilised to distinguish between breast cancer molecular subgroups. Cheang et al. used the Ki-67 along with a panel of receptors [estrogen receptor (ER), progesterone receptor (PR), and HER2NEU] and discovered that a Ki-67 level of 13% could distinguish luminal A cancer with a good prognosis from luminal B BC with a poor prognosis. Nine hundred and forty-three patients with node-negative BC who had not received systemic therapy were subtyped using these four immunohistochemistry markers (IHC4): ER, PR, HER2, and Ki-67, and were monitored for relapse and 10-year cancer-specific survival.

Luminal B BC patients with a Ki-67 of >14 percent had a significantly poorer prognosis for recurrence and mortality than luminal A BC patients with a Ki-67 of 14 percent.⁶²

In a prior study, a Ki-67 of 14 percent was used to distinguish high risk from low risk. However, the cut-points utilised to make this differentiation in the literature have ranged from a Ki-67 of 5-30%.⁶³ Because of the large range of cut-points used in Ki-67 assays, comparing proliferative activity values from different breast cancer centres has proven difficult. The ongoing disagreement over techniques of labelling and counting neoplastic cells in paraffin sections has added to the problem. Some pathologists prefer to count stained nuclei at "hot spots" and near the malignancy's invasive edge, while others score cell numbers in a field that is representative of the entire section.⁹ Because of this dispute, the Ki 67 index was not included the list of approved biomarkers for clinical practise in the "American Society of Clinical Oncology" 2007 guidelines.¹⁰

In 2010, an international "Ki-67 in Breast Cancer Working Group" was formed to investigate the utility of Ki-67 as a repeatable prognostic index.⁶⁴ The organisation released guidelines for measuring Ki-67, detailing the type of biopsy to be performed, the fixative to be used, storage durations, and antigen retrieval methods. It was discussed which monoclonal antibody to employ as a reagent for immunohistochemistry and staining procedures. The working group has also established guidelines for scoring, data analysis, and interpretation of the results.

Yet, there is no agreement on a single cut off point or a range. This is due in part to the fact that the Ki-67 has a continuous distribution and that preanalytic and analytical methodological variances remain.⁶⁵ These issues are at the root of the ongoing controversy over the Ki-67 assay's use and repeatability.

However most of the specialists who commented on the treatment-oriented classification of BC said that Ki-67 index should be evaluated in the range of local laboratory values.¹² The group of specialists used the example of a laboratory with a median Ki-67 index of 20%.

Nonetheless, in 2015 “St Gallen International Breast Cancer Conference” consensus statement acknowledged that value of assessing and correlating hormone receptor levels and proliferation activity to evaluate prognosis and to guide adjuvant chemotherapy.⁶⁶

The consensus also stated that "international collaboration has contributed to gains in Ki-67 score concordance," promoting the marker's ongoing usage and standardisation.

KI-67 And Metastasis:

Advanced surgical procedures, larger radiation field, breakthroughs in cytotoxic medications and targeted therapy together have resulted in longer disease-free survival and lower mortality rate. However, it is yet impossible to declare a fraction of people "cancer-free." After extended anti-oestrogen therapy, node-negative ER positive tumours return at a frequency of 2%/ year for at least 15 years. This prompted researchers to look for a scoring system that could distinguish BC patients at low risk compared to those at high enough risk of recurrence to warrant chemotherapy. “Genomic Health 21-gene recurrence score (6H1-RS)”, which was derived from a tumor-related gene assay and commercially marketed as Oncotype DX®.⁶⁷ The 6H1-RS score was generated for lymphnode-negative, ER-positive, HER2-neu negative BC patients who didn’t receive adjuvant chemotherapy in the “Arimidex, Tamoxifen, Alone or in Combination (ATAC) trial”. The Oncotype DX® was found to be a predict distant recurrence better than patient age, tumour stage, grade, or ER expression by these researchers. 6 of the Oncotype DX ®'s cancer-related

genes are associated with proliferation, IHC4 score was found as effective as the 21-gene score in anticipating distant illness 5 years after treatment completion.⁶⁸

Choice Of Therapy

Ki-67 index is useful in prognostication of BC as well as in selection of the appropriate medication for its treatment. Dividing cells are more susceptible to cytotoxic medications. A higher Ki-67 level is linked to favourable response to NACT. Strongly ER-positive tumours with a low Ki-67 score, respond better to 4-8 months of neoadjuvant hormone therapy. The ability of baseline Ki-67 readings to predict response to a specific adjuvant chemotherapy regimen, has yet to be determined.⁶⁵

While baseline Ki-67 staining may help guide initial therapy choices, monitoring patient response to current treatment has become a critical component of patient care. In the Immediate Preoperative Anastrozole, Tamoxifen, or Combination with Tamoxifen (IMPACT) experiment, the Ki-67 in a core biopsy was assessed two and twelve weeks after starting treatment.⁷⁰ The inhibition of Ki-67 by anastrozole was larger than that seen with tamoxifen or the combination at both time intervals. At the ATAC trial's 31-month evaluation, anastrozole's stronger suppression of Ki-67 was significantly associated with increased recurrence-free survival rate of patients on this drug.⁷¹

Assessment Of Residual Risk

In majority of patients with invasive BC, Chemotherapy yields a clinical response, whereas only a small percentage of them have a complete pathological response. Profiling of the residual cancer in excision specimens act as a guide to adjuvant therapy. In 283 patients with ER-negative, invasive non-metastatic BC who didn't have a pathological response, an analysis of Ki-67 before and after NACT was done. Patients with high

baseline Ki-67 index responded well to NACT, while those with higher Ki-67 had considerably worse recurrence. -successful survival.⁷² A high Ki-67 index in residual cancer indicates the need for additional non-cross-resistant treatment.

Association Between Ki67 And Clinical Parameters And Histological Parameters Of Carcinoma Breast

A retrospective study by Liang, Q et al,⁷³ analyzed the interaction between Ki-67 and histological grade and their prognostic role in different breast cancer subtypes. Using the median Ki-67 index 15% as the cut-off for low/high Ki-67 expression. Recurrence-free survival (RFS) was calculated and compared, and the results indicated that Ki-67 index was significantly associated with histological grade in all breast cancer patients ($p < 0.001$) and in each immunohistochemical (IHC)-based subtype ($p < 0.001$). Both high Ki-67 expression and grade 3 tumours were independent predictors of inferior RFS in all patients, especially in those with luminal-like tumours ($p < 0.05$). Ki-67 index was an independent prognostic factor for RFS in grade 1, 2 patients with luminal-like tumours (adjusted hazard ratio [HR] = 1.92, 95% confidence interval [CI]: 1.22-3.03, $p = 0.005$), but not in the other subtypes. Similarly, histological grade predicted shorter RFS in patients with low Ki-67 expression who had luminal-like tumours (adjusted HR = 2.12, 95% CI: 1.13-3.99, $p = 0.02$) but not in the other subtypes. Conversely, Ki-67 showed no prognostic value for patients with grade 3 tumours and vice versa.

Nigam, J et al,⁷⁴ analysed the correlation of Ki-67 with clinicopathological parameters of breast cancer. They studied 129 cases of core needle biopsy and mastectomy specimens. The patient's mean age and median age were 47.41 and 47 years, respectively. Only 56 specimens of mastectomy were received. T2 (26/56) was the most common tumor size. Grading was done in 46 cases, and grade 2 (23/46) was the most common. Estrogen,

progesterone, and Her2neu were positive in 65, 61, and 59 cases, respectively. Only estrogen receptor (ER) expression ($p = 0.035$) and Her2neu ($p = 0.035$) overexpression was significantly associated with Ki-67. Ki-67 expression had correlated with clinicopathological factors. Only ER expression and Her2neu overexpression were significantly associated with Ki-67. Hence, patients with high Ki-67 expression may have better responses to hormonal therapy and chemotherapy.

A prospective study by L, Madhushankar et al,⁷⁵ analysed all the excised mastectomy specimens of patients with carcinoma breast to analyse the relationship with Ki67. They analysed 41 cases of age between 25 to 75 years. The mean age of presentation was 49.22 ± 11.21 years. 75.6% patients had Ki67 between 22-40% indicating that younger the age group more aggressive is the breast cancer. Ki67 expression decreased as the patient's age increased. Tumors were between 1.6 to 10 cm in size in greatest dimension and most were between 3 to 6 cm. As tumor size increased, an increase in Ki-67 level was noticed. A positive relationship was observed between involved lymph nodes and the mean level of Ki67 expression. On histopathological examination tumour grade-III had high Ki67 and proliferative index was gradually increasing from grade-I to grade-III. Proliferative index Ki67 was also compared with stage of disease in non-metastatic breast cancer, was higher in later stage of disease. This study demonstrated HER2/-neu positivity with higher frequency of Ki67. A significant relationship was also found between Ki67 and tumor grade and age of the patient. A positive relationship was seen between the mean level of Ki67 expression and involved lymph nodes. Ki67 expression thus affects the prognosis along with other factors, including the size and grade of tumor. Ki-67 expression along with IHC markers for ER, PR and HER2neu correlated with histopathological grades, however, it was discovered to be an independent prognostic and predictive factor in BC. High index labelled Ki67 is considered as an unfavourable factor that influences tumour

progression with poor prognosis. It helps in counselling the patient about prognosis of the disease. In conclusion, Ki-67 has great potential as prognostic biomarker in aggressive breast cancers and such prognostic information could be beneficial for development of therapeutic strategy. It would be easy to include it in the panel of markers routinely assessed in clinical practice.

Correlation Of Prognostic Factors Of Carcinoma Breast With Ki 67 Proliferation Assay

Ragab, H et al,⁷⁶ analysed 92 patients with developed non metastatic breast cancer and 10 women had benign breast tumor served as controls. They measured the serum level by ELISA technique and tissue expression of Ki-67 by immunohistochemical technique. The results showed that there were no statistically significant differences in serum Ki-67 levels between the two studied groups. As for Ki-67 expression in breast cancer cells, the score increases with increase of tumor size, grade, premenopausal, Ki-67 expression in ER and PR positive tumors showed lower values than estrogen and progesterone negative tumors, while higher Ki-67 expression was more frequently associated with HER2-positive. This study supports the finding that tissue Ki-67 expression may provide additional information regarding the prognosis to that obtained from classical prognostic factors and can provide data of significant value to other important prognostic indicators such as pathological grading, and lymphnode involvement.

A study by Kang, Y et al,⁷⁷ aimed to assess the prognostic value of Ki-67 according to PR expression in patients who have ER- positive, HER2NEU negative early breast cancer. among 1848 patients, 223 (12%) patients had high ($\geq 10\%$) Ki-67, and 1625 (88%) had low Ki-67 expression. Significantly poor RFS and OS was seen in the high vs. low Ki-67 expression only when the PR was low ($< 20\%$) ($p < 0.001$ and 0.005 , respectively, for RFS and OS). No significant difference was found in RFS and OS according to Ki-67 when the

PR was high ($p=0.120$ and 0.076). RFS of four groups according to high/low Ki-67 and PR expression was compared. The low PR and high Ki-67 expression group showed worst outcome among them ($p<0.001$). In a multivariate analysis, high Ki-67 was an independent prognostic factor when the PR was low (HR 3.05; 95% CI 1.50-6.19; $p=0.002$). Hence this study showed Ki-67 had a value as a prognostic factor only under low PR expression level in early breast cancer. PR should be considered in evaluating the prognosis of BC patients using Ki-67.

Min, K et al,⁷⁸ evaluated Ki67 and BCL2 expression with 203 cases of breast cancer. They found a significant correlations between Ki67/BCL2 index and clinicopathological findings such as age, tumour stage, size and necrosis, histological grade, extensive intraductal component, lymphatic and vascular invasion, oestrogen receptor, progesterone receptor, HER2NEU and p53 expression (all $p<0.05$). In univariate and multivariate analyses, high Ki67/BCL2 index correlated with shorter DFS and OS in patients with early stage invasive ductal carcinoma (all $p<0.05$). The results suggested that Ki67/BCL2 index should be considered as a prognostic predictor in patients with early stage invasive ductal carcinoma.

A study by Alco, Gul et. Al,⁷⁹ aimed to identify the optimal Ki-67 cut-off value in BC patients, and investigate the association of Ki-67 expression levels with other prognostic factors. The correlation between Ki-67 assay and other prognostic factors age, size, expression, human epidermal growth factor. The multivariate analysis showed that a Ki-67 value of $\geq 15\%$ was associated with the largest number of poor prognostic factors. In addition, a Ki 67 value of $\geq 15\%$ was identified to be statistically significant in association with certain luminal subtypes. Following the correlation analysis for the Ki-67 index and

the other prognostic factors, a Ki 67 value of $\geq 15\%$ was revealed to be the optimal cut-off level for BC patients.⁷⁹

Soliman, N et al,⁸⁰ aimed to see how useful the Ki 67 assay is in predicting recurrence in various molecular subtypes of breast cancer. In 107 cases of primary breast cancer, the Ki-67 level was determined. Approximately 44, 23, 15, and 25 cases were grouped as luminal A, luminal B, HER2 subtype, and triplenegative (TN), respectively. No luminal A patients showed Ki-67 level higher than 15%, and their recurrence was 20%. In luminal B group, Ki-67 level higher than 15% was observed in 69% of patients, and recurrence was 39%. In HER2 subtype, Ki-67 was higher than 15% in 34% of cases, and recurrence was 40%. In triple-negative cases, Ki-67 was higher than 15% in 60% of cases, and recurrence was detected in 32% of patients. Patients with Ki-67 less than 15% displayed better overall survival than those with higher Ki-67, i.e $> 15\%$ ($P = 0.01$). Patients having Ki-67 $> 15\%$ had higher rate of metastasis and recurrence than those with Ki-67 $< 15\%$ ($P = 0.000$). The study results suggested Ki-67 may be considered as a valuable biomarker in BC patients.

Ferguson, N et al,⁸¹ conducted a study to see how breast cancer subtypes, the Ki-67 proliferation index, and pathologic tumour features affected survival in Caucasian women with BC. The results showed that patients with stage IIB through stage IV breast carcinomas were 2.1-16 times more likely to die than patients with stages IA-B and IIA disease, respectively (95% CI 1.17-3.81 through 9.68-28.03, respectively), irrespective of ER/PR/HER2 subtype. Similar effect was seen with T2, N2/N3, or M1 tumors in comparison with T1, N0/N1, and M0 tumors. Chances of dying increase approximately 5% for every year increase in age..

LACUNAE OF LITERATURE

Ki67 index is a valuable biomarker of BC as higher ki67 correlates with higher tumor grade. The correlation of Ki 67 with histological and molecular subtypes have been established in several studies. Its assessment in BC with various clinic pathological parameters is well studied. The prognostic value of Ki67 in breast cancer is extensively studied. However, no independent prognostic significance of ki67 index could be established by many of the studies as its association with nodal metastasis or any other prognostic factor in breast cancer.

MATERIAL & METHODS



MATERIALS & METHODS

Study site: This study was conducted in the Department of General Surgery at R.L. Jalappa Hospital, Kolar.

Study population: All the eligible patients admitted at Department of General Surgery, R.L. Jalappa hospital with diagnosis of carcinoma of breast were included study.

Study design: The current study was a cohort study

Sample size: 98

Sampling method: All the eligible subjects were recruited into the study consecutively by convenient sampling till the sample size is reached.

Study duration: The data collection for the study was done between Dec 2019 to June 2021.

Inclusion Criteria:

1. All biopsy proven carcinoma breast were included in this study

Exclusion criteria:

1. Patients who are treated with neoadjuvant chemotherapy.
2. Male carcinoma breast patients.
3. Recurrent carcinoma breast patients.
4. Patients with distant metastasis.

Ethical considerations: Study was approved by institutional human ethics committee. Informed written consent was obtained from all the study participants and only those participants willing to sign the informed consent were included in the study. The risks and benefits involved in the study and voluntary nature of participation were explained to the participants before obtaining consent. Confidentiality of the study participants was maintained.

Data Collection Tools: All the relevant parameters were documented in a structured study proforma.

Methodology:

Patients admitted with diagnosis of carcinoma of breast were included in the study from the period of Dec 2019 to June 2021. Specimen was sent in 10% buffered formalin. The paraffin blocks of primary tissue and metastatic lymph node was sent for tumour marker study using IHC. The value of ki67 were studied and compared with other prognostic markers using appropriate statistical analysis methods.

Following Investigations Are Done:

1. Complete Blood Count
2. Renal function tests
3. Serum electrolytes
4. Chest radiograph
5. ECG
6. Mammography
7. Core needle biopsy of lump
8. USG abdomen and pelvis.
9. ER/PR/Her2Neu Receptor Status
10. Immunohistochemistry marker study from the tumour tissue/ nodal tissue for ki67

Statistical Methods

ki67 proliferation index was considered as primary outcome variable. Prognostic factors were considered as explanatory variables. Descriptive analysis was carried out by mean and standard deviation for quantitative variables, frequency and proportion for categorical variables. All quantitative variables were checked for normal distribution. For normally distributed quantitative parameters the mean values were compared using independent sample t-test. Categorical outcomes were compared using Chi square test /Fisher's Exact test (If the overall sample size was < 20 or if the expected number in any one of the cells is < 5 , Fisher's exact test was used.). Data was also represented using appropriate diagrams like bar diagram, pie diagram and cluster bar diagram. P value < 0.05 was considered statistically significant.

Data was analyzed by using S PSS software, V.22. (1).

RESULTS



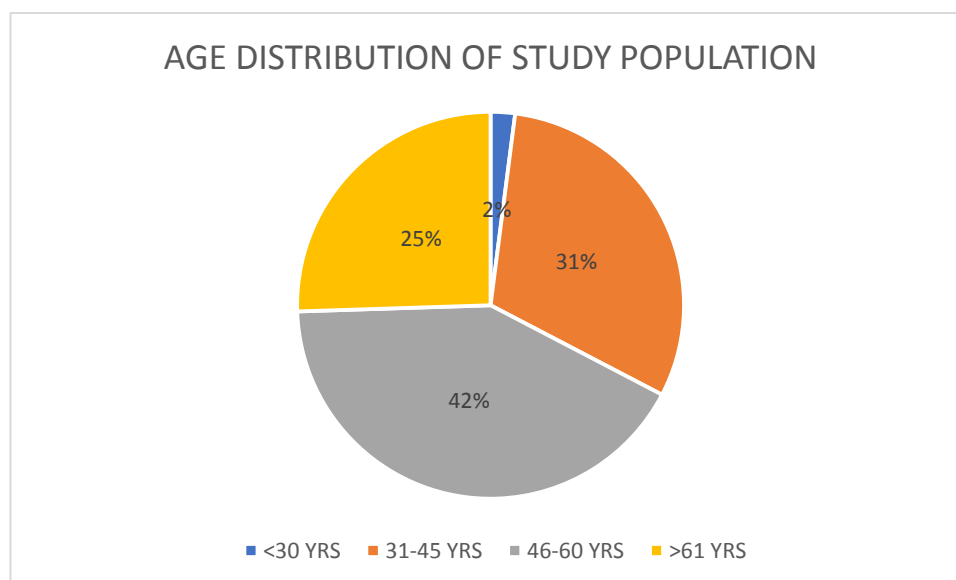
OBSERVATIONS AND RESULTS

A total of 98 subjects were considered in the study.

Table 4: Descriptive Analysis of Age (In Years) In Study Population (N=98)

AGE	NUMBER OF PATIENTS	PERCENTAGE(%)
<30 YRS	2	2.04
31-45 YRS	30	30.61
46-60 YRS	41	41.83
>61 YRS	25	25.51

Figure 6: Pie Chart Showing Age Distribution of Study Population



The study population consisted of patients aged between 30 to 80 years with a mean age of 53.61 ± 12.48 years. (Table 4 & Figure 6)

Table 5: Descriptive Analysis of Occupation In The Study Population

Occupation	Frequency	Percentages
House wife	75	76.53%
Working class	23	23.47%

Among the study population, 75(76.53%) were housewives and 23(23.47%) were working class. (Table 5 & Figure 3)

Figure 7: Pie Chart of Occupation In The Study Population (N=98)

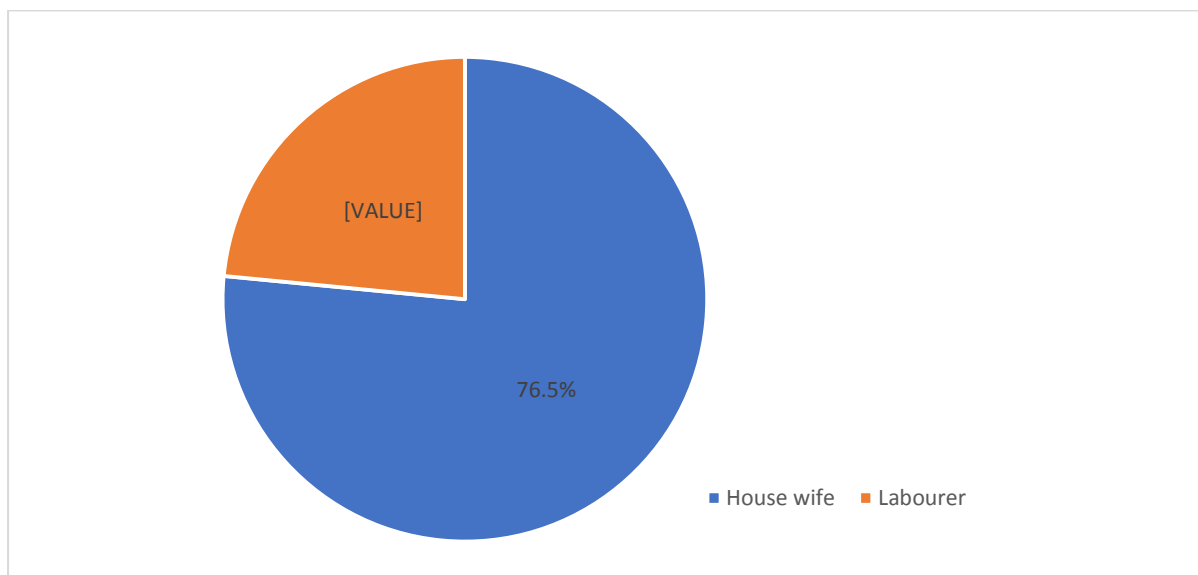


Table 6: Descriptive Analysis of Presenting Complaint in the Study Population (N=98)

Presenting Complaint	Frequency	Percentages
Lump in right breast	53	54.08%
Lump in left breast	45	45.92%

Among presenting complaint, 53 (54.08%) had lump in right breast and 45 (45.92%) had lump in left breast. (Table 6 & Figure 8)

Figure 8: Pie Chart of Presenting Complaint In The Study Population (N=98)

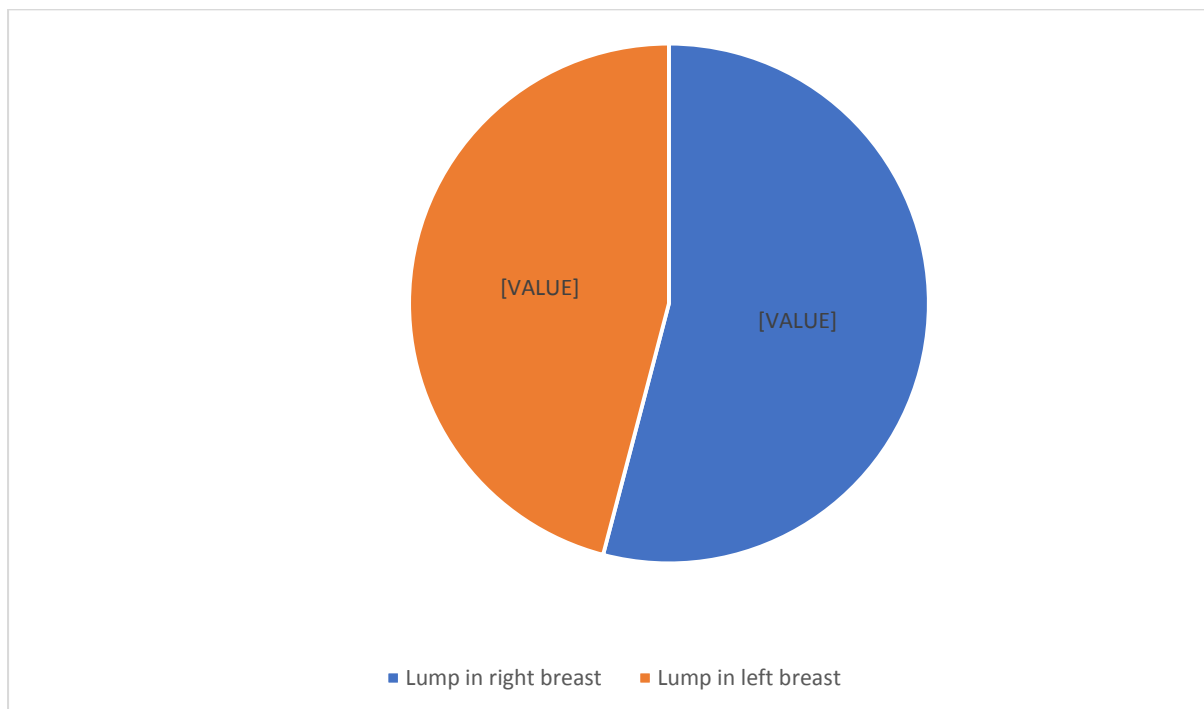
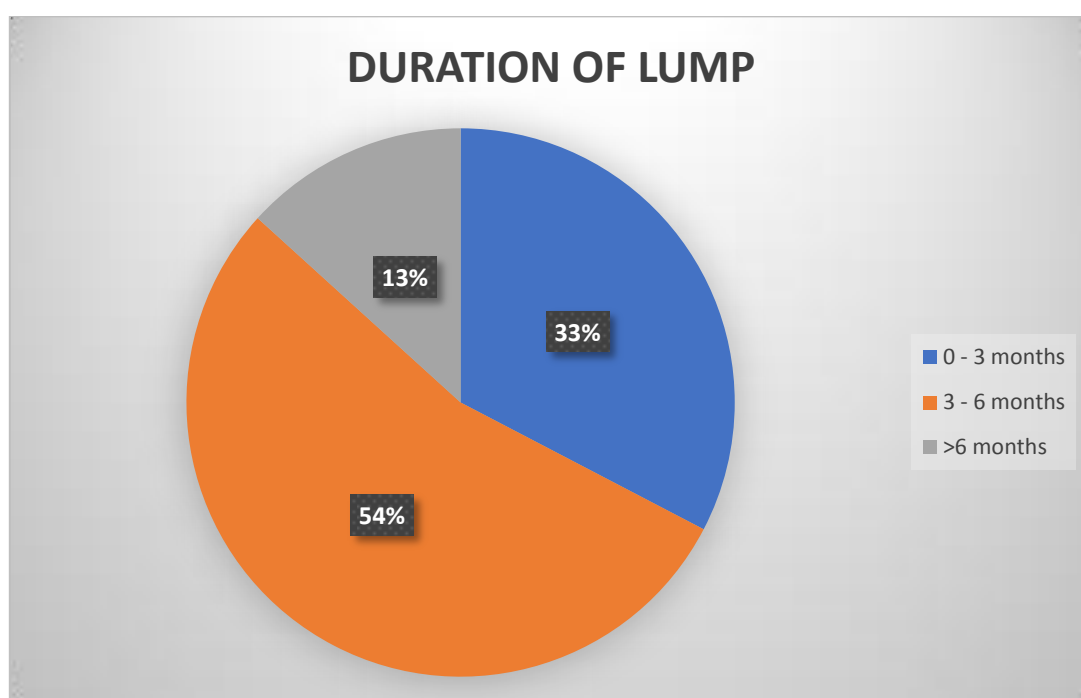


Table 7: Descriptive Analysis of Duration of Symptoms In Study Population (N=98)

DURATION OF LUMP	FREQUENCY
0 - 3 months	32
3 - 6 months	53
>6 months	13

Figure 9: Pie Chart Showing Descriptive Analysis of Duration Of Symptoms In Study Population (N=98)



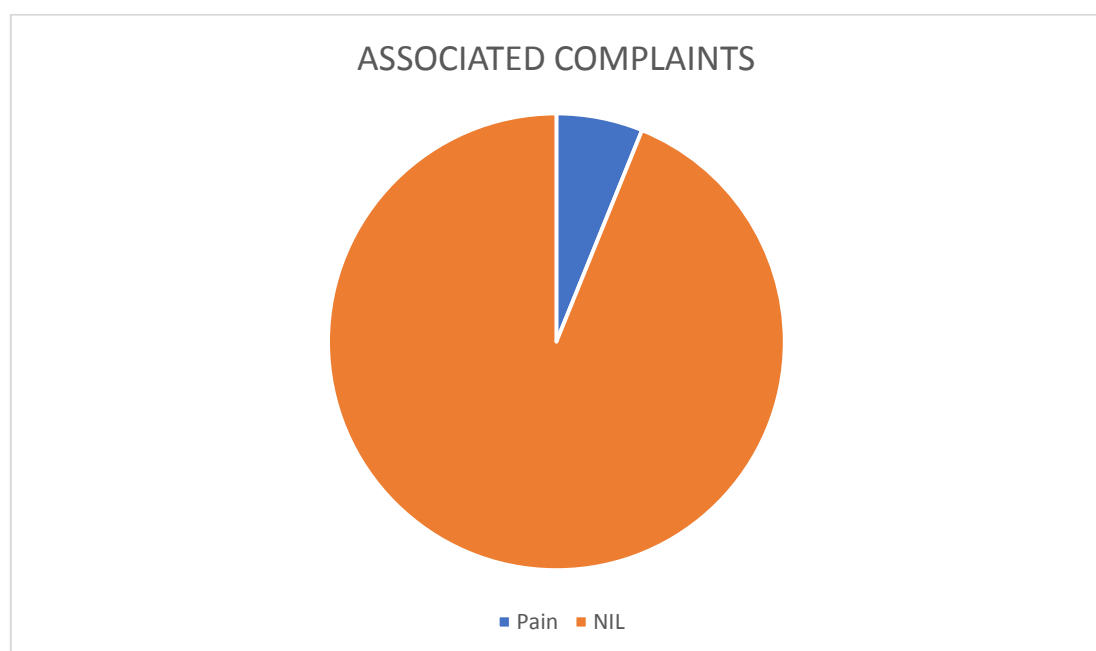
Most patients in the study population presented with a lump of duration 3-6 months (54%)

The mean duration of lump was 4.62 ± 2.18 months (Table 7 & Figure 9)

Table 8: Descriptive Analysis of Associated Complaints In The Study Population (N=98)

Associated Complaints	Frequency	Percentages
Pain	6	6.12%
No symptoms	92	93.88%

Figure 10: Pie Chart of Associated Complaints In The Study Population (N=98)



Out of 98 participants, only 6.12% had pain associated with the lump. (Table 8 & Figure 10)

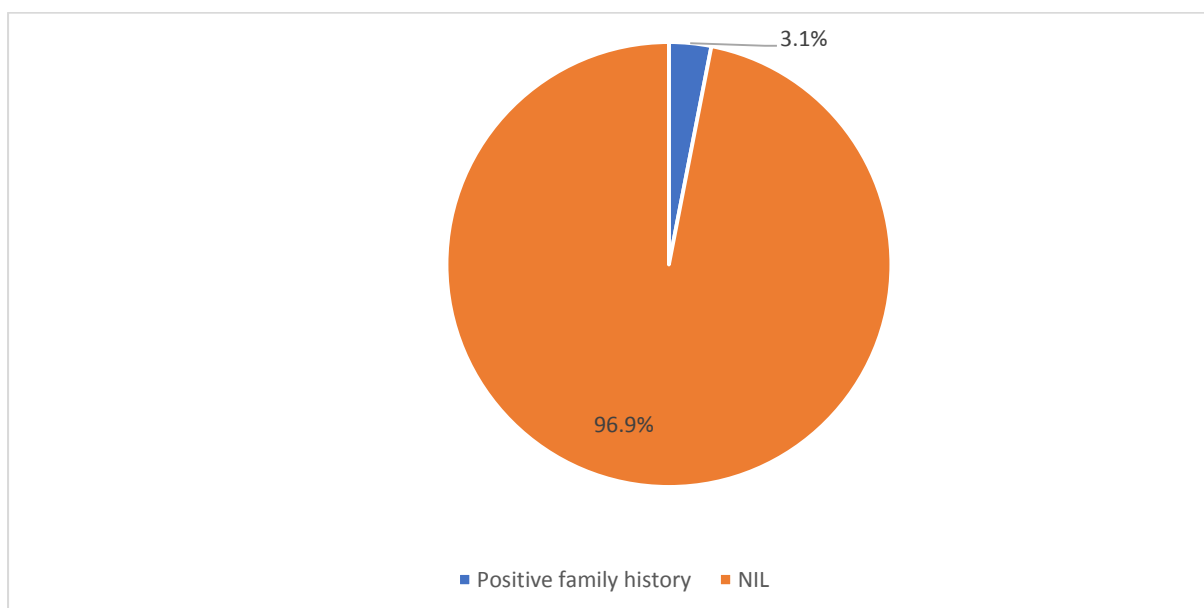
Table 9: Descriptive Analysis of Past History In The Study Population (N=98)

PAST HISTORY	FREQUENCY	PERCENTAGES
Contralateral Breast Cancer	2	2.04%
Diabetes Mellitus	5	5.10%
Hypertension	11	11.22%
No comorbidities	82	83.67%

Among the study population, 2 patients had a history of contralateral breast cancer, 5 had diabetes mellitus and 11 had hypertension. (Table 9)

Table 10: Descriptive Analysis of Family History In The Study Population (N=98)

FAMILY HISTORY	FREQUENCY	PERCENTAGES
Positive Family History	3	3.06%
No family history	95	96.94%

Figure 11: Pie Chart of Family History In The Study Population (N=98)

Out of 98 participants, 3(3.06%) had positive family history. (Table 10 & figure 11)

Table 11: Descriptive Analysis of Menstrual History In The Study Population (N=98)

MENTRUAL HISTORY	FREQUENCY	PERCENTAGE
PRE-MENOPAUSAL	33	33.67
POST MENOPAUSAL	65	66.33

Among the subjects considered for the study most of them (66.3%) were of post-menopausal age group. (Table 11 & figure 12)

Figure 12: Pie Chart of Menstrual History In The Study Population (N=98)

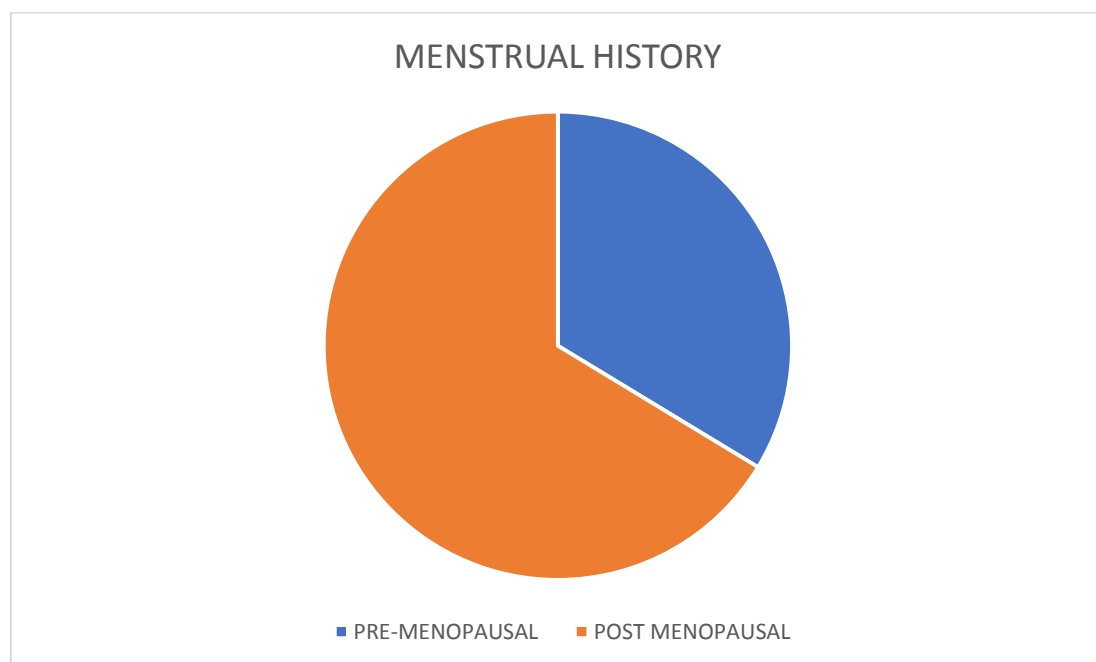
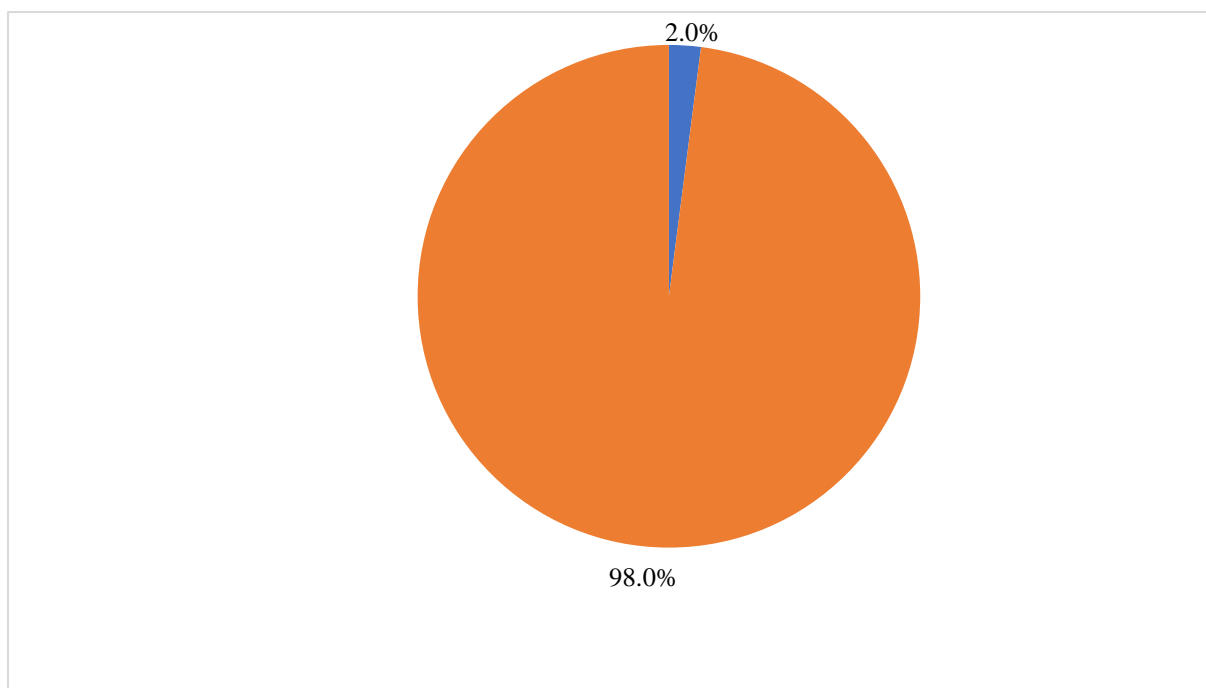


Table 12: Descriptive Analysis of Obstetric Score In The Study Population (N=98)

Obstetric score	Frequency	Percentages
Nullipara	2	2.04%
Multipara	96	97.96%

Figure 13: Pie Chart Of Obstetric Score In The Study Population (N=98)

Among the study population, 2(2.04%) were nullipara and 96(97.96%) were multi para.
(Table 12 & figure 13)

Table 13: Descriptive Analysis of General Physical Examination In The Study Population (N=98)

General physical examination	Frequency	Percentages
Build		
Moderate	96	97.96%
Well	2	2.04%
Nourishment		
Moderate	85	86.73%
Poor	11	11.22%
Well	2	2.04%
Pallor		
Present	1	1.02%
Absent	97	98.98%
Icterus (Absent)	98	100%
Cyanosis (Absent)	98	100%
Clubbing (Absent)	98	100%
Generalised lymphadenopathy (Absent)	98	100%
Edema (Absent)	98	100%
Spine (Normal)	98	100%

Among the study population, 96(97.96%) were moderately built, 2(2.04%) well built, 85(86.73%) were moderately nourished, 11(11.22%) poorly nourished. Only 1 patient had pallor. None were found to have icterus, cyanosis, clubbing, generalized lymphadenopathy or edema.(Table 13)

Table 14: Descriptive Analysis of Inspectory Findings In The Study Population (N=98)

Inspectory findings	Frequency	Percentages
Breast Symmetry		
Asymmetrical	89	90.82%
Symmetrical	9	9.18%
Nipple Retraction	16	16.33%
Nipple Discharge (blood tinged)	1	1.02%
Scars	3	3.06%
Site		
Left-all quadrants	2	2.04%
Left lower outer quadrant	4	4.08%
Left upper inner quadrant	5	5.10%
Left upper outer quadrant	32	32.65%
Right- all quadrants	5	5.10%
Right lower inner quadrant	7	7.14%
Right lower outer quadrant	5	5.10%
Right upper inner quadrant	11	11.22%
Right upper outer quadrant	27	27.55%
Borders		
Ill defended	77	78.57%
Well defended	21	21.43%
Surface		
Irregular	12	12.24%
Smooth	86	87.76%
Skin Changes		
Peau d orange	22	22.45%
Tethering	13	13.27%
Ulcer	13	13.27%
Skin nodules	1	1.02%
None	49	50.00%

Figure 14: Pie Chart of Site of Lump In The Study Population (N=98)

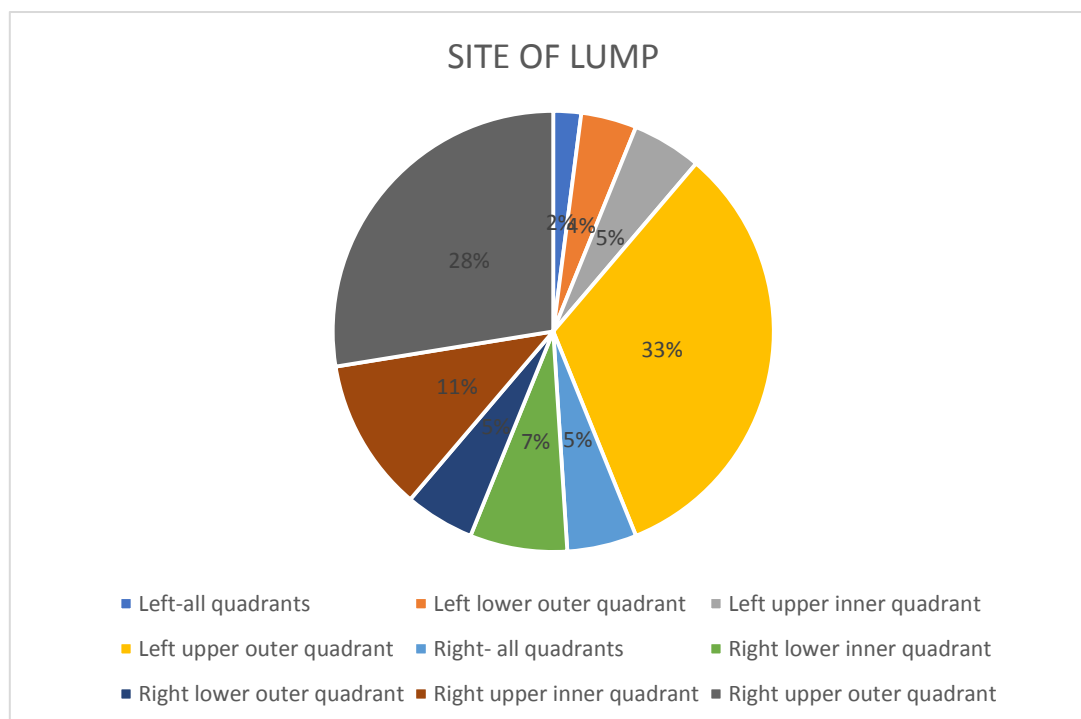


Figure 15: Pie Chart of Border In The Study Population (N=98)

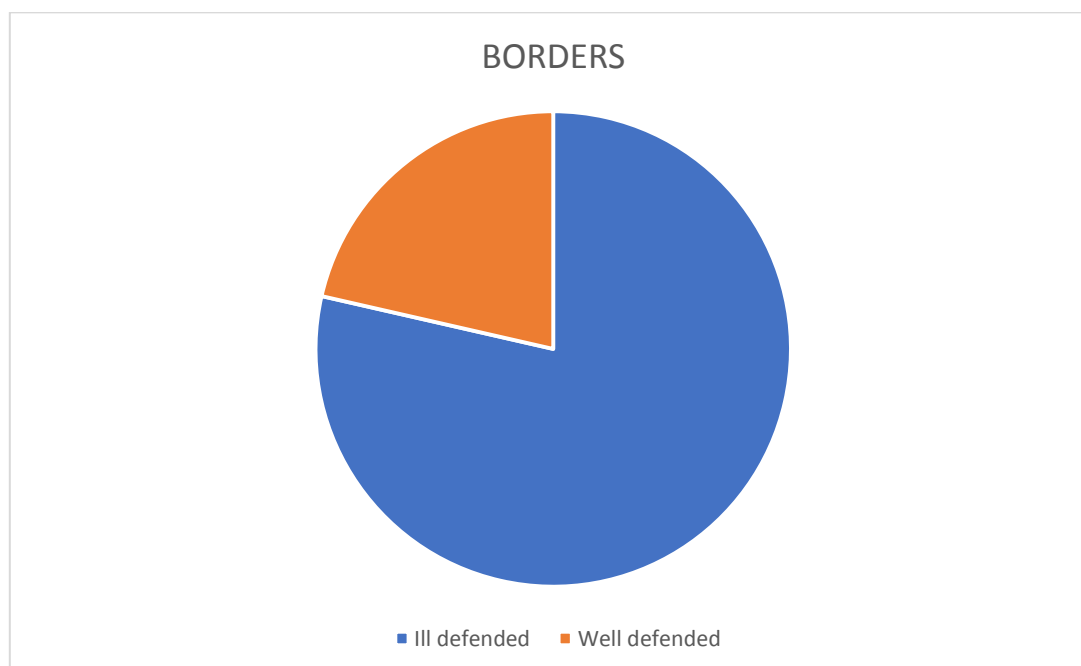


Figure 16: Pie Chart of Surface In The Study Population (N=98)

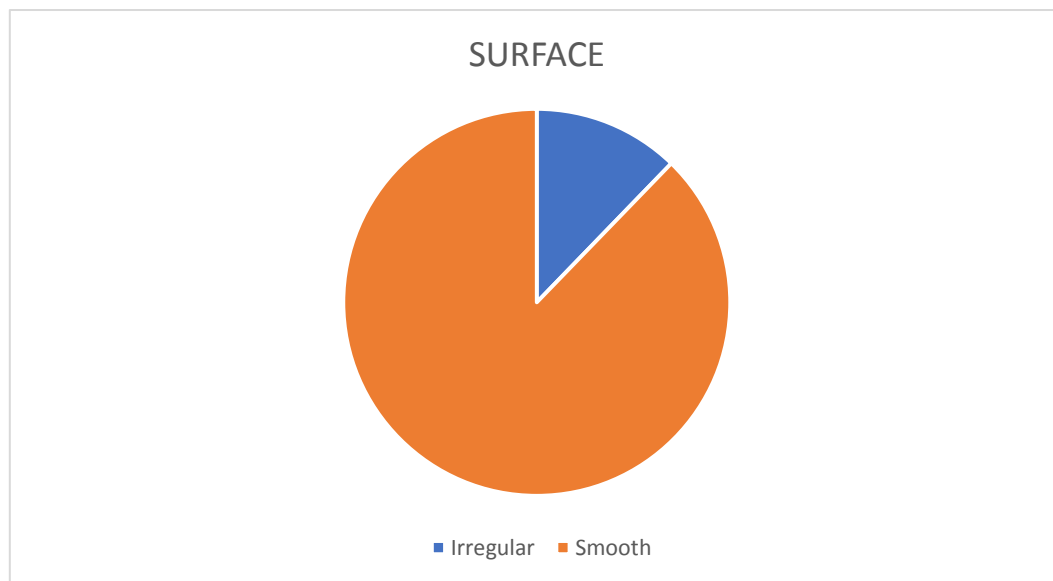
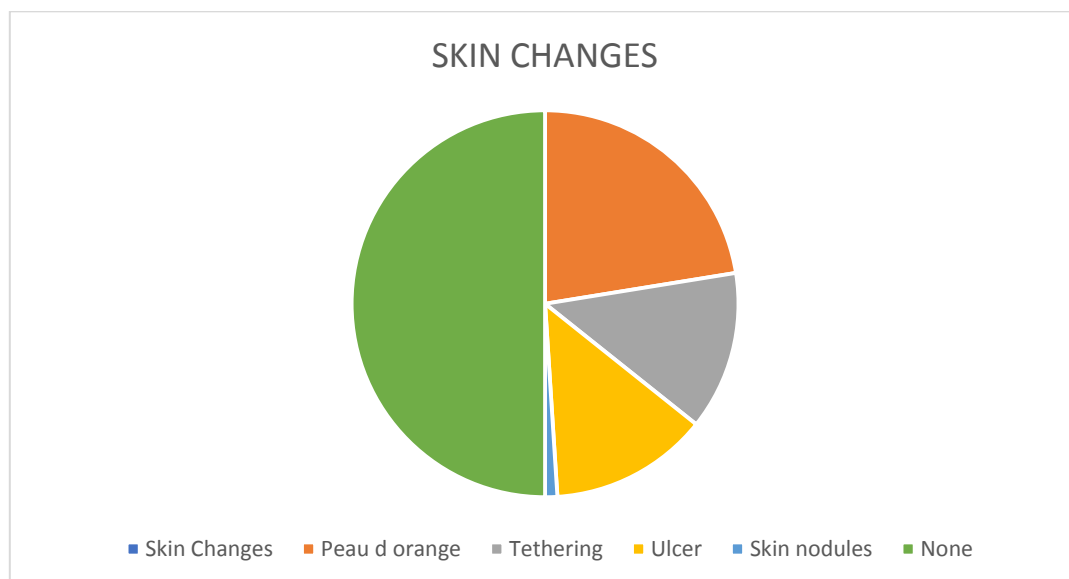


Figure 17: Pie Chart of Skin Changes In The Study Population (N=98)



Among the study population of 98 subjects, on inspection breast asymmetry was noted in 90.82%. 16.33% had nipple retraction and 1.02% had blood tinged nipple discharge. On inspection most common location of lump was upper outer quadrant – left in 32.65% and right 27.55% of the subjects. Most of them had ill-defined borders(78.57%). Skin changes was seen in 50% of the cases most common manifestation being Peau'D Orange(22.45%). (Table 14 & Figure 14 to 17)

Table 15: Descriptive Analysis Of Palpatory Findings In The Study Population (N=98)

Palpatory findings	Frequency	Percentages
Contralateral Breast		
Normal	98	100.00%
Temperature		
LOCAL RISE	3	3.06%
Normal	95	96.94%
Tenderness		
TENDER	18	18.37%
NON-TENDER	80	81.63%
Site		
Left-all quadrants	2	2.04%
Left lower outer quadrant	4	4.08%
Left upper inner quadrant	6	6.12%
Left upper outer quadrant	33	33.67%
Right- all quadrants	5	5.10%
Right lower inner quadrant	7	7.14%
Right lower outer quadrant	5	5.10%
Right upper inner quadrant	10	10.20%
Right upper outer quadrant	26	26.53%
Number(single)	98	100.00%
Borders		
Ill defined	6	6.12%
Well defined	92	93.88%
Surface		
Irregular	6	6.12%
Smooth	92	93.88%
Consistency		
Firm	4	4.08%
Hard	94	95.92%
Mobility		
Mobile	90	91.8%
Restricted mobility	6	6.1%
Fixed/ Not Mobile	2	2.04%

Figure 18: Pie Chart Of Site Of Lump On Palpation In The Study Population (N=98)

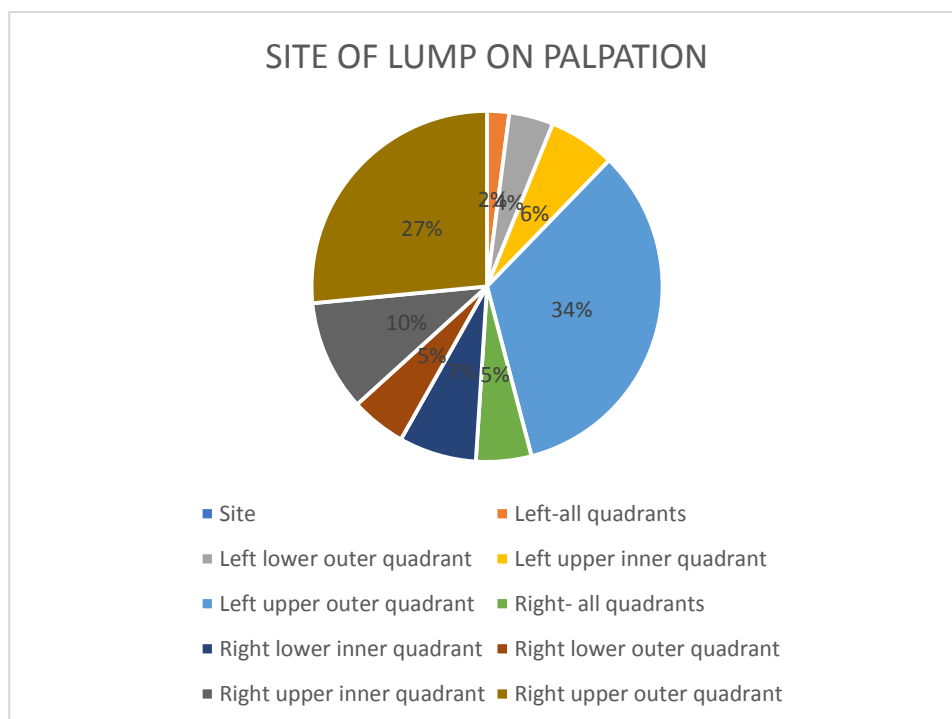


Figure 19: Pie Chart Of Borders On Palpation In The Study Population (N=98)

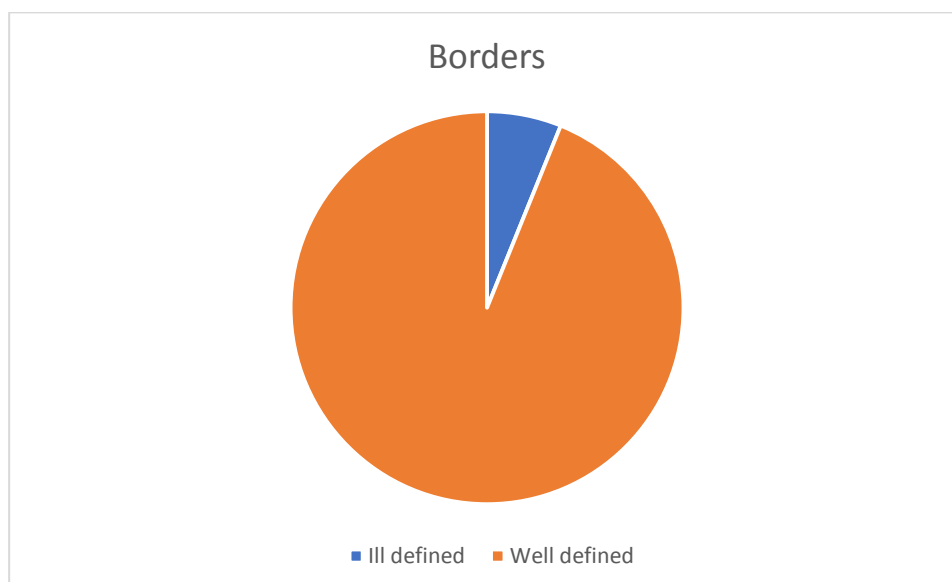


Figure 20: Pie Chart Of Surface On Palpation In The Study Population (N=98)

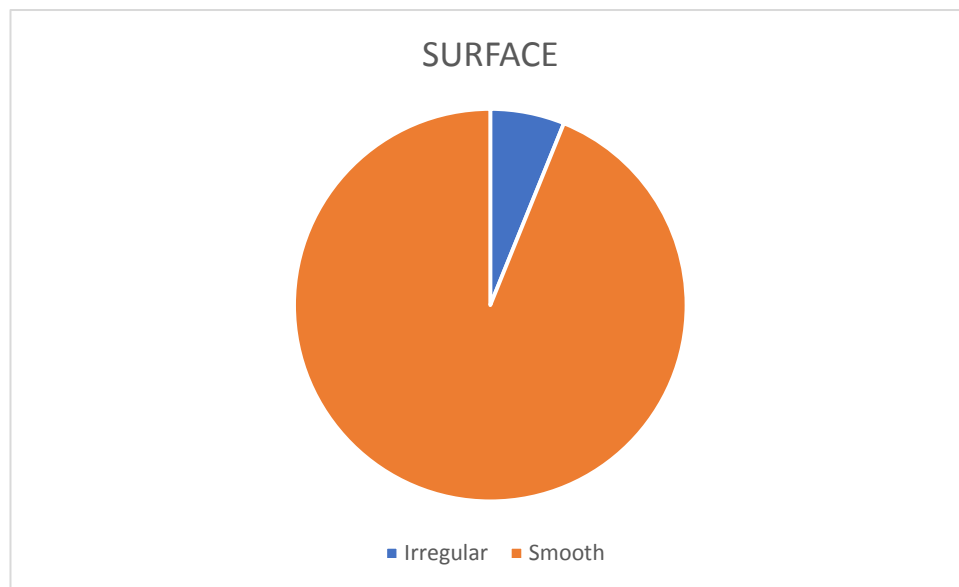
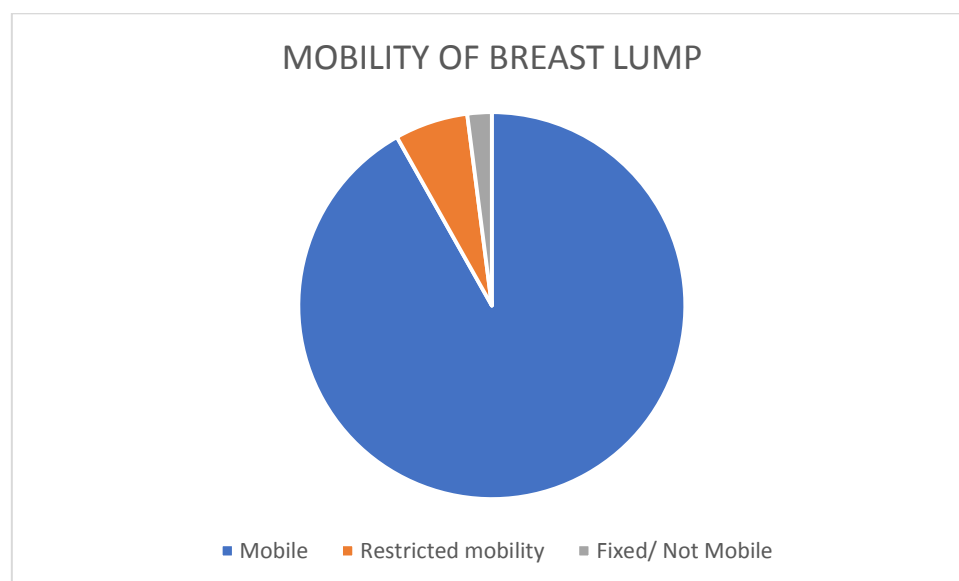


Figure 21: Pie Chart Of Mobility In The Study Population (N=98)



On palpation, contralateral breast examination was found to be normal among all 98 subjects. Local rise of temperature was found in 3 of them. 80 (81.63%) had non-tender breast lump. As seen on inspection, on palpation also upper outer quadrant was the most common site of lump with left accounting for 33.67 and right 26.53%. 93.88% of them had well defined borders and smooth surface.~96% of the lumps examined were hard in consistency. 91.8% of

the subjects had a mobile breast lump whereas 6.1% had restricted mobility and 2% were found to have a immobile breast lump. (Table 15 & Figure 18 to 21)

Table 16: Descriptive Analysis Of Size Of Breast Lump In The Study Population (N=98)

Parameter	Mean \pm SD	Median	Minimum	Maximum
Length (in cm)	4.94 \pm 1.56	5.00	1.00	12.0
Width (in cm)	4.03 \pm 1.65	3.00	2.00	8.0

The mean size of the breast lump among the study population was found to be 4.94 \pm 1.56 x 4.03 \pm 1.65. (Table 16)

Table 17: Descriptive Analysis Of Lymphadenopathy In The Study Population (N=98)

Lymphadenopathy	Frequency	Percentages
Axilla		
Single	42	42.86%
Multiple	6	6.12%
No axillary lymphadenopathy	50	51.02%
Consistency(N=48)		
FIRM	2	4.08%
HARD	46	95.92%
Fixity(N=48)		
Fixed	5	10.20%
Mobile	43	89.80%

Among the study population, 48 had axillary lymphadenopathy. 42(42.86%) of them had single palpable lymph node, 6(6.12%) had multiple palpable lymph nodes. Out of 48 participants, 46(95.92%) were hard in consistency, 5(10.20%) were fixed and 43(89.80%) were mobile. (Table 17)

Table 18: Descriptive Analysis Of Systemic Examination In The Study Population**(N=98)**

Systemic examination	Frequency	Percentages
CVS (S1 S2 heard)	98	100.00%
RS (Bilateral NVBS+)	98	100.00%
PA(NAD)	98	100.00%
CNS(NAD)	98	100.00%

On systemic examination, all 98 subject were found to be normal. (Table 18)

Table 19: Descriptive Analysis Of Diagnosis In The Study Population (N=98)

Diagnosis	Frequency	Percentages
Carcinoma Right Breast	53	54.08%
Carcinoma Left Breast	45	45.92%

Out of 98 participants, 53(54.08%) participants were diagnosed with carcinoma right breast and 45(45.92%) with carcinoma left breast. (Table 19 & figure 22)

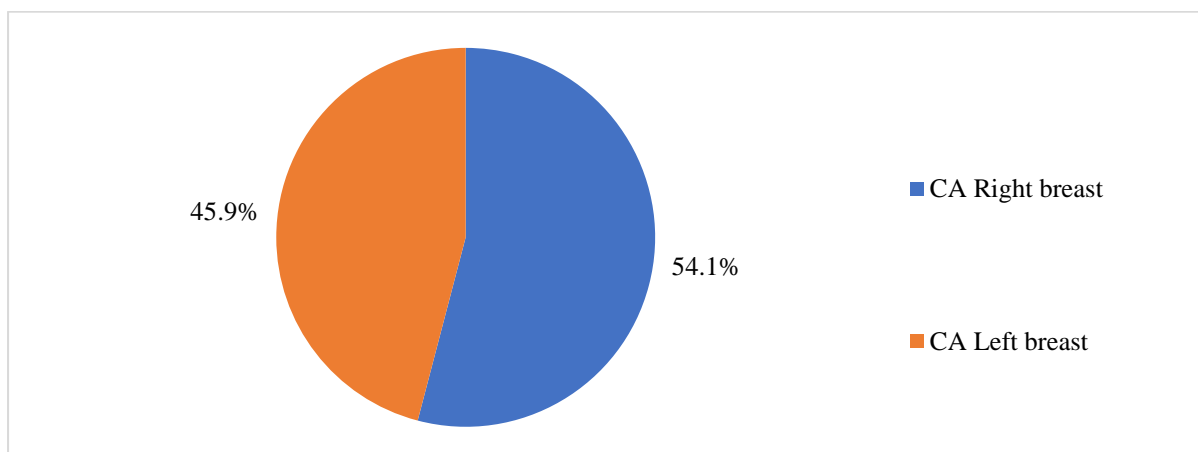
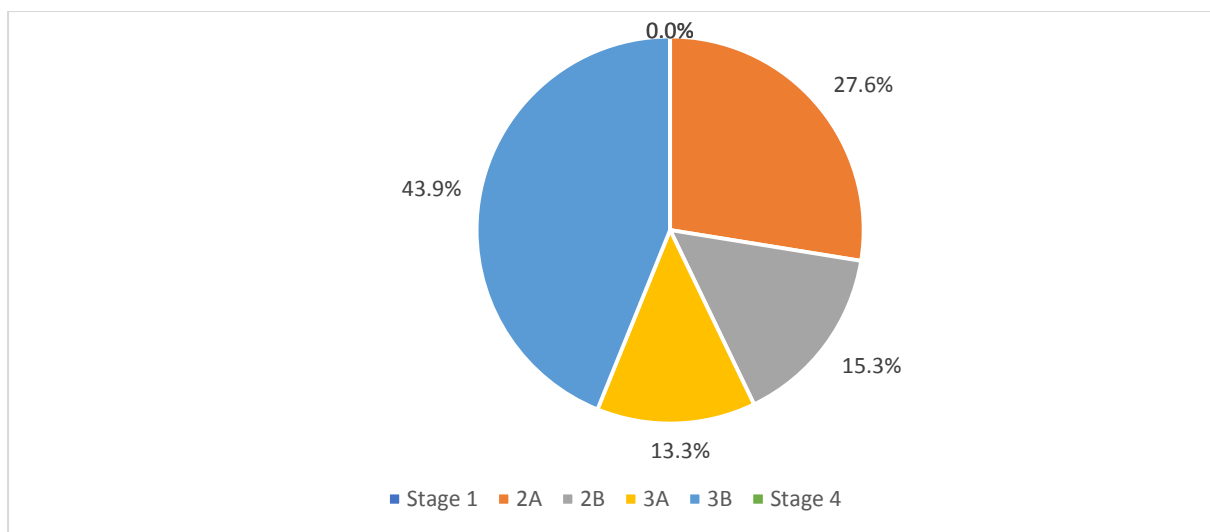
Figure 22: Pie Chart Of Diagnosis In The Study Population (N=98)

Table 20: Descriptive Analysis Of Staging In The Study Population (N=98)

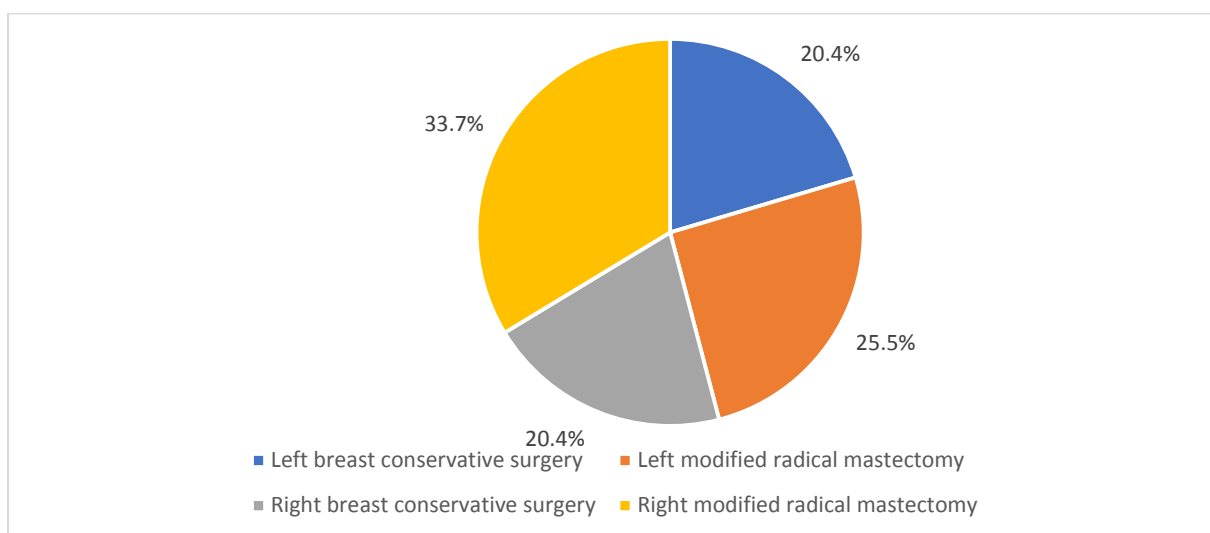
Staging	Frequency	Percentages
I	0	0%
IIA	27	27.55%
IIB	15	15.31%
IIIA	13	13.27%
IIIB	43	43.88%
IV	0	0%

Figure 23: Pie Chart Of Staging In The Study Population (N=98)

On staging the disease among the study population, most of them diagnosed with breast cancer were of stage IIIB(43.88%) followed by IIA(27.55%) (Table 20 & figure 23).

Table 21: Descriptive Analysis of Surgery Done In The Study Population (N=98)

Surgery Done	Frequency	Percentages
Left breast conservative surgery	20	20.41%
Left modified radical mastectomy	25	25.51%
Right breast conservative surgery	20	20.41%
Right modified radical mastectomy	33	33.67%

Figure 24: Pie Chart Of Surgery Done In The Study Population (N=98)

All the 98 subjects in the study population were managed surgically. 60% of them underwent modified radical mastectomy while 40% of the subjects underwent breast conservation surgery. (Table 21 & figure 24)

Table 22: Descriptive Analysis of Investigation Findings In The Study Population (N=98)

Investigation findings	Frequency	Percentages
Histopathology		
Infiltrating ductal carcinoma	98	100.00%
Estrogen receptor status		
Positive	43	43.88%
Negative	55	56.12%
Progesterone receptor status		
Positive	42	42.86%
Negative	56	57.14%
Her2Neu status		
Equivocal	2	2.04%
Positive	36	36.73%
Negative	60	61.22%

Among the investigation findings, all of them had infiltrating ductal carcinoma , 43(43.88%) had estrogen receptor positive status, 42(42.86%) had progesterone receptor positive status and 2(2.04%) had equivocal expression of hormone receptor status and 36(36.73%) had her2neu positivity (Table 22 & Figure 25 to 27)

Figure 25: Pie Chart of Estrogen Receptor Status In The Study Population (N=98)

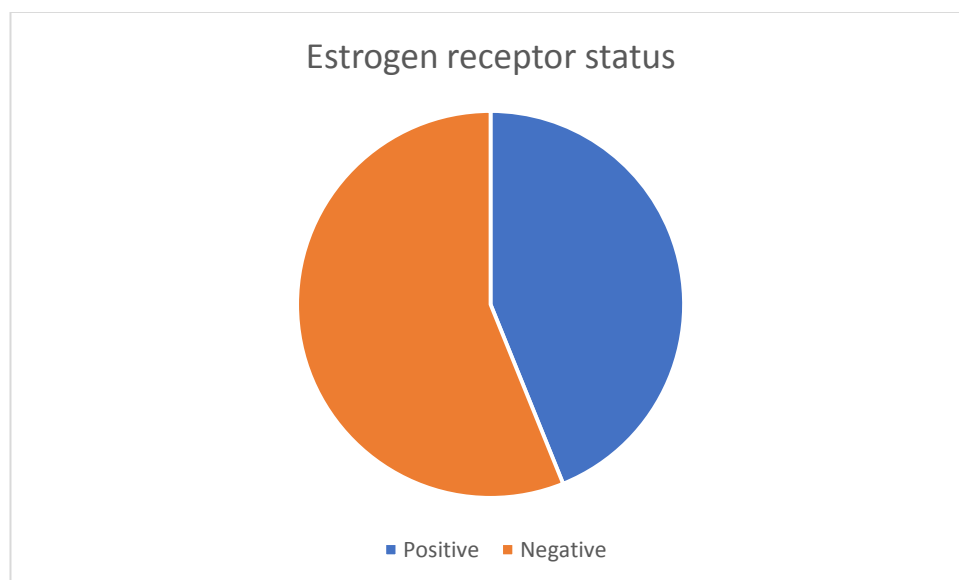


Figure 26: Pie Chart of Progesterone Receptor Status In The Study Population (N=98)

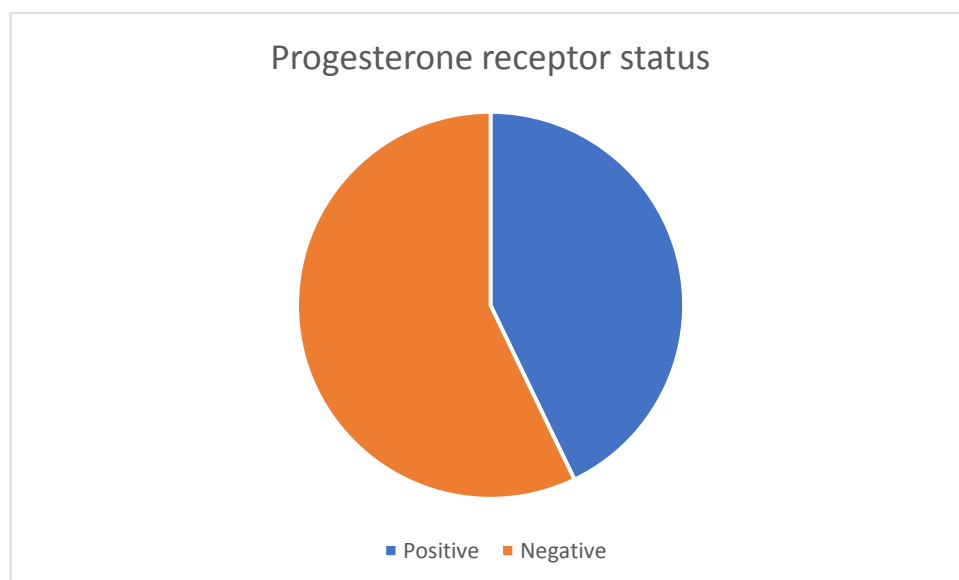


Figure 27: Pie Chart of Her2neu Status In The Study Population (N=98)

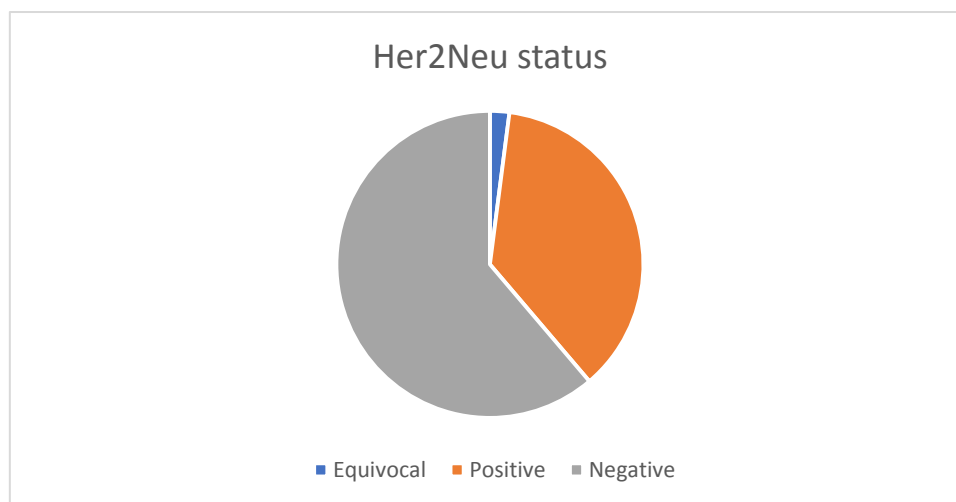


Table 23: Descriptive Analysis Of Ki 67 Classification In Study Population(N=98)

Ki 67 Classification	Frequency	Percentages
<20	29	29.59%
≥20	69	70.4%

Among the study population, 69(70.40%) had ki67 proliferation index ≥ 20 and 29(29.59%) had <20 . (Table 23 & figure 28)

Figure 28: Pie Chart Of Ki 67 Index In The Study Population (N=98)

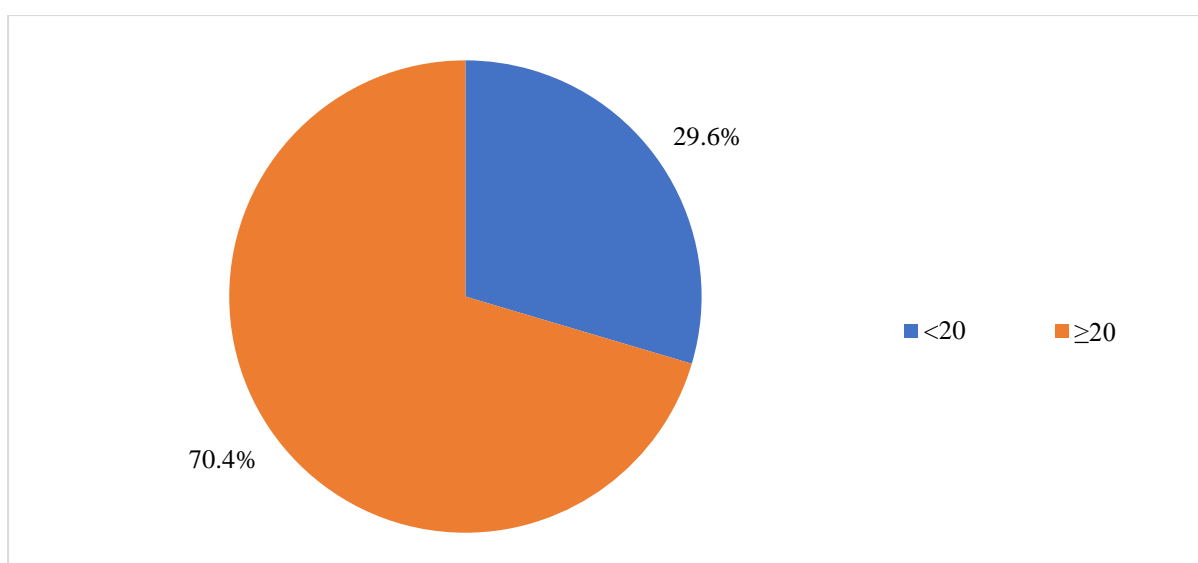


Table 24: Comparison Of Baseline Parameter With Ki 67 Index (N=98)

Age Group (in years)	Ki 67 Classification		P value
	<20	≥20	
Upto 30 years (N=2)	2 (100%)	0 (0%)	*
31 to 45 years (N=30)	4 (13.33%)	26 (86.67%)	
46 to 60 years (N=41)	10 (24.39%)	31 (75.61%)	
61 years (N=25)	13 (52%)	12 (48%)	
Duration of Lump			
≤6 Months (N=85)	22 (25.88%)	63 (74.12%)	0.053†
>6 Months (N=13)	7 (53.85%)	6 (46.15%)	

*No statistical test was applied- due to 0 subjects in the cells †-Fishers exact test

Among the study population, ki67 proliferation index ≥ 20 was more prevalent in all age groups and highest in the subjects of age group 46-60yrs. The difference in occupation between ki67 classification is found to be insignificant with a P- value of 1.000. Most subjects who presented with with a lump of duration ≤ 6 months had a ki67 index ≥ 20 . The difference in duration of lump between ki67 classification is found to be insignificant with a P- value of 0.053 (Table 24 & Figure 29)

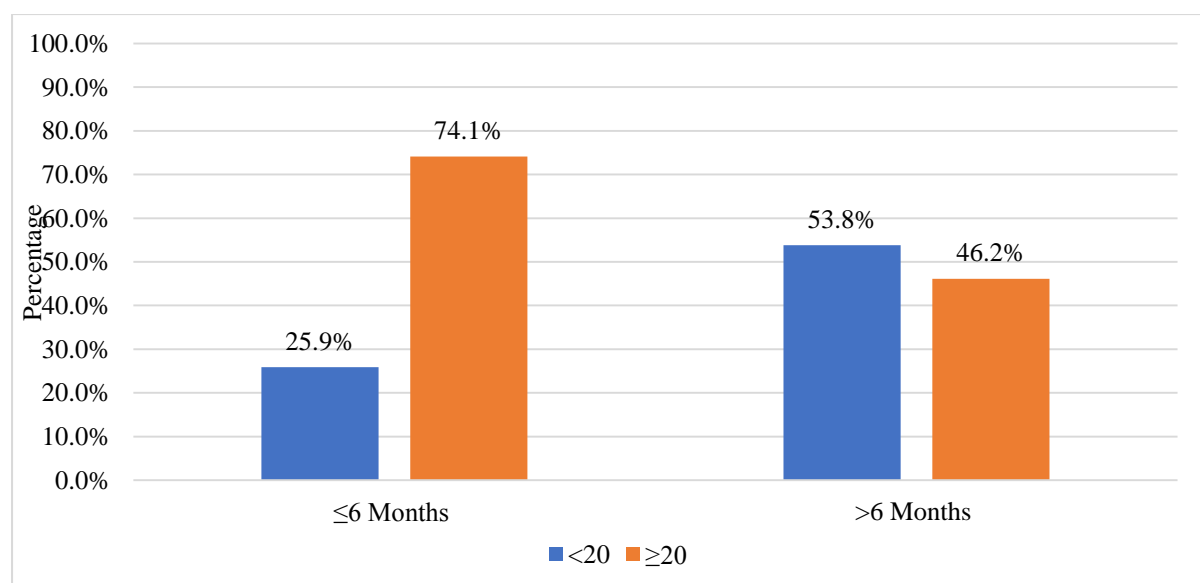
Figure 29: Cluster Bar Chart Of Comparison Of Duration Of Lump And Ki 67 Index (N=98)

Table 25: Comparison Of Examination Findings With Ki67 Index (N=98)

Parameter	Ki 67 Classification		P value
	<20	≥20	
Breast Symmetry			
Asymmetrical (N=89)	28 (31.46%)	61 (68.54%)	0.274†
Symmetrical (N=9)	1 (11.11%)	8 (88.89%)	
Nipple Retraction (N=16)	7 (43.75%)	9 (56.25%)	0.231†
Site			
Left-all quadrants (N=2)	0 (0%)	2 (100%)	*
Left lower outer quadrant (N=4)	0 (0%)	4 (100%)	
Left upper inner quadrant (N=5)	3 (60%)	2 (40%)	
Left upper outer quadrant (N=32)	8 (25%)	24 (75%)	
Right- all quadrants (N=5)	2 (40%)	3 (60%)	
Right lower inner quadrant (N=7)	2 (28.57%)	5 (71.43%)	
Right lower outer quadrant (N=5)	2 (40%)	3 (60%)	
Right upper inner quadrant (N=11)	4 (36.36%)	7 (63.64%)	
Right upper outer quadrant (N=27)	8 (29.63%)	19 (70.37%)	
Borders			
Ill defined (N=6)	1 (16.67%)	5 (83.33%)	0.667†
Well defined (N=92)	28 (30.43%)	64 (69.57%)	
Surface			
Irregular (N=12)	1 (8.33%)	11 (91.67%)	0.103†
Smooth (N=86)	28 (32.56%)	58 (67.44%)	
Skin Changes			
Peau d orange (N=22)	6 (27.27%)	16 (72.73%)	*
Tethering (N=13)	3 (23.08%)	10 (76.92%)	
Ulcer (N=13)	5 (38.46%)	8 (61.54%)	
Skin Nodules (N=1)	0 (0%)	1 (100%)	
None (N=49)	15 (30.61%)	34 (69.39%)	

*No statistical test was applied- due to 0 subjects in the cells †-Fishers exact test ‡- chi

square test

Out of 32 participants in left upper outer quadrant, 8 (25%) had <20 ki67 and 24(75%) had ≥ 20 ki67. out of 5 participants in right all quadrants, 2 (40%) had <20 ki67 and 3 (60%) had ≥ 20 ki67. Out of 7 participants in right lower inner quadrant, 2 (28.57%) had <20 ki67 and 5 (71.43%) had ≥ 20 ki67. Out of 5 participants in right lower outer quadrant, 2 (40%) had <20 ki67 and 3 (60%) had ≥ 20 ki67. Out of 11 participants in right upper inner quadrant, 4 (36.36%) had <20 ki67 and 7 (63.64%) had ≥ 20 ki67. Out of 27 participants in right upper outer quadrant, 8(29.63%) had <20 ki67 and 19 (70.37%) had ≥ 20 ki67. The difference in borders between ki67 classification is found to be insignificant with a P- value of 0.667. The difference in surface between ki67 classification is found to be insignificant with a P- value of 0.103. Among the skin changes, out of 22 participants in Peau d orange, majority 16(72.73%) had ≥ 20 ki67, out of 13 participants in tethering, majority 10 (76.92%) had ≥ 20 ki67. Out of 13 participants in ulcer, majority 8 (61.54%) had ≥ 20 ki67. And out of 1 participant, in skin nodules, all of them had ≥ 20 ki67. (Table 25 & figure 30)

Figure 30: Cluster Bar Chart Of Comparison Of Breast Symmetry And Ki 67 Index (N=98)

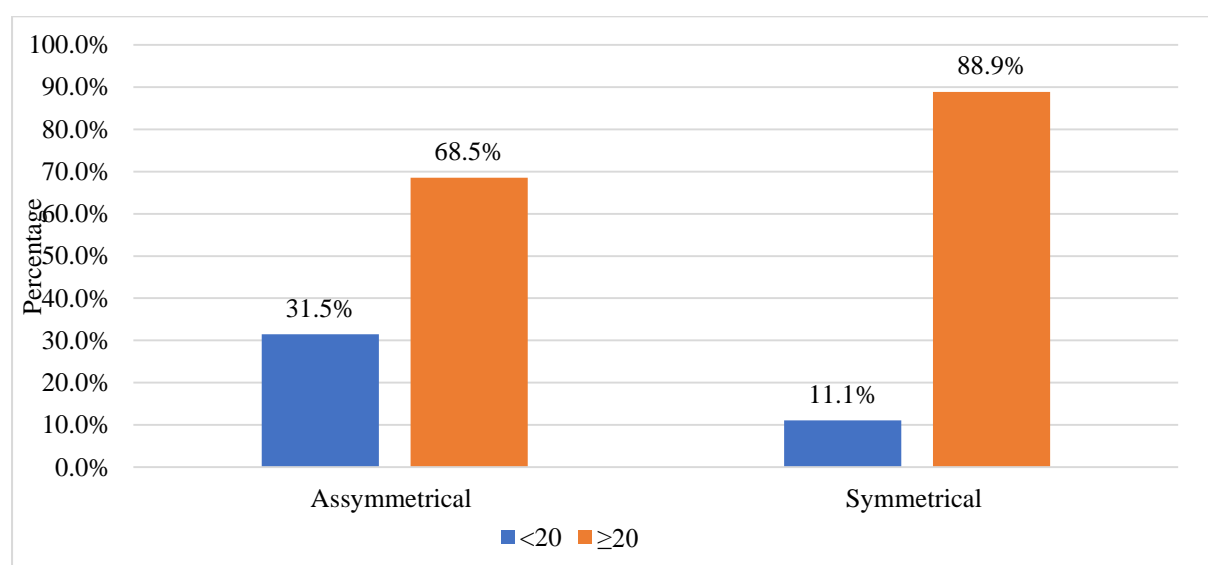


Table 26: Comparison Of Mean Size Of Lump With Ki 67 Index(N=98)

Parameter	KI 67 classification (Mean± SD)		P value
	<20 (N=29)	≥20 (N=69)	
Length (in cm)	5.17 ± 1.42	4.84 ± 1.61	0.339
Width (in cm)	4.24 ± 1.68	3.94 ± 1.63	0.414

The mean <20 ki67 classification in size of length was 5.17 ± 1.42cm and the ≥20 ki67 in length was .84 ± 1.61 cm, the association between two groups was statistically not significant (P value 0.339). The mean <20 ki67 classification in size of width was 4.24 ± 1.68 cm and the ≥20 ki67 in length was 3.94 ± 1.63cm, the association between two groups was statistically not significant (P value 0.414). (Table 26)

Table 27: Comparison Of Lymphadenopathy With Ki 67 Index (N=98)

Parameter	Ki 67 Classification		P value
	<20	≥20	
Axilla			
Single (N=42)	13 (30.95%)	29 (69.05%)	*
Multiple (N=6)	0 (0%)	6 (100%)	
No axillary lymphadenopathy (N=50)	16 (32%)	34 (68%)	
Consistency(N=49)			
Firm (N=2)	0 (0%)	2 (100%)	*
Hard (N=47)	14 (24.56%)	33 (70.21%)	
Fixity(N=49)			
Fixed /immobile(N=5)	3 (60%)	2 (40%)	*
Restricted mobility	0 (0%)	0 (0%)	
Mobile (N=44)	12 (27.27%)	32 (72.73%)	
Supraclavicular lymphadenopathy(N=1)	0 (0%)	1 (100%)	*

†-Fishers exact test ‡- chi square test *No statistical test was applied- due to 0 subjects in the cells

Out of 42 participants in single axilla, 13 (30.95%) had <20 ki67 classification and 29 (69.05%) had ≥ 20 had single axilla. Out of 6 participants in multiple axilla, 6 (100%) had ≥ 20 ki67 had single axilla. Out of 2 firm consistency, all of them 2 (100%) had. Out of 47 participants in hard consistency, 14 (24.56%) had <20 ki67 and 33 (70.21%) had ≥ 20 ki67 consistency.

Out of 49 participants in fixity, 5 participants were fixed/ immobile and 44 participants were mobile. Out of 1 participant, 1 (100%) had ≥ 20 ki67. (Table 27,figure 31)

Figure31: Cluster Bar Chart Of Comparison Of Axillary Lymphadenopathy With Ki 67

Index (N=98)

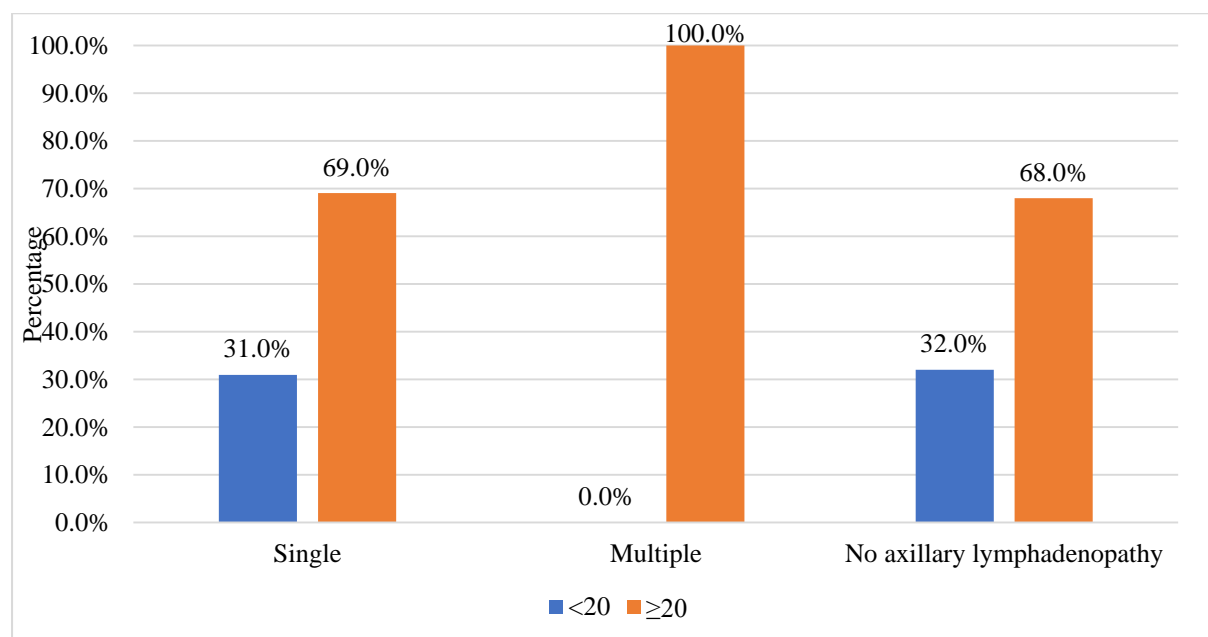


Table 28: Comparison Of Staging With Ki 67 Index (N=98)

Staging	Ki 67 Classification		Chi square	P value
	<20	≥20		
Stage I	0(0%)	0(0%)	2.556	0.465
IIA (N=27)	7 (25.93%)	20 (74.07%)		
IIB (N=15)	3 (20%)	12 (80%)		
IIIA (N=13)	6 (46.15%)	7 (53.85%)		
IIIB (N=43)	13 (30.23%)	30 (69.77%)		
Stage IV	0(0%)	0(0%)		

Stage IIIB (43) was the most prevalent stage among the subjects considered in the study.

Among them 30 had a ki67 index ≥ 20 which was not statistically significant. (Table 28)

Table 29: Comparison Of Investigation Findings With Ki 67 Index (N=98)

Investigation findings	Ki 67 Classification		P value
	<20	≥20	
Estrogen receptor			
Positive (N=43)	18 (41.86%)	25 (58.14%)	0.019
Negative (N=55)	11 (20%)	44 (80%)	
Progesterone receptor			
Positive (N=42)	19 (45.24%)	23 (54.76%)	0.003
Negative (N=56)	10 (17.86%)	46 (82.14%)	
Her2Neu			
Equivocal (N=2)	0 (0%)	2 (100%)	*
Positive (N=36)	9 (25%)	27 (75%)	
Negative (N=60)	20 (33.33%)	40 (66.66%)	

*No statistical test was applied- due to 0 subjects in the cells ‡- chi square test

On comparing positive estrogen receptor status and ki67, it is found to be significant with a P- value of 0.019 with majority of 25 (58.14%) participants had ≥ 20 ki67. The difference in positive progesterone receptor status and ki67 is found to be significant with a P- value of

0.003 with majority of 23 (54.76%) participants had ≥ 20 ki67. Out of 2 participants with equivocal receptor expression, all of them 2 (100%) had ≥ 20 ki67. Out of 36 participants in positive her2neu, majority 27 (75%) had ≥ 20 ki67. (Table 29 & figure 32, 33)

Figure 32: Cluster Bar Chart Of Comparison Of Estrogen Receptor With Ki 67 Index (N=98)

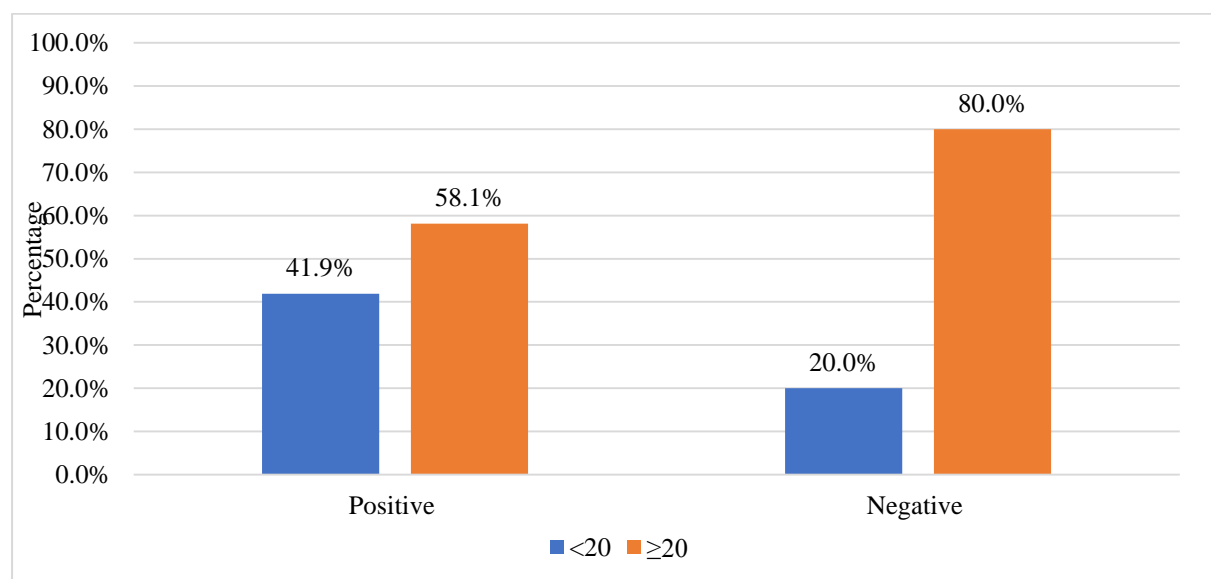
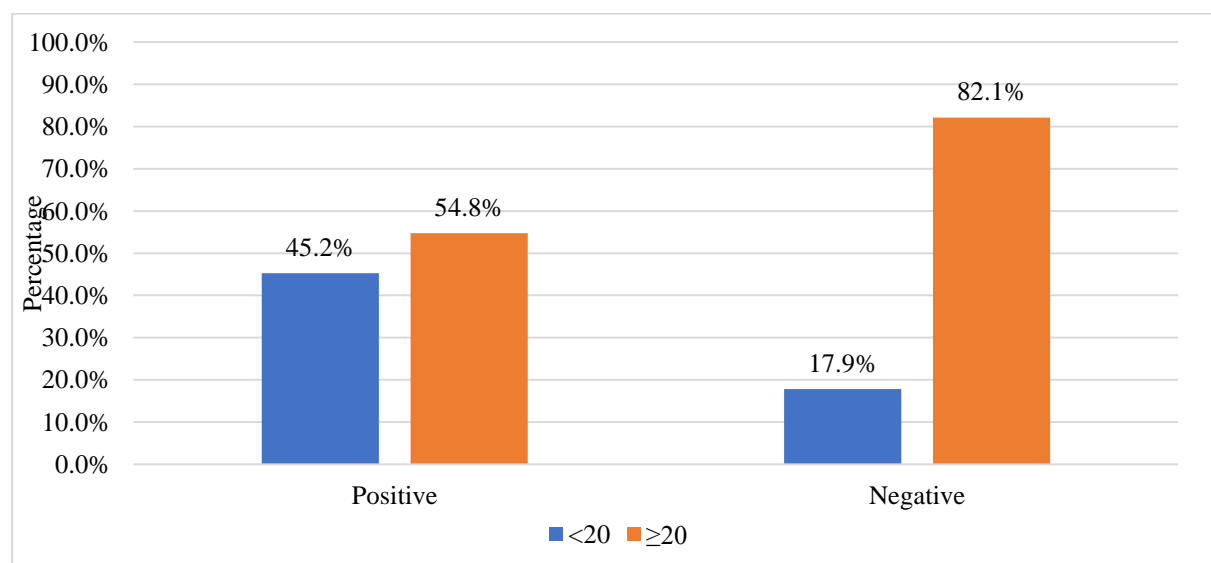


Figure 33: Cluster Bar Chart Of Comparison Of Progesterone Receptor With Ki 67 Index (N=98)



DISCUSSION



DISCUSSION:

The commonest cancer in women is breast cancer, which accounts for one-third of all malignancies in women. Breast cancer has a high spreading potential, resulting in a high mortality rate. Early discovery of this disease leads to a better prognosis and a higher survival rate. Prognostic markers such tumor size, grade, age, histological type and hormone receptor status influence the therapy decision. Proliferation is a defining feature of malignant tumours and a critical measure for predicting therapeutic response.⁶⁶ Ki 67 is a protein found in the nucleus in late G1, S, G2, and M phase of cell cycle, showing the proportion of cells capable of proliferating.⁶⁶ Tumor size, axillary lymph node involvement, nuclear grade, estrogen & progesterone receptor status, and HER2 status are all important biological markers in primary breast cancer. The goal of this study is to determine the utility of Ki 67 assay as a prognostic marker in BC, as well as its relationship to clinical and histological markers. Patients attending the General Surgery Department of R. L. Jalappa Hospital with biopsy proven carcinoma of the breast are included in the study. Ki-67 Proliferation index, is the primary outcome variable. Prognostic factors are explanatory variables.

A total of 98 patients with a mean age of 53.61 ± 12.48 years ranging from 30 to 80 years, out of which 54.08% with right breast lump and 45.92% with left breast lump were included in the final analysis. Our study is a cohort of females with biopsy proven breast carcinoma patients. Soliman et al. had a similar age group in their study with a mean age of 54.6 ± 12 years ranging from 31 to 88 years.⁸² The patients were aged between 20-75 years, with a mean age of 47.41 ± 11.36 years in Nigam et al.'s study.⁸³ The mean age of patients was 47.4 years (24 to 76 years) in Kamranzadeh et al.'s study.⁸⁴ Alco et al. had a study group with a median age of 49 years, ranging from 23 to 87 years, with 24.5% of the patients younger than 40 years old.⁸⁵

The mean duration of lump was 4.62 ± 2.18 months and only 6.12% had the complaint of pain. Among the comorbidities, 2.04% had carcinoma in the contralateral breast, 5.10% had diabetes and 11.22% had hypertension. Only 3.06% had family history of breast carcinoma. In our study group, majority of them had stage IIIB carcinoma at 43.88%, followed by stage IIA at 27.55%, 15.31% stage IIB, 13.27% stage IIIA. Approximately 42% of the patients were grade 2, and 95% of the cases displayed tumor size of more than 2 cm in Soliman et al.'s study.⁸² The most frequent stage of presentation was IIA (31.7%), followed by IIB and IIIB at 26.8% each, while stages IIIA (9.8%) and IIIC (4.9%) were under 10% in Madhushanker et al.'s study.⁸⁶

Table 30: Histopathological Features Of Subjects Across Studies

Study	Lymph node involvement		Histopathology	Estrogen receptor		Progesterone receptor		Her2Neu	
	+ve %	_ve %		+ve	_ve	+ve	_ve	+ve	_ve
Current study	48.98	51.02	IDC* 100%	43.88	56.12	42.86	57.14	36.73	61.22
Kamranzadeh et al. ⁸⁴	60.49	39.51		64.85	35.15	59.39	40.61	24.24	
Madhushankar. ⁸⁶	60	40	IDC* 93%	58.5		51.2		39.0	
Alco et al. ⁸⁵	45.2	54.8	IDC* 79.7%	81.4	18.6	66.9	33.1	21.4	78.6
Soliman et al. ⁸²	75.7	24.3	IDC* 94.4%	53.3	46.7	55.1	44.9	19.6	80.4

*IDC: Invasive ductal carcinoma

The appropriate cut-off point is still a matter of debate among oncologists. Hence, the most suitable cut-off point for Ki-67 in clinical practice is widely investigated.⁸⁷ Cases with $\geq 20\%$ positive nuclei were classified as high Ki-67 expression, and those with $< 20\%$ were classified as low Ki-67 expression in our study. At this cut off value, 70.40% had ≥ 20 Ki-67 & 29.59% had < 20 Ki-67 in our study. Soliman et al. used 15% as the cutoff point in their study,⁸² while Kamranzadeh et al.⁸⁴, Alco et al.⁸⁵, and Nigam et al.⁸³ considered Ki67 $> 10\%$ as positive status.⁸⁴ Liang et al. chose the median value of 15% for Ki-67 as the threshold.⁸⁸ In their study, Kermani et al. found that 53 percent of tumours were Ki-67 positive, with $> 1\%$ tumour nuclei stained, and 24 percent had tumours with more than 15% Ki-67 expression.⁸⁹ Kamranzadeh et al.⁸⁴ reported 69.16% of BC patients had Ki-67 $> 10\%$.

In our study, patients in the age group of 31 to 60 years, majority of them had ≥ 20 Ki-67 but age showed no significant association with Ki-67. Axillary nodal metastasis was one of the most important prognostic factors. The survival rate is determined by the number of lymph nodes involved, fixity, and the presence of extranodal extension. Duration of lump, mensural history, physical characteristics of the affected breast, physical characteristics of the lump, size of the lump, staging and nodal status showed no significant association with the Ki-67 expression. Kermani et al. discovered no correlation between Ki-67 expression and age, tumour size, or grade, but a marginally significant correlation between nodal status and Ki 67 expression.⁸⁹ At a cut off value of Ki-67 ≥ 20 , Ragab et al. reported as the tumor size increased, nodal affection increased and with advanced grade, Ki-67 expression showed higher values in their study.⁹⁰ In accordance with our study, Kamranzadeh et al. found no significant relationship between Ki-67 levels and menopausal status ($P = 0.53$), lymph node status, metastasis, or tumour size, but their findings revealed that Ki-67 levels were associated with BC stage ($P = 0.03$), higher levels of Ki-67 was found in more invasive tumours. In a prospective observational study, Madhushankar et al. observed that a high Ki-

67 index ($\geq 20\%$) significantly correlated with younger age demonstrating more aggressive tumor and has poor prognosis. They also found a positive relationship between lymph nodes involvement, histological grade, and the mean level of Ki67 expression.⁸⁶

Contrary to our finding, Min et al. found significant correlations between Ki-67 and clinicopathological findings such as age, tumour stage, size and necrosis, histological grade, extensive intraductal component, lymphovascular invasion (all $p < 0.05$).⁹¹ Nigam et al. discovered no significant correlation between Ki-67 and age, tumour size, lymph node status, lymphovascular invasion, perineural invasion, or histological grade, which is consistent with our findings.⁸³

Positive oestrogen receptor status is associated with a favourable response to hormone therapy, a good prognosis, and long disease-free and overall survival in breast cancer, however the progesterone receptor's enhanced prognostic and predictive utility has been a source of debate.⁹² While the expression of estrogen receptor had significant association with Ki-67 with p value 0.019 in our study, the expression of progesterone receptor also showed a significant correlation with Ki-67 with p 0.003 with 54.76% of the participants with positive progesterone receptor having ≥ 20 Ki-67. With regards to HER2Neu status, those with equivocal HER2Neu, all had ≥ 20 Ki-67 and those with positive HER2Neu, 75% had ≥ 20 Ki-67 but also among those with negative Her2Neu, 66.66% had ≥ 20 Ki-67. Therefore, based on Chi square test, our study demonstrated a significant association between expression of estrogen receptor, progesterone receptor and Ki-67. Similar to our findings, Kermani et al. discovered a strong link between the expression of the progesterone receptor and Ki-67, but their investigation also revealed a substantial association between the oestrogen receptor and Ki-67.⁸⁹ Ragab et al. found that the expression in estrogen receptor positive tumors showed lower values than estrogen negative tumors in their study. They

found higher Ki-67 expression more frequently associated with HER2-negative status, High Ki-67 index ($\geq 15\%$) was significantly correlated with ER-/PR- and also high tumor grade.⁹⁰

Solilman et al. found no significant association between high Ki-67 positivity and positive HER2/neu which may be due to the considerably small number of HER2+ positive cases in their study. They discovered that a high Ki-67 index (15%) was substantially associated with poor prognostic variables and ER/PR negative. Ki-67 expression is a predictor of disease-free survival and overall survival, according to their findings.⁸² Kamranzadeh et al.⁸⁴ found no evidence of a link between Ki-67 and prognostic variables such hormone receptors ($p = 0.29$) and HER2Neu status ($p = 0.65$). At Ki-67 $\geq 15\%$, Alco et al.'s study demonstrated it to be negatively correlated with ER/PR expression ($P < 0.001$). A younger age (≤ 40 years old), an IDC tumor type, HG/NG III, LVI, HR-negativity, HER-2 positivity and pT stage (tumor size) were revealed as poor prognostic factors associated with high expression levels of Ki-67.⁸⁵

Table 31: Association Of Ki-67 With Other Clinicopathological Factors Across Studies:

Study (year)	Ki-67	Not associated/correlated with	Associated/correlated with
Current study (2020)	<20 vs ≥ 20	Age, duration of lump, menstrual history, physical characteristics of the breast and lump, size of the lump, stage, lymph node involvement, ER expression, HER2Neu	ER expression, PR expression
Nigam et al. (2020) ⁸³	$\leq 10\%$ vs $> 10\%$	Age, tumor size, lymph node status, lymphovascular invasion, perineural invasion, histological grade, Nottingham prognostic	ER expression, Her2 expression

		index, PR expression, molecular subtypes	
Kamranzadeh et al. (2019) ⁸⁴	≤10 % vs >10%	Menopausal status, ER expression, PR expression, Her2 expression, lymph node involvement, tumor size, tumor grade	Pathological stage
Ragab et al. (2018) ⁹⁰	<20% vs >20%		Age, tumor grade, tumor size, lymph node involvement, ER expression, PR expression, Her2 expression
Soliman et al. (2016) ⁸²	<15% vs >15%	Age, tumor size, lymph node status, tumor stage, histological type, Her2 expression	Tumor grade, mitotic count, ER expression, PR expression, molecular subtype, alive or dead, recurrence and metastasis
Min et al. (2016) ⁹¹			ER expression, PR expression, HER2Neu and p53 expression

SUMMARY



SUMMARY

- A total of 98 patients with a mean age of 53.61 ± 12.48 years ranging from 30 to 80 years, out of which 54.08% with right breast lump and 45.92% with left breast lump were considered in the final analysis.
- The mean duration of lump was 4.62 ± 2.18 months and only 6.12% had the complaint of pain. Among the comorbidities, 2.04% had disease in the contralateral breast, 5.10% had diabetes and 11.22% had hypertension.
- 3.06% had positive family history of breast carcinoma. In our study group, majority of them had stage IIIB carcinoma at 43.88%, followed by stage IIA at 27.55%, 15.31% stage IIB, 13.27% stage IIIA.
- At a cut off value of 20%, 70.40% had ki67 proliferation index ≥ 20 and 29.59% had < 20 . in our study.
- In our study, patients in the age group of 31 to 60 years, majority of them had ≥ 20 Ki-67 but age showed no significant association with Ki-67.
- Duration of lump, menstrual history, physical characteristics of the effected breast, physical characteristics of the lump, size of the lump, stage, lymph node involvement had no significant association with the Ki-67 expression.
- While the expression of estrogen receptor had significant association with Ki-67 with p value 0.019 in our study with 58.14 % of the participants with positive estrogen receptor having ≥ 20 Ki-67, the expression of progesterone receptor showed a significant correlation with Ki-67 with p 0.003 with 54.76 % of the participants with positive progesterone receptor having ≥ 20 Ki-67. With regards to HER2Neu status, those with equivocal HER2Neu, all had ≥ 20 Ki-67 and those with positive HER2Neu,

75% had ≥ 20 Ki-67 but also among those with negative Her2Neu, 66.66% had ≥ 20 Ki-67.

- Based on Chi square test, our study demonstrated a significant association between expression of progesterone receptor, estrogen receptor and Ki-67.

CONCLUSION



CONCLUSION

Breast cancer is the most common cancer among women, and it is also the second largest cause of death. Prognostic factors are important in the diagnosis of breast cancer because they help identify patients who are at high risk. Proliferation of the cells is linked to a poor prognosis.⁸⁹ Ki-67 is a nuclear antigen, which exists in proliferative cells. This study is conducted in the Department of General Surgery, R.L. Jalappa Hospital, Kolar on a cohort of patients admitted with biopsy-proven diagnosis of carcinoma of breast from the period of Dec 2019 to June 2021. Proliferation index, Ki-67 is the primary outcome variable and prognostic factors are explanatory variables. A total of 98 patients with a mean age of 53.61 ± 12.48 years ranging from 30 to 80 years, out of which 54.08% with right breast lump and 45.92% with left breast lump are included in the final analysis. At a cut off value of 20%, 70.40% had ki67 proliferation index ≥ 20 and 29.59% had < 20 . In our study Age, duration of lump, menstrual history, physical characteristics of the effected breast, physical characteristics of the lump, size of the lump, staging and lymph node status had no significant association with the Ki-67 expression. Based on Chi square test, our study demonstrated a significant association between expression of estrogen & progesterone receptor with Ki-67.

LIMITATIONS

Because this was a single tertiary center study the sample size is small. To confirm these findings, large-scale population studies are required.

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BIBLIOGRAPHY

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ANNEXURES



PROFORMA

Name:

Age:

Sex:

Occupation:

UHID number:

Phone number:

Address:

DOA:

DOD:

Presenting complaints:

Previous history:

Family history:

Past history:

Menstrual history:

Obstetric history:

GENERAL PHYSICAL EXAMINATION:

- Built and nourishment:
- Pallor/Cyanosis/Icterus/Clubbing/edema/Generalized lymphadenopathy

VITAL DATA:

- Pulse:
- Temperature:
- BP:
- Respiration rate:

Systemic examination

- Per abdomen:
- Respiratory system:
- Cardio vascular system:
- Central nervous system:

LOCAL EXAMINATION:

Inspection:

- Site:
- Size:
- Symmetry: symmetrical/asymmetrical
- Number:
- Borders: well defined/ill defined
- Surface: smooth/irregular
- Skin changes:
 - Peau d'orange: yes / no
 - Dimpling: yes / no
 - Ulceration and fungation: yes / no
- Nipple discharge: yes / no
- Scars: yes / no

Palpation:

- Local rise of temperature: present / absent
- Tenderness: present / absent
- Number:
- Size:
- Borders: well defined / ill defined
- Consistency: soft / firm / hard
- Fluctuation: present / absent
- Transillumination: present / absent
- Surface: smooth / irregular
- Axillary lymphadenopathy:
 - Location:
 - Number:
 - Consistency:
 - Fixity
- Supraclavicular lymphadenopathy:
 - Number
 - Consistency
 - Fixity

INVESTIGATIONS:

Routine:

- Haemoglobin:
- Total count:
- Differential Count:
- ESR:
- Blood group:
- BT:
- CT:
- HIV:
- HBsAg:
- RBS:
- Blood urea:
- Serum creatinine:
- Chest X-ray:

Specific:

HISTOPATHOLOGICAL EXAMINATION:

Tumour grade:

Lymph node status:

ER: positive/negative

PR: positive/negative

Her2/neu: positive/negative

Ki67(%):

PATIENT INFORMATION SHEET

STUDY TITLE: “CORRELATION OF PROGNOSTIC FACTORS OF CARCINOMA BREAST WITH KI67 PROLIFERATION ASSAY”

GUIDE: DR. SREERAMULU.P. N

CO-GUIDE: DR. HEMALATHA.A

DR. MANJUNATH.G.N

STUDY CONDUCTED BY DR.Y. ROHIT KUMAR

Study location: R L Jalappa Hospital and Research Centre attached to Sri Devaraj Urs Medical College, Tamaka, Kolar.

The purpose of the study is explained in detail to us and all information collected is for study purpose only. The data collected is submitted to the department of surgery, SDUMC, Kolar and confidentiality ensured .The merits and demerits explained briefly to us

All Patients diagnosed with carcinoma breast will be included in this study. Patients in this study will undergo routine investigations, cbc ,rft, FNAC/Biopsy of breast tissue,ER,PR,Her2neu and in addition ki67 proliferation index will be done and correlation of clinical and pathological factors with ki67 will be done to find a significant correlation. Standard of the care will be maintained throughout the study.

Please read the following information and discuss with your family members. You can ask any question regarding the study. If you agree to participate in the study, we will collect information (as per proforma) from you or a person responsible for you or both. Relevant history will be taken. This information collected will be used only for dissertation and publication.

All information collected from you will be kept confidential and will not be disclosed to any outsider. Your identity will not be revealed. This study has been reviewed by the Institutional Ethics Committee and you are free to contact the member of the Institutional Ethics Committee.

There is no compulsion to agree to this study. The care you will get will not change if you don't

wish to participate. You are required to sign/ provide thumb impression only if you voluntarily agree to participate in this study.

For further information contact:

left thumb impression/signature of the patient

Dr.Y.Rohit Kumar [post graduate]

Department of General Surgery

SDUMC, Kolar

left thumb impression / signature of the witness

Phone number

8971056679

CONSENT FORM

Title: Assessment of Correlation of Prognostic Factors of Carcinoma Breast with ki67 Proliferation Assay

Principal investigator: Dr.Y.Rohit Kumar

I, Mrs. have been explained in my own understandable language, that I will be included in a study which is assessment of correlation of prognostic factors of carcinoma breast with ki67 proliferation assay, being conducted in RL JALAPPA HOSPITAL.

I have been explained that my clinical findings, investigations, preoperative and post-operative findings will be assessed and documented for study purpose.

I have been explained my participation in this study is entirely voluntary and I can withdraw from the study any time and this will not affect my relation with my doctor or treatment for my ailment.

I have been explained about the risk/benefit of the study.

I understand that the medical information produced by this study will become part of institutional records and will be kept confidential by my said institute.

I agree not to restrict the use of any data or result that arise from this study provided such a use is only for scientific purpose(s).

I have principal investigator mobile number for enquiries.

I have been informed that standard of care will be maintained throughout the treatment period.

I in my sound mind give full consent to be added in the part of this study.

Investigator: Dr.Y. Rohit Kumar

Participant's signature/ thumb impression

Name:

Signature/thumb impression of the witness:

Date:

Name:

Relation to patient

ರೋಗಿಯ ಮಾಹಿತಿ ನಮೂನೆ

ಅಧ್ಯಯನ ಶೀರ್ಷಿಕೆ : ಅನ್ನೂಡಿಯನ್ ಅನೇಸ್ಮೆಂಟ್ ಆಫ್ ಕೊರೋನಾ ವೈರಸ್ ಫ್ಯಾಲ್ಸ್ ಕಾರ್ಸಿನೋಮಾ ಸ್ತನ ಜೋತೆ ಕೆ167
ಪ್ರಮಾಣೀಕರಣ ಸಹಾಯದಿಂದ”

ಮಾರ್ಗದರ್ಶಿ: ಡಾ. ಶ್ರೀರಾಮೂಲು. ಪಿ.ಎನ್

ಡಾ.ರೋಹಿತ್ ಕುಮಾರ್ ಅವರಿಂದ ಅಧ್ಯಯನ

ಅಧ್ಯಯನ ಸ್ಥಳ: ಆರ್.ಎಲ್.ಜೆ. ಆಸ್ಪತ್ರೆ ಮತ್ತು ಸಂಶೋಧನಾ ಕೇಂದ್ರ, ಜೋಡಿಸಲಾದ ಶ್ರೀ ದೇವರಾಜ ಅರಸು ವೈದ್ಯಕೀಯ ಕಾಲೇಜು, ಟಮಕ, ಕೋಲಾರ.

ವಿವರಗಳು-

ವಿಷಯ ಆಯ್ಕೆ:

ನೀವು, ರೋಗಿಯನ್ನು ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಆಯ್ಕೆ ಮಾಡಲಾಗಿದೆ ಏಕೆಂದರೆ ನೀವು ಆಧಾರವಾಗಿರುವ ಸ್ಥಿತಿಯನ್ನು ಹೊಂದಿದ್ದೀರಿ.

ನಿಯೋಜ್ಯವಂಟ್ ಕೀಮೋಥರಪಿ ಮುಂಚಿತವಾಗಿ ಚಿಕಿತ್ಸೆ ನೀಡಿದ್ದರೆ ಮತ್ತು ನೀವು ಕಾರ್ಸಿನೋಮಾ ಸ್ತನದ ಪುನರಾವರ್ತಿತ ಪ್ರಕರಣವಾಗಿದ್ದರೆ ನೀವು ರೋಗಿಯನ್ನು ಈ ಅಧ್ಯಯನದಿಂದ ಹೊರಗಿಡಬಹುದಿತ್ತು.

ಕಾರ್ಸಿನೋಮಾ ಸ್ತನದಿಂದ ಕರ್ಣೀಯವಾಗಿರುವ ಎಲ್ಲಾ ರೋಗಿಗಳನ್ನು ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಸೇರಿಸಲಾಗುವುದು. ಈ ಅಧ್ಯಯನದ ರೋಗಿಗಳು ದಿನನಿತ್ಯದ ತನಿಖೆಗೆ ಒಳಗಾಗುತ್ತಾರೆ, ಸಿಬಿಸಿ, ಆರ್ಎಫ್ಪಿ, ಎಫ್ಎನ್ಎಸ್ / ಸ್ತನ ಅಂಗಾಂಶದ ಬಯಾಪ್ಸಿ ಮತ್ತು ಆಸ್ಪಿರಿ ದುಗ್ಧರಸ ಗ್ರಂಥಿ, ಇಆರ್, ಪಿಆರ್, ಹರ್ 2 ನ್ಯೂ ಮತ್ತು ಹೆಚ್ಚುವರಿಯಾಗಿ ಕಿ 67 ಪ್ರಸರಣ ಸೂಚ್ಯಂಕವನ್ನು ಮಾಡಲಾಗುವುದು ಮತ್ತು ಕಿ 67 ರೊಂದಿಗೆ ಕ್ಲಿನಿಕಲ್ ಮತ್ತು ರೋಗಶಾಸ್ತ್ರೀಯ ಅಂಶಗಳ ಪರಸ್ಪರ ಸಂಬಂಧವನ್ನು ಮಾಡಲಾಗುತ್ತದೆ. ಮಹತ್ವದ ಪರಸ್ಪರ ಸಂಬಂಧವನ್ನು ಕಂಡುಹಿಡಿಯಲು. ಅಧ್ಯಯನದ ಮೂಲಕ ಆರೈಕೆಯ ಗುಣಮಟ್ಟವನ್ನು ಕಾವಾಡಿಕೊಳ್ಳಲಾಗುತ್ತದೆ.

ದಯವಿಟ್ಟು ಈ ಕೆಳಗಿನ ಮಾಹಿತಿಯನ್ನು ಓದಿ ಮತ್ತು ನಿಮ್ಮ ಕುಟುಂಬ ಸದಸ್ಯರೊಂದಿಗೆ ಚರ್ಚಿಸಿ. ಅಧ್ಯಯನಕ್ಕೆ ಸಂಬಂಧಿಸಿದಂತೆ ನೀವು ಯಾವುದೇ ಪ್ರಶ್ನೆಯನ್ನು ಕೇಳಬಹುದು. ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸಲು ನೀವು ಒಪ್ಪಿದರೆ ನಾವು ನಿಮ್ಮಿಂದ ಜವಾಬ್ದಾರರಾಗಿರುವ ವ್ಯಕ್ತಿಯಿಂದ ಮಾಹಿತಿಯನ್ನು (ಪ್ರೊಫಾರ್ಮಾದ ಪ್ರಕಾರ) ಸಂಗ್ರಹಿಸುತ್ತೇವೆ. ಸಂಬಂಧಿತ ಇತಿಹಾಸವನ್ನು ತೆಗೆದುಕೊಳ್ಳಲಾಗುವುದು. ಸಂಗ್ರಹಿಸಿದ ಈ ಮಾಹಿತಿಯನ್ನು ಪ್ರಬಂಧ ಮತ್ತು ಪ್ರಕಟಣೆಗೆ ಮಾತ್ರ ಬಳಸಲಾಗುತ್ತದೆ.

ನಿಮ್ಮಿಂದ ಸಂಗ್ರಹಿಸಿದ ಎಲ್ಲಾ ಮಾಹಿತಿಯನ್ನು ಗೌಪ್ಯವಾಗಿರಿಸಲಾಗುವುದು, ಮತ್ತು ಯಾವುದೇ ಹೊರಗಿನವರಿಗೆ ಬಹಿರಂಗಪಡಿಸಲಾಗುವುದಿಲ್ಲ. ನಿಮ್ಮ ಗುರುತನ್ನು ಬಹಿರಂಗಪಡಿಸಲಾಗುವುದಿಲ್ಲ. ಈ ಅಧ್ಯಯನವು ಸಾಂಸ್ಥಿಕ ನೀತಿಶಾಸ್ತ್ರ ಸಮಿತಿಯಿಂದ ಪರಿಶೀಲಿಸಲ್ಪಟ್ಟಿದೆ ಮತ್ತು ನೀವು ಸಂಸ್ಥೆಯ ಸಾಂಸ್ಥಿಕ ನೈತಿಕ ಸಮಿತಿಯ ಸದಸ್ಯರನ್ನು ಸಂಪರ್ಕಿಸಲು ಮುಕ್ತರಾಗಿದ್ದೀರಿ. ಈ ಅಧ್ಯಯನಕ್ಕೆ ಒಪ್ಪಿಗೆ ನೀಡಲು ಯಾವುದೇ ಕಡ್ಡಾಯವಿಲ್ಲ ಮತ್ತು ಸಮಯದ ಯಾವುದೇ ಹಂತದಲ್ಲಿ ನೀವು ಅಧ್ಯಯನದಿಂದ ಹಿಂಪಡೆಯಲು ಸ್ವತಂತ್ರರಾಗಿರುತ್ತೀರಿ. ನೀವು ಭಾಗವಹಿಸಲು ಬಯಸದಿದ್ದರೆ ನೀವು ಪಡೆಯುವ ಕಾಳಜಿ ಬದಲಾಗುವುದಿಲ್ಲ. ಪ್ರಮಾಣಿತ ಪ್ರೋಟೋಕಾಲ್ ಪ್ರಕಾರ ರೋಗಿಯು ಸೂಕ್ತವಾದ ತನಿಖೆಗೆ ಒಳಗಾಗುತ್ತಾನೆ ಮತ್ತು ತನಿಖೆಗಳಿಗೆ ಹೆಚ್ಚುವರಿ ಶುಲ್ಕಗಳು ತೆಗೆದುಕೊಳ್ಳಲಾಗುವುದಿಲ್ಲ. ಈ ಅಧ್ಯಯನದಲ್ಲಿ ನೀವು ಸ್ವಯಂಪ್ರೇರಣೆಯಿಂದ ಒಪ್ಪಿಕೊಳ್ಳುವುದಾದರೆ ಮಾತ್ರ ಸಹಿ/ಹೆಬ್ಬೆಚ್ಚಿನ ಗುರುತು ಒದಗಿಸುವ ಅಗತ್ಯವಿದೆ.

ರೋಗಿಯ ಸಹಿ / ಹೆಬ್ಬರಳು ಗುರುತು

ಸಾಕ್ಷಿ ಸಹಿ / ಹೆಬ್ಬರಳು ಗುರುತು

ಹೆಚ್ಚಿನ ಮಾಹಿತಿಗಾಗಿ ಸಂಪರ್ಕಿಸಿ:

ಡಾ.ರೋಹಿತ್ ಕುಮಾರ್ [ಸ್ನಾತಕೋತ್ತರ ಪದವೀಧರ]

ಸಾಮಾನ್ಯ ಶಸ್ತ್ರಚಿಕಿತ್ಸೆ ಇಲಾಖೆ

SDUMC, ಕೋಲಾರ್

ದೂರವಾಣಿ ಸಂಖ್ಯೆ: 8971056679

ರೋಗಿಯ ತಿಳಿವಳಿಕೆಯ ಸಮ್ಮತಿ ನಮೂನೆ

ಅಧ್ಯಯನ ಶೀರ್ಷಿಕೆ : ಅಸ್ಕೂಡಿಯನ್ ಅನಿಸ್ಟೆಂಟ್ ಆಫ್ ಕೊರೋನಾ ವೈರಸ್‌ನ ಪ್ರಾಚೀನ ಕಾರ್ಬೋನೇಟ್ ಸ್ತನ ಕೆ167 ಪ್ರಮಾಣೀಕರಣ ಸಹಾಯದಿಂದ”

ಅನುಗುಣವಾದ ಲೇಖಕ: ಡಾ. ರೋಹಿತ್ ಕುಮಾರ್

ನಾನು ಶ್ರೀ/ಶ್ರೀಮತಿ..... ನನ್ನ ಸ್ವಂತ ಅರ್ಥವಾಗುವಂತಹ ಭಾಷೆಯಲ್ಲಿ ವಿವರಿಸಲಾಗಿದೆ. ನಾನು ನಡೆಸಿದ ಅಧ್ಯಯನದಲ್ಲಿ ನೇರಿಸಲಾಗುವುದು. ಅಸ್ಕೂಡಿಯನ್ ಅನಿಸ್ಟೆಂಟ್ ಆಫ್ ಕೊರೋನಾ ವೈರಸ್‌ನ ಪ್ರಾಚೀನ ಕಾರ್ಬೋನೇಟ್ ಸ್ತನ ಕೆ167 ಪ್ರಮಾಣೀಕರಣ ರೋಗನಿರ್ಣಯದ ಅಂಶಗಳ ಪರಸ್ಪರ ಸಂಬಂಧದ ಮೌಲ್ಯಮಾಪನವಾಗಿದೆ. ಅಧ್ಯಯನ ನನ್ನ ವೈದ್ಯಕೀಯ ಸಂಶೋಧನೆಗಳು, ತನಿಖೆಗಳು, ಅಧ್ಯಯನ ಉದ್ದೇಶಕ್ಕಾಗಿ ಮೌಲ್ಯಮಾಪನ ಮಾಡಲಾಗುವುದು ಮತ್ತು ದಾಖಲಾಗಿವೆ ಎಂದು ನನಗೆ ವಿವರಿಸಲಾಗಿದೆ.

ನನ್ನ ಕ್ಲಿನಿಕಲ್ ಅವಿಷ್ಕಾರಗಳು, ತನಿಖೆಗಳು, ಪೂರ್ವಭಾವಿ ಮತ್ತು ಶಸ್ತ್ರಚಿಕಿತ್ಸೆಯ ನಂತರದ ಸಂಶೋಧನೆಗಳನ್ನು ಮೌಲ್ಯಮಾಪನ ಮತ್ತು ಅಧ್ಯಯನದ ಉದ್ದೇಶಕ್ಕಾಗಿ ದಾಖಲಿಸಲಾಗುತ್ತದೆ ಎಂದು ನನಗೆ ವಿವರಿಸಲಾಗಿದೆ.

ಈ ಅಧ್ಯಯನದ ನನ್ನ ಪಾಲ್ಗೊಳ್ಳುವಿಕೆಯು ಸಂಪೂರ್ಣವಾಗಿ ಸ್ವಯಂಪ್ರೇರಿತವಾಗಿರುವುದನ್ನು ನಾನು ವಿವರಿಸಿದ್ದೇನೆ. ಮತ್ತು ಯಾವುದೇ ಸಮಯದಲ್ಲಿ ನಾನು ಈ ಅಧ್ಯಯನದಿಂದ ಹಿಂತೆಗೆದುಕೊಳ್ಳಬಹುದು ಮತ್ತು ಇದು ನನ್ನ ವೈದ್ಯರೊಂದಿಗೆ ನನ್ನ ಸಂಬಂಧವನ್ನು ಅಥವಾ ನನ್ನ ಕಾಯಿಲೆಯ ಚಿಕಿತ್ಸೆಗೆ ಪರಿಣಾಮ ಬೀರುವುದಿಲ್ಲ.

ನನ್ನ ಸ್ವಂತ ಅರ್ಥವಾಗುವ ಭಾಷೆಯಲ್ಲಿ ವಿವರಿಸಲಾಗಿದೆ. ಅನುಸರಣೆ ವಿವರಗಳು ಮತ್ತು ಸಂಭವನೀಯ ಪ್ರಯೋಜನಗಳು ಮತ್ತು ವಿಪತ್ತುಗಳ ಬಗ್ಗೆ ನನಗೆ ವಿವರಿಸಲಾಗಿದೆ.

ಅಧ್ಯಯನದ ಸಮಯದಲ್ಲಿ ನನ್ನ ವಿವರಗಳನ್ನು ಗೌಪ್ಯವಾಗಿರಿಸಲಾಗುವುದು, ಮತ್ತು ಪ್ರಕಟಣೆ ಮಾಡುವಾಗ ಅಥವಾ ಅವಿಷ್ಕಾರಗಳ ಹಂಚಿಕೆಯ ಸಂದರ್ಭದಲ್ಲಿ ನನ್ನ ವಿವರಗಳನ್ನು ಮರೆಮಾಡಲಾಗುವುದು ಎಂದು ನಾನು ಅರ್ಥಮಾಡಿಕೊಂಡಿದ್ದೇನೆ.

ವಿಚಾರಣೆಗಾಗಿ ನಾನು ಪ್ರಧಾನ ತನಿಖಾಧಿಕಾರಿ ಮೊಬೈಲ್ ಸಂಖ್ಯೆಯನ್ನು ಹೊಂದಿದೆ.

ನಾನು ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಸ್ವಯಂಪ್ರೇರಣೆಯಿಂದ ಸಮ್ಮತಿಯನ್ನು ನೀಡುತ್ತೇನೆ.

ತನಿಖಾಧಿಕಾರಿ: ಡಾ.ರೋಹಿತ್ ಕುಮಾರ್.ವೈ

ಭಾಗವಹಿಸುವವರ ಸಹಿ / ಹೆಬ್ಬರಳು ಅನಿಸಿಕೆ

ಹೆಸರು:

KEY TO MASTERCHART

R-ALL QUADRANTS	Right all quadrants
R-LO	Right lower outer quadrant
R-LI	Right lower inner quadrant
R- L 1/2	Right lower half
R-UO	Right upper outer quadrant
R-UI	Right upper inner quadrant
R-U 1/2	Right upper half
L-ALL QUADRANTS	Left All Quadrants
L-LO	Left lower outer quadrant
L-LI	Left lower inner quadrant
L- L 1/2	Left lower half
L-UO	Left upper outer quadrant
L-UI	Left upper inner quadrant
L-U 1/2	Left upper half
PDO	Peau'D Orange
NAD	No Abnormalities Detected
L-MRM	Left Modified Radical Mastectomy
R-MRM	Right Modified Radical Mastectomy
L-BCS	Left Breast conservation surgery
R-BCS	Right Breast conservation surgery
NEG	Negative
POS	Positive

MASTER CHART

S. No.	UID	AGE	COLOCATION	PRESENTING COMPLAINT	DURATION	ASSOCIATED COMPARIS	RAS HISTORY	FAMILY HISTORY	MEDICAL HISTORY	ONSET/CLINICAL	RASID	DOUGMENT	PALOR	EXTENS	CYNOSID	CLUBBING	GEN. UNWELL/ANOMALY	EDMA	SPINE	PULSES	BP	TEMPERATURE	HRP. RATE	BREAST SWELLING	NGUL RETRACTION	NGUL DISCHARGE	SCARS	STES	ROMBOS	SURFACE	SKIN CHANGES	UNWELL/ANOMALY	CONVULSIONAL BREAST	TEMPERATURE	TENDRUS	STES	NUMBER	SIZE	ROMBOS	SURFACE	COMFORT	MOBILITY	PULSATILITY	FLUCTUATION	TRANSLUMINATION	ANAL	CVS	RS	PA	ONS	ENDURANCE	STAGE	EMERGENTONE	HEALTHCARE	EX	PE	HRP. RATE	R. EP				
1	87679	18	HOUSEWIFE	LUMP IN LEFT BREAST	3 M	NIL	NIL	NIL	POST MENOPUSAL	P.12.1	MODERATE	MODERATE	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	NORMAL	82	110/70	98	AFEBRILE	14	ASYMMETRICAL	PRESENT	ABSENT	ABSENT	R. ALL QUADRANTS	R. ALL QUADRANTS	POO	NIL	NORMAL	NORMAL	TENDER	R. ALL QUADRANTS	SINGLE	7X7	WELL DEFINED	SMOOTH	HARD	FIXED TO BREAST TISSUE	ABSENT	ABSENT	ABSENT	MULTIPLE	HARD	MOBILE	ABSENT	51.52 HEARD	B/L W/BS +	NAD	NAD	CA LEFT BREAST	74891M	R. BMN	INFLTRATING DUCTA CA	NEG	NEG	POS	100%
2	873206	15	HOUSEWIFE	LUMP IN RIGHT BREAST	3 M	NIL	NIL	NIL	POST MENOPUSAL	P.12.1	MODERATE	MODERATE	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	NORMAL	80	120/80	98	AFEBRILE	15	ASYMMETRICAL	ABSENT	ABSENT	ABSENT	R. ALL QUADRANTS	R. ALL QUADRANTS	POO	NIL	NORMAL	NORMAL	NON TENDER	R. ALL QUADRANTS	SINGLE	5X5	WELL DEFINED	SMOOTH	HARD	FIXED TO BREAST TISSUE	ABSENT	ABSENT	ABSENT	SINGLE	HARD	MOBILE	ABSENT	51.52 HEARD	B/L W/BS +	NAD	NAD	CA RIGHT BREAST	74891M	R. BMN	INFLTRATING DUCTA CA	NEG	NEG	POS	100%
3	759213	15	HOUSEWIFE	LUMP IN RIGHT BREAST	4 M	NIL	NIL	NIL	REGULAR CYCLES	P.12.2	MODERATE	MODERATE	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	NORMAL	82	120/80	98	AFEBRILE	14	ASYMMETRICAL	PRESENT	ABSENT	ABSENT	R. ALL QUADRANTS	R. ALL QUADRANTS	POO	NIL	NORMAL	NORMAL	NON TENDER	R. ALL QUADRANTS	SINGLE	8X8	WELL DEFINED	SMOOTH	HARD	FIXED TO BREAST TISSUE	ABSENT	ABSENT	ABSENT	SINGLE	FRM	MOBILE	ABSENT	51.52 HEARD	B/L W/BS +	NAD	NAD	CA RIGHT BREAST	74891M	R. BMN	INFLTRATING DUCTA CA	NEG	NEG	POS	100%
4	81736	15	HOUSEWIFE	LUMP IN LEFT BREAST	3 M	NIL	HTN	NIL	POST MENOPUSAL	P.12.1	MODERATE	MODERATE	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	NORMAL	80	110/70	98	AFEBRILE	17	ASYMMETRICAL	PRESENT	ABSENT	ABSENT	R. ALL QUADRANTS	R. ALL QUADRANTS	POO	NIL	NORMAL	NORMAL	NON TENDER	R. ALL QUADRANTS	SINGLE	4X4	WELL DEFINED	SMOOTH	HARD	FIXED TO BREAST TISSUE	ABSENT	ABSENT	ABSENT	SINGLE	HARD	FIXED	ABSENT	51.52 HEARD	B/L W/BS +	NAD	NAD	CA LEFT BREAST	74891M	R. BMN	INFLTRATING DUCTA CA	NEG	NEG	POS	100%
5	812028	13	HOUSEWIFE	LUMP IN LEFT BREAST	3 M	NIL	NIL	NIL	REGULAR CYCLES	P.12.1	MODERATE	MODERATE	PRESENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	NORMAL	72	110/70	98	AFEBRILE	14	SYMMETRICAL	ABSENT	ABSENT	ABSENT	R. ALL QUADRANTS	R. ALL QUADRANTS	POO	NIL	NORMAL	NORMAL	NON TENDER	R. ALL QUADRANTS	SINGLE	7X5	ILL DEFINED	IRREGULAR	HARD	FIXED TO BREAST TISSUE	ABSENT	ABSENT	ABSENT	MULTIPLE	HARD	MOBILE	ABSENT	51.52 HEARD	B/L W/BS +	NAD	NAD	CA LEFT BREAST	74891M	R. BMN	INFLTRATING DUCTA CA	NEG	NEG	POS	100%
6	80441	46	HOUSEWIFE	LUMP IN RIGHT BREAST	4 M	NIL	HTN	NIL	POST MENOPUSAL	P.12.1	MODERATE	MODERATE	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	NORMAL	84	110/70	98	AFEBRILE	16	SYMMETRICAL	ABSENT	ABSENT	ABSENT	R. ALL QUADRANTS	R. ALL QUADRANTS	POO	NIL	NORMAL	NORMAL	NON TENDER	R. ALL QUADRANTS	SINGLE	6X6	WELL DEFINED	SMOOTH	HARD	FIXED TO BREAST TISSUE	ABSENT	ABSENT	ABSENT	SINGLE	HARD	MOBILE	ABSENT	51.52 HEARD	B/L W/BS +	NAD	NAD	CA RIGHT BREAST	74891M	R. BMN	INFLTRATING DUCTA CA	NEG	NEG	POS	100%
7	705227	43	HOUSEWIFE	LUMP IN RIGHT BREAST	3 M	NIL	NIL	NIL	IRREGULAR CYCLES	P.12.1	MODERATE	MODERATE	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	NORMAL	80	110/70	98	AFEBRILE	15	ASYMMETRICAL	ABSENT	ABSENT	ABSENT	R. ALL QUADRANTS	R. ALL QUADRANTS	POO	NIL	NORMAL	NORMAL	NON TENDER	R. ALL QUADRANTS	SINGLE	8X7	WELL DEFINED	SMOOTH	HARD	FIXED TO BREAST TISSUE	ABSENT	ABSENT	ABSENT	SINGLE	HARD	MOBILE	ABSENT	51.52 HEARD	B/L W/BS +	NAD	NAD	CA RIGHT BREAST	74891M	R. BMN	INFLTRATING DUCTA CA	NEG	NEG	POS	100%
8	786513	42	HOUSEWIFE	LUMP IN LEFT BREAST	4 M	NIL	NIL	NIL	IRREGULAR CYCLES	P.12.1	MODERATE	MODERATE	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	NORMAL	78	120/80	98	AFEBRILE	16	ASYMMETRICAL	PRESENT	ABSENT	ABSENT	R. ALL QUADRANTS	R. ALL QUADRANTS	POO	NIL	NORMAL	NORMAL	NON TENDER	R. ALL QUADRANTS	SINGLE	5X5	WELL DEFINED	SMOOTH	HARD	FIXED TO CHEST WALL	ABSENT	ABSENT	ABSENT	SINGLE	HARD	MOBILE	ABSENT	51.52 HEARD	B/L W/BS +	NAD	NAD	CA LEFT BREAST	74891M	R. BMN	INFLTRATING DUCTA CA	POS	POS	POS	100%
9	774433	45	LABOURER	LUMP IN LEFT BREAST	3 M	NIL	CA LEFT BREAST	NIL	POST MENOPUSAL	P.12.1	MODERATE	MODERATE	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	NORMAL	83	110/70	98	AFEBRILE	15	ASYMMETRICAL	ABSENT	ABSENT	ABSENT	R. ALL QUADRANTS	R. ALL QUADRANTS	POO	NIL	NORMAL	NORMAL	NON TENDER	R. ALL QUADRANTS	SINGLE	5X5	WELL DEFINED	SMOOTH	HARD	FIXED TO BREAST TISSUE	ABSENT	ABSENT	ABSENT	SINGLE	HARD	MOBILE	ABSENT	51.52 HEARD	B/L W/BS +	NAD	NAD	CA LEFT BREAST	74891M	R. BMN	INFLTRATING DUCTA CA	NEG	NEG	POS	100%
10	760394	30	HOUSEWIFE	LUMP IN RIGHT BREAST	3 M	NIL	NIL	NIL	REGULAR CYCLES	P.12.2	MODERATE	MODERATE	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	NORMAL	83	110/70	98	AFEBRILE	18	ASYMMETRICAL	ABSENT	ABSENT	ABSENT	R. ALL QUADRANTS	R. ALL QUADRANTS	POO	NIL	NORMAL	NORMAL	NON TENDER	R. ALL QUADRANTS	SINGLE	3X2	WELL DEFINED	SMOOTH	HARD	FIXED TO BREAST TISSUE	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	51.52 HEARD	B/L W/BS +	NAD	NAD	CA LEFT BREAST	74891M	R. BMN	INFLTRATING DUCTA CA	POS	POS	POS	100%
11	76046	30	HOUSEWIFE	LUMP IN RIGHT BREAST	3 M	NIL	CA LEFT BREAST	NIL	POST MENOPUSAL	P.12.1	MODERATE	MODERATE	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	NORMAL	82	110/70	98	AFEBRILE	16	ASYMMETRICAL	PRESENT	ABSENT	ABSENT	R. ALL QUADRANTS	R. ALL QUADRANTS	POO	NIL	NORMAL	NORMAL	NON TENDER	R. ALL QUADRANTS	SINGLE	3X2	WELL DEFINED	SMOOTH	HARD	FIXED TO BREAST TISSUE	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	51.52 HEARD	B/L W/BS +	NAD	NAD	CA LEFT BREAST	74891M	R. BMN	INFLTRATING DUCTA CA	POS	POS	POS	100%
12	755897	35	HOUSEWIFE	LUMP IN RIGHT BREAST	3 M	NIL	NIL	NIL	POST MENOPUSAL	P.12.1	MODERATE	MODERATE	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	NORMAL	82	120/80	98	AFEBRILE	18	ASYMMETRICAL	PRESENT	ABSENT	ABSENT	R. ALL QUADRANTS	R. ALL QUADRANTS	POO	NIL	NORMAL	NORMAL	NON TENDER	R. ALL QUADRANTS	SINGLE	4X3	WELL DEFINED	SMOOTH	HARD	FIXED TO BREAST TISSUE	ABSENT	ABSENT	ABSENT	SINGLE	HARD	MOBILE	ABSENT	51.52 HEARD	B/L W/BS +	NAD	NAD	CA RIGHT BREAST	74891M	R. BMN	INFLTRATING DUCTA CA	POS	POS	NEG	100%
13	83445	72	HOUSEWIFE	LUMP IN LEFT BREAST	2 M	NIL	NIL	NIL	POST MENOPUSAL	P.12.1	MODERATE	MODERATE	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	NORMAL	80	110/70	98	AFEBRILE	16	ASYMMETRICAL	ABSENT	ABSENT	PRESENT	R. ALL QUADRANTS	R. ALL QUADRANTS	POO	NIL	NORMAL	NORMAL	NON TENDER	R. ALL QUADRANTS	SINGLE	3X2	WELL DEFINED	SMOOTH	HARD	FIXED TO BREAST TISSUE	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	51.52 HEARD	B/L W/BS +	NAD	NAD	CA LEFT BREAST	74891M	R. BMN	INFLTRATING DUCTA CA	NEG	NEG	NEG	100%
14	820817	42	LABOURER	LUMP IN RIGHT BREAST	3 M	NIL	NIL	NIL	REGULAR CYCLES	P.12.1	MODERATE	MODERATE	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	NORMAL	82	130/80	98	AFEBRILE	15	ASYMMETRICAL	ABSENT	ABSENT	ABSENT	R. ALL QUADRANTS	R. ALL QUADRANTS	POO	NIL	NORMAL	NORMAL	NON TENDER	R. ALL QUADRANTS	SINGLE	4X5	WELL DEFINED	SMOOTH	HARD	FIXED TO BREAST TISSUE	ABSENT	ABSENT	ABSENT	SINGLE	HARD	MOBILE	ABSENT	51.52 HEARD	B/L W/BS +	NAD	NAD	CA RIGHT BREAST	74891M	R. BMN	INFLTRATING DUCTA CA	POS	POS	NEG	100%
15	834245	34	LABOURER	LUMP IN RIGHT BREAST	2 M	NIL	NIL	NIL	REGULAR CYCLES	P.12.2	MODERATE	MODERATE	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	NORMAL	84	100/60	98	AFEBRILE	18	ASYMMETRICAL	PRESENT	ABSENT	ABSENT	R. ALL QUADRANTS	R. ALL QUADRANTS	POO	NIL	NORMAL	NORMAL	NON TENDER	R. ALL QUADRANTS	SINGLE	5X5	ILL DEFINED	IRREGULAR	HARD	FIXED TO BREAST TISSUE	ABSENT	ABSENT	ABSENT	SINGLE	HARD	MOBILE	ABSENT	51.52 HEARD	B/L W/BS +	NAD	NAD	CA RIGHT BREAST	74891M	R. BMN	INFLTRATING DUCTA CA	NEG	NEG	POS	100%
16	840227	43	LABOURER	LUMP IN RIGHT BREAST	3 M	NIL	NIL	NIL	REGULAR CYCLES	P.12.1	MODERATE	MODERATE	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	NORMAL	82	120/80	98	AFEBRILE	16	ASYMMETRICAL	ABSENT	ABSENT	ABSENT	R. ALL QUADRANTS	R. ALL QUADRANTS	POO	NIL	NORMAL	NORMAL	NON TENDER	R. ALL QUADRANTS	SINGLE	8X7	WELL DEFINED	SMOOTH	HARD	FIXED TO BREAST TISSUE	ABSENT	ABSENT	ABSENT	SINGLE	HARD	MOBILE	ABSENT	51.52 HEARD	B/L W/BS +	NAD	NAD	CA RIGHT BREAST	74891M	R. BMN	INFLTRATING DUCTA CA	POS	POS	POS	100%
17	887319	70	HOUSEWIFE	LUMP IN RIGHT BREAST	6 M	NIL	NIL	NIL	POST MENOPUSAL	P.12.1	MODERATE	MODERATE	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	NORMAL	68	110/70	98	AFEBRILE	15	ASYMMETRICAL	PRESENT	ABSENT	ABSENT	R. ALL QUADRANTS	R. ALL QUADRANTS	POO	NIL	NORMAL	NORMAL	NON TENDER	R. ALL QUADRANTS	SINGLE	4X5	WELL DEFINED	SMOOTH	HARD	FIXED TO BREAST TISSUE	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	51.52 HEARD	B/L W/BS +	NAD	NAD	CA RIGHT BREAST	74891M	R. BMN	INFLTRATING DUCTA CA	POS	POS	NEG	100%
18	82008	45	LABOURER	LUMP IN LEFT BREAST	3 M	NIL	NIL	NIL	REGULAR CYCLES	P.12.2	MODERATE	MODERATE	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	NORMAL	76	140/70	98	AFEBRILE	16	ASYMMETRICAL	ABSENT	ABSENT	ABSENT	R. ALL QUADRANTS	R. ALL QUADRANTS	POO	NIL	NORMAL	LOCAL RISE +	TENDER	R. ALL QUADRANTS	SINGLE	7X5	WELL DEFINED	SMOOTH	HARD	FIXED TO BREAST TISSUE	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	51.52 HEARD	B/L W/BS +	NAD	NAD	CA LEFT BREAST	74891M	R. BMN	INFLTRATING DUCTA CA	POS	POS	NEG	100%
19	84805	40	LABOURER	LUMP IN RIGHT BREAST	3 M	NIL	NIL	NIL	REGULAR CYCLES	P.12.1	MODERATE	MODERATE	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	NORMAL	82	130/80	98	AFEBRILE	15	ASYMMETRICAL	ABSENT	ABSENT	ABSENT	R. ALL QUADRANTS	R. ALL QUADRANTS	POO	NIL	NORMAL	NORMAL	NON TENDER	R. ALL QUADRANTS	SINGLE	8X6	WELL DEFINED	IRREGULAR	HARD	FIXED TO BREAST TISSUE	ABSENT	ABSENT	ABSENT	MULTIPLE	HARD	MOBILE	ABSENT	51.52 HEARD	B/L W/BS +	NAD	NAD	CA RIGHT BREAST	74891M	R. BMN	INFLTRATING DUCTA CA	POS	POS	NEG	100%
20	85577	76	HOUSEWIFE	LUMP IN RIGHT BREAST	5 M	NIL	NIL	NIL	POST MENOPUSAL	P.12.1	MODERATE	MODERATE	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	NORMAL	88	130/80	98	AFEBRILE	17	ASYMMETRICAL	ABSENT	ABSENT	ABSENT	R. ALL QUADRANTS	R. ALL QUADRANTS	POO	NIL	NORMAL	NORMAL	NON TENDER	R. ALL QUADRANTS	SINGLE	5X3	WELL DEFINED	SMOOTH	HARD	FIXED TO BREAST TISSUE	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	51.52 HEARD	B/L W/BS +	NAD	NAD	CA RIGHT BREAST	74891M	R. BMN	INFLTRATING DUCTA CA	NEG	NEG	POS	100%
21	84805	40	LABOURER	LUMP IN RIGHT BREAST	3 M	NIL	NIL	NIL	REGULAR CYCLES	P.12.1	MODERATE	MODERATE	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	NORMAL	82	110/70	98	AFEBRILE	16	ASYMMETRICAL	ABSENT	ABSENT	ABSENT	R. ALL QUADRANTS	R. ALL QUADRANTS	POO	NIL	NORMAL	NORMAL	NON TENDER	R. ALL QUADRANTS	SINGLE	8X7	WELL DEFINED	SMOOTH	HARD	FIXED TO BREAST TISSUE	ABSENT	ABSENT	ABSENT	SINGLE	HARD	MOBILE	ABSENT	51.52 HEARD	B/L W/BS +	NAD	NAD	CA RIGHT BREAST	74891M	R. BMN	INFLTRATING DUCTA CA	POS	POS	NEG	100%
22	82475	31	LABOURER	LUMP IN RIGHT BREAST	4 M	NIL	NIL	NIL	REGULAR CYCLES	P.12.1	MODERATE	MODERATE	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	NORMAL	84	120/80	98	AFEBRILE	18	ASYMMETRICAL	ABSENT	ABSENT	ABSENT	R. ALL QUADRANTS	R. ALL QUADRANTS	POO	NIL	NORMAL	NORMAL	NON TENDER	R. ALL QUADRANTS	SINGLE	4X3	WELL DEFINED	SMOOTH	HARD	FIXED TO BREAST TISSUE	ABSENT	ABSENT	ABSENT	SINGLE	HARD	MOBILE	ABSENT	51.52 HEARD	B/L W/BS +	NAD	NAD	CA RIGHT BREAST	74891M	R. BMN	INFLTRATING DUCTA CA	NEG	NEG	POS	100%
23	80757	40	LABOURER	LUMP IN RIGHT BREAST	6 M	NIL	HTN	NIL	POST MENOPUSAL	P.12.1	MODERATE	MODERATE	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	NORMAL	80	140/80	98	AFEBRILE	16	ASYMMETRICAL	PRESENT	ABSENT	ABSENT	R. ALL QUADRANTS	R. ALL QUADRANTS	POO	NIL	NORMAL	NORMAL	NON TENDER	R. ALL QUADRANTS	SINGLE	6X6	WELL DEFINED	SMOOTH	HARD	FIXED TO BREAST TISSUE	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	51.52 HEARD	B/L W/BS +	NAD	NAD	CA LEFT BREAST	74891M	R. BMN	INFLTRATING DUCTA CA	POS	POS	NEG	100%
24	820817	42	LABOURER	LUMP IN RIGHT BREAST	3 M	NIL	NIL	NIL	REGULAR CYCLES	P.12.1	MODERATE	MODERATE	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	NORMAL	82	130/80	98	AFEBRILE	15	ASYMMETRICAL	ABSENT	ABSENT	ABSENT	R. ALL QUADRANTS	R. ALL QUADRANTS	POO	NIL	NORMAL	NORMAL	NON TENDER	R. ALL QUADRANTS	SINGLE	5X4	WELL DEFINED	SMOOTH	HARD	FIXED TO BREAST TISSUE	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	51.52 HEARD	B/L W/BS +	NAD	NAD	CA RIGHT BREAST	74891M	R. BMN	INFLTRATING DUCTA CA	POS	POS	NEG	100%
25																																																														