Innovations

A Complete Guide to Breast Cancer and its Management

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Abstract: *Breast cancer remains a major global health concern, characterized by heterogeneous histopathological and molecular subtypes that influence prognosis and therapeutic response. Both modifiable factors, including lifestyle, diet, obesity, and alcohol use, and non-modifiable factors, such as genetics, hormonal influences, and family history, contribute to disease risk. Advances in diagnostic tools—mammography, ultrasound, MRI, and confirmatory biopsy—have improved early detection and accuracy. Current treatment strategies integrate surgery, chemotherapy, radiotherapy, hormone therapy, immunotherapy, and targeted therapy, while non-pharmacological measures such as lifestyle modification and psychosocial support enhance outcomes. Despite progress, triple-negative breast cancer, accounting for 15–25% of cases, remains a therapeutic challenge due to its aggressive course and limited responsiveness to conventional regimens. Male breast cancer, though rare, warrants equal recognition in diagnosis and management. Preventive strategies and awareness programs, such as Pink Ribbon initiatives, further improve survival through early detection. A comprehensive understanding of breast cancer biology, diagnostics, and personalized therapy is crucial, with future directions emphasizing precision medicine, predictive biomarkers, and innovative therapies tailored to individual tumor characteristics.*

Key Words: *Breast cancer Types, Risk factors, Pathophysiology, Signs & symptoms, Treatment*

Introduction

Breasts are present in both sexes but serve different roles. In females, they produce milk for nursing and contribute to sexual pleasure [1,2], while in males they have no biological function but remain sensitive and erotically responsive [3].Externally, the most visible parts are the nipples and areolas, with most people having two breasts [4].

Anatomy of Breast:

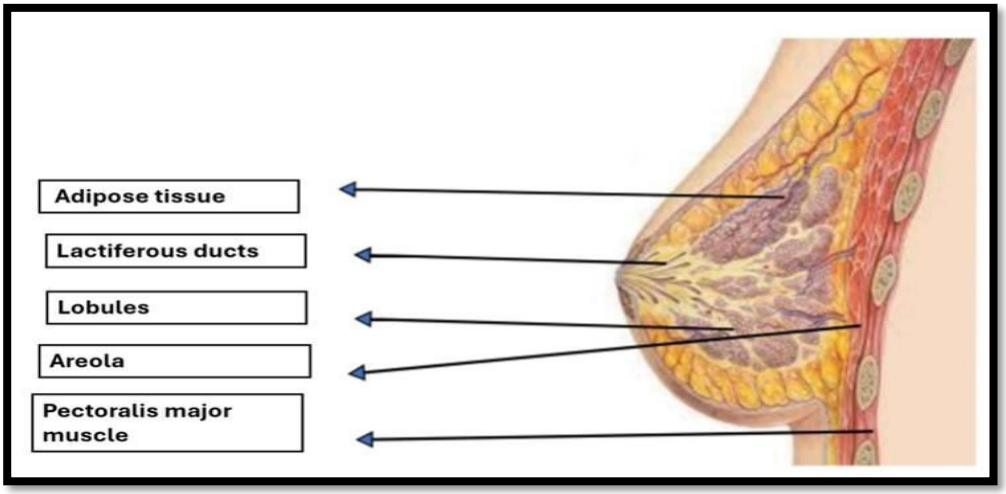


Fig 1. Anatomy of Breast

The female breast consists mainly of adipose tissue extending from the collarbone to the armpit [5]. Each breast has 15–20 lobes with lobules that produce milk, connected by ducts leading to the nipple [6]. The nipple, rich in nerve endings and milk ducts, sits at the center of the areola, which contains Montgomery's glands for lubrication [7]. Blood vessels support metabolism, lymphatics drain to chest/axillary nodes for immune defense, and nerves—especially in the nipple–areola complex confer high sensitivity [7,8].

Physiology of breast:

Breast development and function are regulated by hormones: oestrogen promotes ductal growth, progesterone (with prolactin) enlarges lobules and dilates breast cells, and prolactin with oxytocin drives milk production and the let-down reflex [9].

Pathophysiology of breast cancer:

Breast cancer arises from malignant growth of breast cells, with risks linked to oestrogen exposure, BRCA1/2 or p53 mutations, DNA damage, and family history. Failure of immune surveillance and DNA repair, along with disrupted stromal–

epithelial signaling via factors like TGF-β and pathways such as Notch, Wnt and NF-κB, drive tumor initiation and progression [10].

Types of Carcinoma:

More than 95 percent of breast cancers are adenocarcinomas, which originate as non-invasive carcinoma in situ in the milk ducts and lobules; however, approximately 70 percent progress by the time of diagnosis, having penetrated the basement membrane to invade surrounding stromal tissue [11].

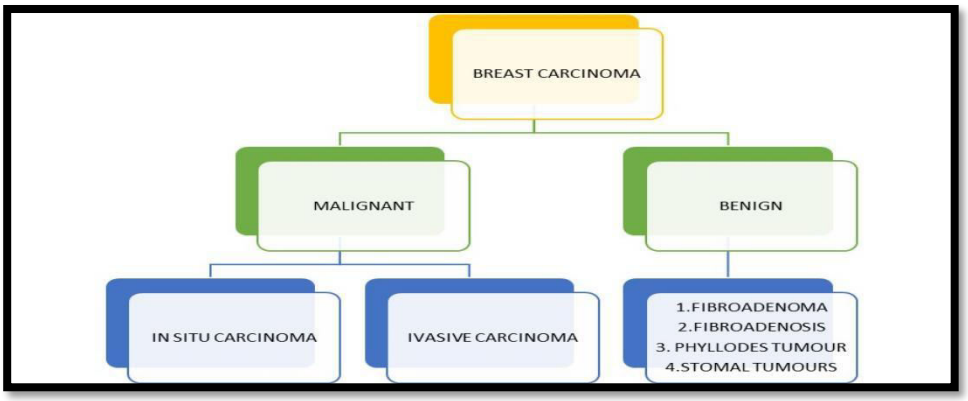


Fig 2. Flow Chart

Fibro Adenoma

Fibro adenomas are benign breast tumors ranging from <1 cm to large masses, typically firm, well-circumscribed, and gray-white with smooth stroma and slit-like space. Histology shows intracanalicular (compressed ducts) or pericanalicular (stromal encasement) patterns. In older women, stromal hyalinization and epithelial shrinkage are common [12].

Fibrocystadenosis

Cyclical mastalgia with nodularity, classified under ANDI, reflects benign hormonedriven breast changes during development and involution. It commonly presents in menstruating women as bilateral, tender, granular breast lumps that worsen premenstrually, sometimes with a blood-good (blue dome) cyst [13].

Phyllodes tumor

Phyllodes tumors range from small nodules to large breast masses, often showing leaf-like stromal projections into cystic spaces, sometimes resembling fibroadenomas. Key distinguishing features include stromal cellularity, mitotic activity, nuclear atypia, stromal overgrowth, and infiltrative margins. Benign tumors show mild atypia and low mitoses, while malignant forms exhibit marked pleomorphism, high mitotic rates

(≥10/10 HPF), stromal overgrowth, infiltrative borders, and occasional heterologous sarcomatous elements [14].

Stromal tumor

The breast has two stromal types: Intralobular stroma, giving rise to biphasic tumors like fibroadenomas and phyllodes tumors via stromal–epithelial interactions, and interlobular stroma, which produces connective tissue–type lesions such as fibrous tumors, myofibroblastomas and stromal hyperplasias [15].

Carcinoma In-situ

- **Ductal carcinoma In-situ**

There are two primary architectural types of DCIScomedo and non-comedoyet most DCIS display a mixed array of growth patterns rather than a single architecture; importantly, nuclear grade and the presence of necrosis are more reliable predictors of local recurrence and disease progression than the architectural subtype itself [16].

- **Comedo DCIS:**

Although DCIS is primarily detected via mammography often appearing as clusters or linear arrangements of microcalcificationsit can occasionally present as a subtle palpable thickening or lump. Histologically, DCIS is characterized by atypical, high-grade nuclei in the cancer cells and frequently exhibits necrosis, resulting from compromised blood supply [17].

- **Non-comedo DCIS**

Non-comedo DCIS lacks central necrosis and high-grade nuclei, presenting with patterns such as cribriform (Swiss-cheese spaces), micropapillary (bulbous epithelial projections without fibrovascular cores), and papillary (true papillae with central cores but absent myoepithelial layer). Calcifications may also occur, linked to intraductal secretions or focal necrosis [18].

- **Lobular carcinoma In-situ**

LCIS consists of uniform, discohesive cells with oval/round nuclei, signet-ring forms, and loss of E-cadherin, filling lobules and sometimes spreading into ducts (pagetoid spread). It typically lacks calcification, necrosis, secretory activity, and nipple involvement, though pagetoid ductal extension may occur. Immunohistochemically, LCIS is ER/PR-positive and HER2-negative [19].

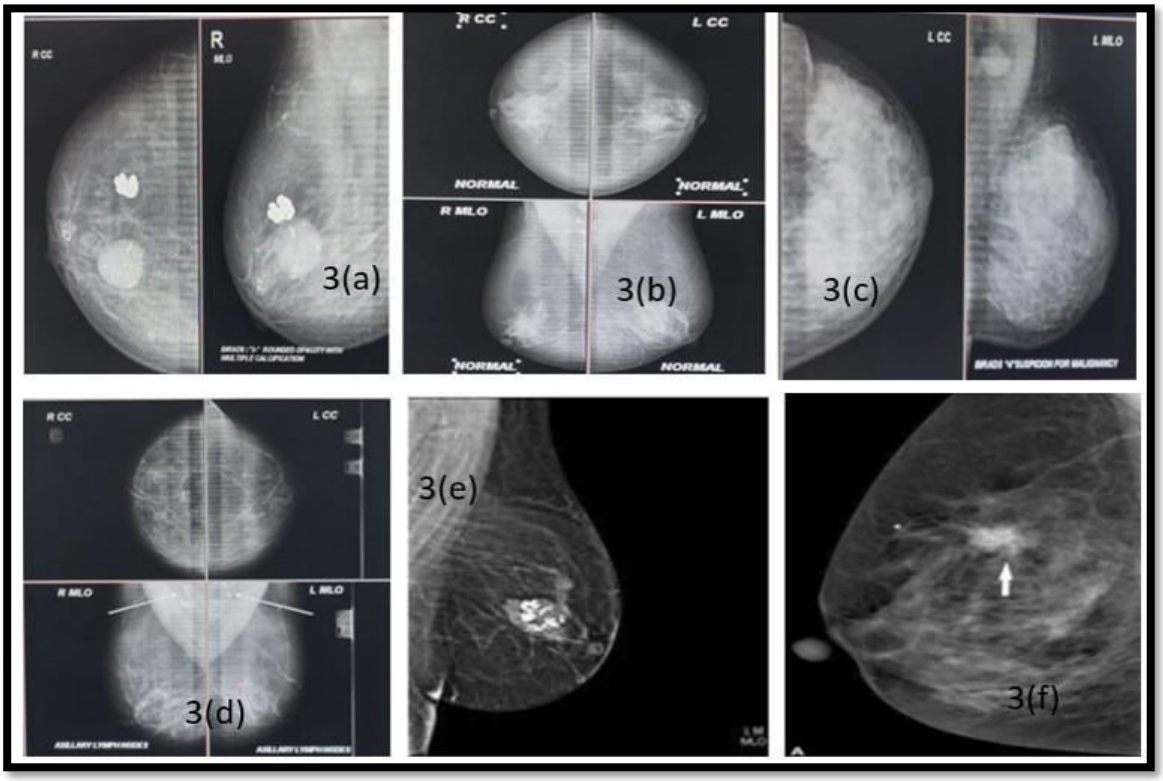
Invasive carcinoma:

On mammography, invasive carcinomas appearing only as classification are usually small (<1 cm), whereas without screening they often present as larger masses (>2–3 cm) [20]. Their appearance varies with stroma, typically showing hard, irregular masses and a grating sound on sectioning from fibrosis. Larger tumors may cause skin dimpling, chest wall tethering, or nipple retraction, and sometimes metastasis

precedes detection of the primary lesion, especially in dense breasts or with weak desmoplastic response [21]. MRI and ultrasound now improve identification of such hidden tumors [22].

Male breast cancer:

Male breast cancer accounts for ~1% of all breast cancers, with a lifetime risk of ~0.11%. In the U.S., ~2,000 cases and 400 deaths occur annually [23,24]. Risk factors mirror those in womenage, family history, oestrogen exposure, radiation, obesity, infertility, and benign breast diseasewith higher rates of ER positivity in men [25]. Due to limited breast tissue, presentation is often nipple discharge or subareolar lumps (2–3 cm), with early skin or chest wall invasion. Metastatic patterns resemble those in women. Management parallels female breast cancer, with mastectomy and axillary dissection for local disease and systemic therapies achieving similar outcomes [26].



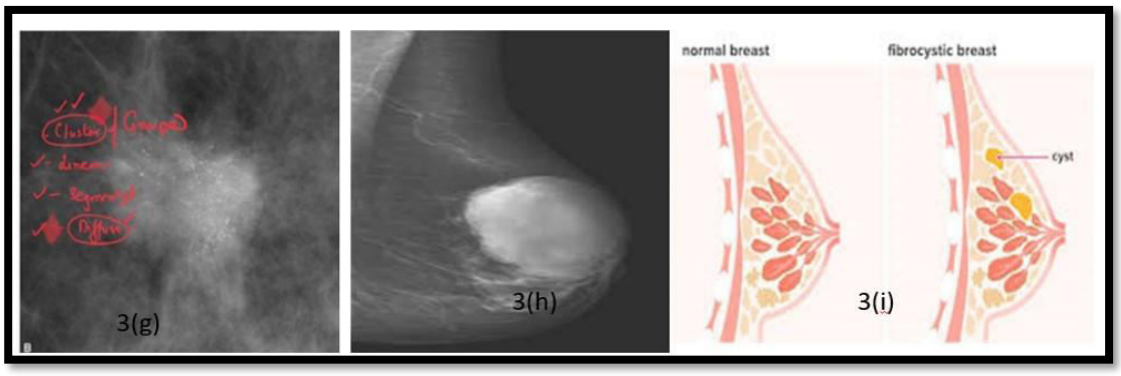


Fig. 3(a). Right breast mammogram (CC and MLO views) showing rounded opacity with multiple calcifications (BI-RADS3). 3(b). Bilateral mammogram (CC and MLO views) showing normal findings. 3(c).Left breast mammogram (CC and MLO views) showing suspicious mass, categorized as BI-RADS4. 3(d). Bilateral mammogram (CC and MLO views) showing axillary lymph nodes. 3(e) Mammogram (MLO view) showing clustered calcifications suggestive of malignancy. 3(f). Mammogram showing an irregular spiculated mass (arrow) highly suggestive of malignancy. 3(g). Mammogram demonstrating grouped (clustered) microcalcifications with annotations for distribution patterns. 3(h). Mammogram showing a well circumscribed breast mass suggestive of a tumor. 3(i). Comparison of a normal breast and a fibrocystic breast showing cyst formation

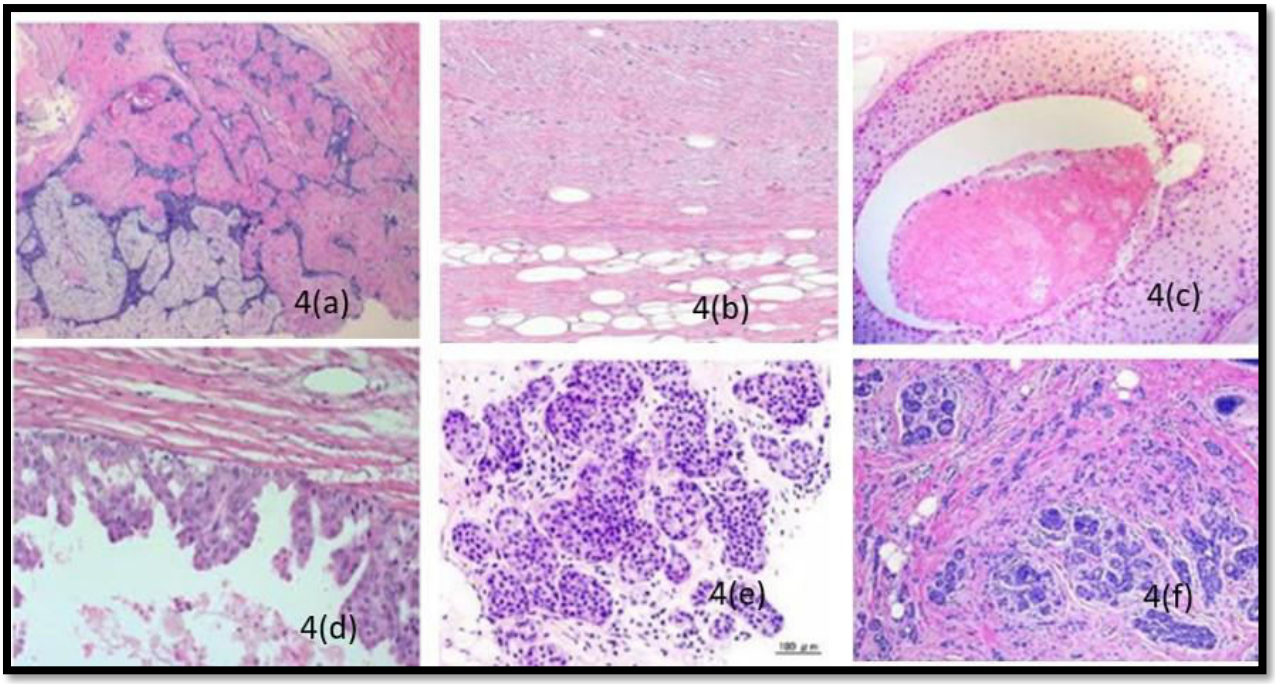


Fig. 4. Histopathology Slides; 4(a). Fibro adenoma; 4(b). Stromal tumor; 4(c). Comedo DCIS; 4(d). Non-Comedo DCIS; 4(e). Lobular DCIS; 4(f). Ivasive Carcinoma

Breast cancer is classified by basement membrane invasion as non-invasive (LCIS, DCIS) or invasive. LCIS fills lobules but is mainly a risk marker, while DCIS subtyped as papillary, cribriform, solid, or comedoretains a myoepithelial layer; low-grade forms progress slowly, whereas solid/comedo types are more aggressive and often precede invasive disease if untreated. Invasive cancers infiltrate stroma, most commonly as invasive ductal carcinoma (IDC, 50–70%), a cohesive mass detectable clinically, or invasive lobular carcinoma (ILC, ~10%), spreading in single-file, making

detection difficult. Special IDC variants include tubular carcinoma (tiny glandular structures), mucinous/colloid carcinoma (abundant extracellular mucin, low-grade), and medullary carcinoma (sheets of high-grade cells with lymphocytic infiltrates and pushing borders) [27].

Signs and symptoms:

A painless breast lump or thickening, alterations In the size, shape, or appearance of the breast, skin dimpling or pitting, and redness or skin changes are among the common symptoms of breast cancer. Other warning signs include nipple inversion or abnormal discharge [28].It is important to note that several benign breast conditions—such as fibroadenomas, cysts, or infections—can produce similar symptoms. Therefore, any unusual changes should prompt a clinical evaluation, imaging, and, if needed, biopsy for accurate diagnosis. Early medical attention improves outcomes by enabling detection of breast cancer at a more treatable stage [29]. The following figure 5 showed how to do the six steps of self examination of breast.

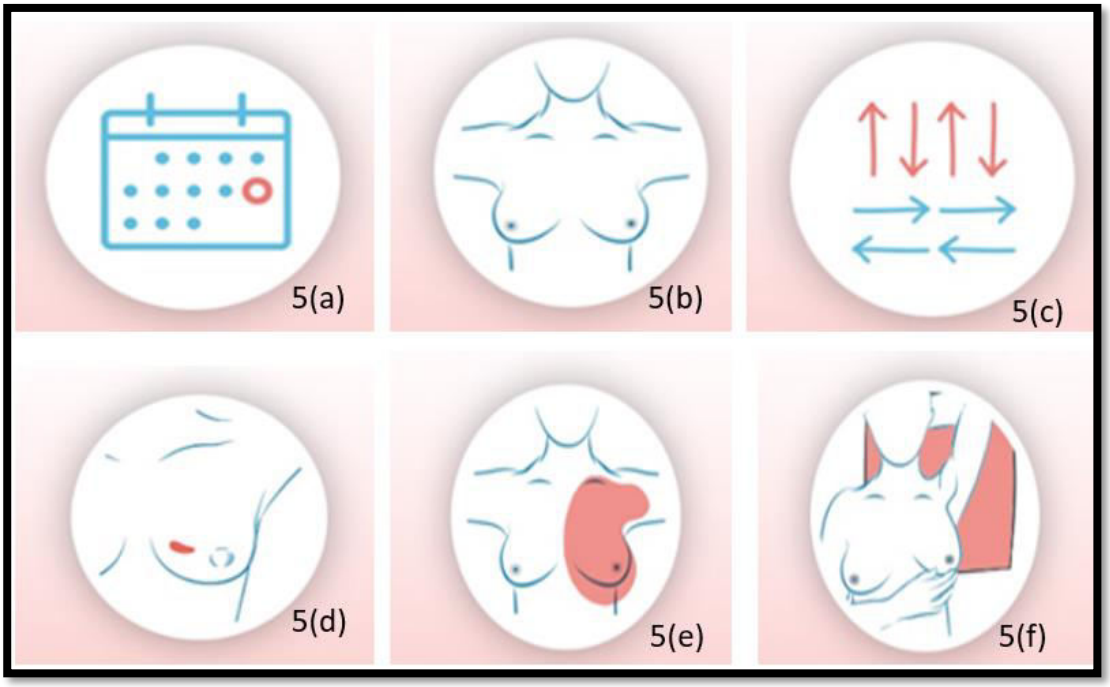


Fig 5(a). Do once a month a week after your period. 5(b). Look in the mirror for any asymmetries. 5(c).Touch all portions of your breasts- up and down & left to right. 5(d). Start feeling for lumps or masses. 5(e).Check from the underarm area to the chest wall and sternum. 5(f). Conduct the self -exam standing up or lying down

Risk factors

A woman's likelihood of developing breast cancer is influenced by both modifiable and non-modifiable risk factors.

Modifiable risk factors:

Modifiable factors involve reproductive history (nulliparity, late age at first childbirth), hormone replacement therapy (HRT), oral contraceptive use, alcohol consumption, obesity, physical inactivity, and exposure to ionizing radiation [30].

Non-modifiable risk factors:

- Non-modifiable factors include age, genetic predisposition (e.g., BRCA1/2 mutations), family history of breast or ovarian cancer, early menarche, late menopause, and personal history of atypical hyperplasia or previous breast cancer.
- Protective factors include breastfeeding, maintaining a healthy weight, regular physical activity, and limiting alcohol.
- Understanding the interplay between these modifiable and non-modifiable categories allows for better risk assessment, preventive strategies, and early detection efforts [31].

Investigations:

Clinical examination:

Visual assessment – inspecting both breasts for asymmetry, skin dimpling, redness, swelling, or nipple changes [31].

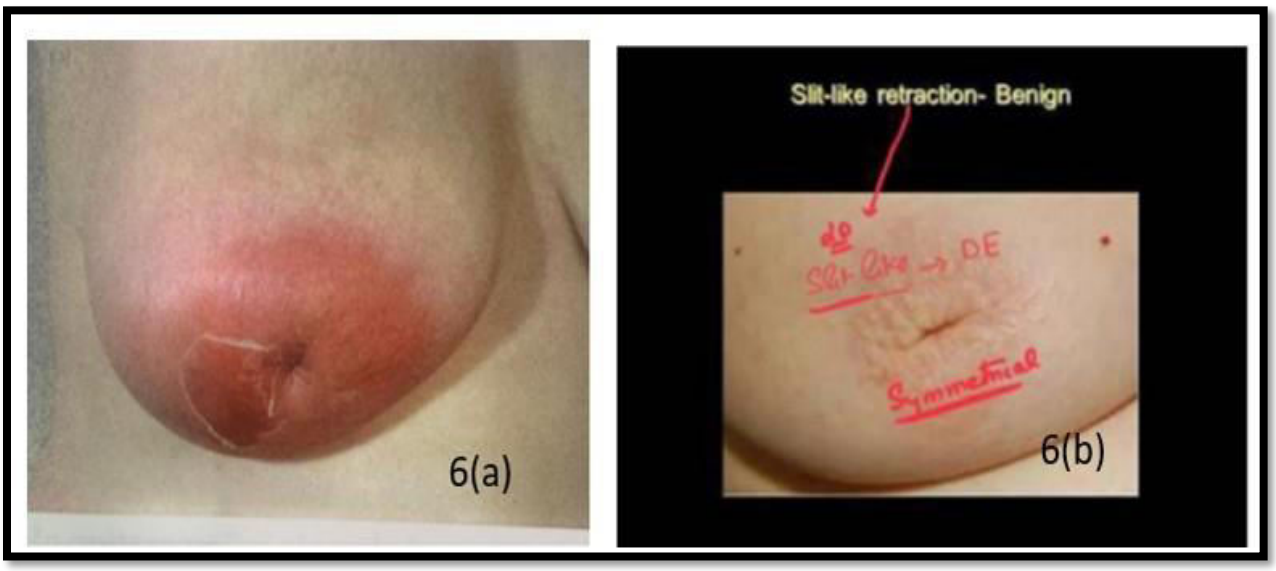


Fig. 6(a). Clinical image showing mastitis with redness, swelling, and inflammation of the breast. 6(b). Slit-like nipple retraction, a benign and symmetrical clinical finding

Inspection

During a breast examination, clinicians should carefully assess for indications of asymmetry, focusing on the following:

- Unusual breast size or shape – asymmetry may indicate underlying pathology rather than normal variation
- Skin colour changes – such as redness, bruising, or other discolourations, which could reflect inflammation or malignancy
- Skin retractions or dimpling – may signal tethering of the skin to underlying tumour or stromal changes
- Unexpected nipple discharge – particularly bloody or unilateral discharge, which may warrant further evaluation

It is essential to remain vigilant for such changes and seek prompt medical consultation to ensure accurate diagnosis and management [33].

Palpitation:

You can more accurately determine whether a breast mass is benign or malignant by closely evaluating its clinical characteristics. Before palpating, ask the woman to identify any lumps she has noticed during breast self-examination (BSE).

When assessing a palpable breast mass, consider the following features:

- Shape – Benign growths such as cysts or fibro adenomas usually have smooth, well-defined borders, whereas malignant lumps often appear irregular or spiculated.
- Consistency – Benign lesions typically feel rubbery, soft, or elastic, while malignant tumours often feel very firm or hard.
- Skin relationship – Masses that are fixed to the skin or underlying tissue are more suspicious for malignancy, whereas benign lumps are usually mobile.
- Changes over time – Rapid growth of a mass over weeks to months raises concern for malignancy, whereas stable lesions are more likely benign.
- Tenderness – Benign masses (e.g., cysts) are often tender, especially with menstrual cycle changes, while malignant tumours are usually painless.

Careful evaluation of these features provides a more precise distinction between benign and malignant breast masses [34].

Lymph nodes:

Axillary lymph nodes are the earliest and most common sites of breast cancer spread, making their examination crucial. Palpation should assess all groups central, lateral, anterior, posterior, and apical for size, fixation, or tenderness. Firm, hard, matted, or immobile nodes suggest malignancy, while soft, tender, mobile nodes are usually

benign. As lymph node status is a key prognostic factor, systematic axillary evaluation is vital for staging and management [35].

Mammogram:
A mammogram is an X-ray test designed for breast tissue and is widely used for early breast cancer detection, even in asymptomatic women. Screening mammography—typically two or more images per breast—can reveal changes years before clinical detection, enabling earlier treatment and lowering mortality [36].

Various imaging modalities for breast cancer diagnosis:

- **Ultrasonography (USG):**
  Breast ultrasonography primarily distinguishes solid tumors from cysts and is valuable for dense breasts, guiding biopsies, and evaluating palpable lumps [37]. Since it can miss micro calcifications, it is not used for routine screening but serves as a diagnostic adjunct to mammography or MRI.

- **Computed Tomography (CT):**
  CT scans are not used for primary breast cancer detection but are essential for staging advanced disease, evaluating metastases (especially in liver and lungs), monitoring therapy, and detecting recurrence. Contrast-enhanced CT further improves visualization of metastatic lesions, supporting accurate diagnosis and treatment planning [38].

- **Magnetic resonance imaging (MRI):**
  Breast MRI offers high-resolution imaging to detect cancers not seen on mammography or ultrasound, making it valuable for dense breasts, high-risk women, and evaluating known cancers [39,40]. It aids in staging, treatment planning, monitoring therapy, and detecting recurrence, though its use is limited by lower specificity and higher cost, so it is often combined with other imaging modalities [41].

- **Positron emission tomography** (PET) [42]
  PET scans visualize tumor biology noninvasively, aiding early diagnosis by detecting over-expressed molecular markers. Using 18F-FDG, PET assesses tumor metabolism, staging, treatment response, and recurrence, while newer tracers targeting ER and HER2 promise more personalized care. Due to limited sensitivity for small lesions and high cost, PET is reserved as an adjunct in advanced disease rather than for primary screening.

Biopsy-Breast Biopsy: A Diagnostic Method [43]

Breast biopsy is performed when imaging or symptoms suggest cancer, by sampling tissue for lab analysis [44]. Techniques include FNA, core needle biopsy (CNB), vacuum-assisted biopsy, and surgical excision, selected based on lesion features. CNB is most common, yielding tissue for histopathology and receptor/HER2 testing to guide therapy. Needle methods are less invasive, faster, and safer than surgery while maintaining high accuracy.

Types of Breast Biopsies: [45]

- **Fine Needle Aspiration (FNA) Biopsy:** A tiny sample of fluid or tissue is taken by inserting a thin needle into the suspicious area or lump.
- **Core Needle Biopsy:** To obtain a tissue sample, a thicker needle is inserted into the lump or trouble spot.
- **Open (Surgical) Biopsy:** To obtain a tissue sample, a surgical incision is made in the breast.

These biopsy methods help doctors determine whether breast cancer is present and what kind it is, which helps them decide on the best course of treatment

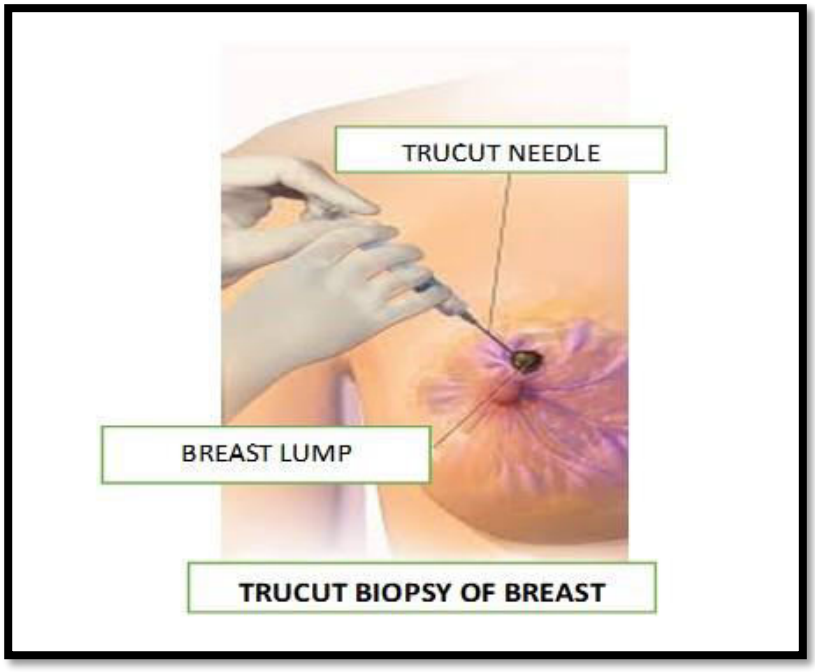


Fig 7. Trucut Biopsy of Breast

Non-pharmaceutical treatment:

A range of non-pharmacological techniques can help reduce stress, alleviate symptoms, and improve overall health in addition to conventional medical treatments.[46]

- Exercise and physical activity can reduce cancer-related fatigue and improve quality of life
- Engaging in mindfulness exercises like yoga, hypnosis, and meditation helps lower stress and enhance emotional well-being
- Making use of artistic therapies, such as music therapy, can support psychological health and relieve anxiety
- Putting relaxation and stress-reduction techniques into practice contributes to better coping and improved daily functioning
- Getting acupressure and massages may alleviate discomfort, reduce fatigue, and promote relaxation

Pharmaceutical treatment:

Surgery:

Surgery is a procedure used to remove breast cancerous tumours.

- Surgery, including mastectomy or lumpectomy, is performed to remove cancerous breast tissue.[47]
- It can be used either by itself or in conjunction with chemotherapy.
- Surgery may be performed alone or combined with chemotherapy, radiotherapy, or hormone therapy depending on the cancer stage and type.

Seroma, haematoma, pain, infection, and cosmetic problems are typical adverse effects.[48]

- **Seroma:** Accumulation of clear fluid at the surgical site after mastectomy or lymph node removal.
- **Haematoma:** Collection of blood causing swelling, bruising, or discomfort post-surgery.
- **Pain:** Postoperative pain due to tissue trauma or nerve injury is common.
- **Infection:** Surgical site infections may occur and require antibiotics.
- **Cosmetic problems:** Scarring, changes in breast shape and asymmetry may affect appearance and selfesteem.

Table 1 List of Drug Formulations for Breast Cancer Treatment

Formulation Type	Example Drugs	Purpose / Remarks
Oral Formulations	Tamoxifen, Letrozole, Anastrozole, Exemestane, Capecitabine	Convenient for long-term use; hormone therapy and oral chemotherapy
IV Injections / Infusions	Doxorubicin, Cyclophosphamide, Paclitaxel, Docetaxel, Trastuzumab, Pertuzumab	Standard for chemotherapy, targeted and antibody therapies
Subcutaneous/IM Injections	Goserelin, Leuprolide, Fulvestrant, SC Trastuzumab	Hormonal therapy; easier administration for some targeted agents
Liposomal Formulations	Pegylated Liposomal Doxorubicin (Doxil, Caelyx)	Reduced toxicity, especially cardiotoxicity
Nanoparticle Formulations	Albumin-bound Paclitaxel (Abraxane)	Enhanced tumor targeting, reduced side effects
Targeted Therapy(Monoclonal Antibodies)	Trastuzumab, Pertuzumab	HER2-positive breast cancer
Antibody-Drug Conjugates (ADC)	Ado-Trastuzumab Emtansine (T-DM1), Trastuzumab Deruxtecan	Antibody + chemotherapy in one formulation
Hormonal Therapies	Tamoxifen (SERM), Letrozole (AI), Fulvestrant (SERD)	Used in ER+/PR+ breast cancers
Immunotherapy	Atezolizumab (PD-L1 inhibitor)	Used in triple-negative breast cancer
Radiopharmaceuticals	Radium-223	Bone metastasis treatment
Topical / Local Delivery	(Less common) under research or palliative care	Limited use in breast cancer
Combination Therapies	CAF regimen: Cyclophosphamide + Doxorubicin + 5-FU	Fixed-dose or sequential use for improved efficacy

Preventive measures for breast carcinoma:

Strategies for Preventing and Reducing Breast Cancer Risk

The risk of getting breast cancer can be reduced in a number of ways: [49]

- **Reproductive history:**
  Breast cancer risk can be lowered by reproductive factors that reduce lifetime exposure to oestrogen, such as early first pregnancy or multiple full-term pregnancies.

- **Hormone therapies:**
  Use of aromatase inhibitors or selective oestrogen receptor modulators (SERMs), like tamoxifen or raloxifene, can reduce breast cancer risk in high-risk women.
- **Risk-reducing mastectomy:**
  Surgically removing one or both breasts (prophylactic mastectomy) can significantly decrease the risk of developing breast cancer, especially in women with BRCA mutations.
- **Ovarian ablation:**
  Removing or suppressing ovarian function (oophorectomy) reduces circulating oestrogen and lowers breast cancer risk, particularly in women at high genetic risk.
- **Frequent exercise:**
  Regular physical activity is associated with a lower risk of breast cancer, likely due to hormonal modulation and weight control.

New development in breast cancer prevention:

The Phase III NATALEE trial showed that adding ribociclib to endocrine therapy lowers recurrence risk in HR-positive, HER2-negative early breast cancer. The FDA has approved ribociclib with aromatase inhibitors for high-risk, early-stage patients, expanding its clinical use [50].

Pink ribbon day:

Every October, the Pink October" campaign promotes global breast cancer awareness, emphasizing access to screening, diagnosis, and treatment October 19 is recognized by WHO as the International Day against Breast Cancer Pink ribbons and the color pink symbolize support for awareness, education, and research worldwide [51].

Conclusion

Breast cancer is a major global health issue, with outcomes improved through advances in early detection and treatment [52] Mammography, MRI, and molecular testing enable timely diagnosis, while ongoing research, tailored therapies, awareness, and accessible healthcare remain essential for reducing its global impact [53].

Conflict Of Interest Statement

The authors declare that there is no conflict of interest regarding the publication of this article.

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