A REVIEW ARTICLE ON BREAST CANCER

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ABSTRACT :

In the United States, breast cancer is among the most frequently diagnosed cancer in women. young women constitute a minority of breast cancer patients, but commonly have distinct concerns and issues compared with older women, including queries regarding fertility, contraception and pregnancy. Breast cancer is a disease in which cells in the breast grow out of control. There are different kinds of breast cancer. The kind of breast cancer depends on which cells in the breast turn into cancer. Breast cancer can begin in different parts of the breast. Breast cancer is classified into four major subtypes: human epidermal growth factor receptor 2 (HER2),Luminal-A, Luminal-B, and Basal-like or triple-negative, based on histopathological criteria including the expression of hormone receptors (estrogen receptor and/or progesterone receptor)and/or HER2.

INTRODUCTION :

Increased incidence of cancer in recent years and its impact on different physical, mental, and social dimensions of human life have turned it to a major problem of the century. [1] The incidence of breast cancer has increased since the widespread uptake of mammography screening and continues to increase with the aging of the population. Globally ,death rates for female breast cancer were conspicuously higher in transitioning countries versus transitioned countries (15.0 per 100,000 versus 12.8 per 1000,000 [2].Mortality rates are highest in the very young (less than age 35) and in very old (greater than age 75) [3].Mammography is a widely used screening approach in the detecting of breast cancer and proved to help reduce the mortality effectively. Other screening methods, such as Magnetic Resonance Imaging (MRI), which is more sensitive than mammography, have also been implemented and studied during the last decade [4].

Key words :breast cancer, symptoms,risk factors, therapies

Table 1: Top 10 countries with the highest number of breast cancer

| Rank	Country	Age standardized rate per 10000(world)
1.	Belgium	111.9
2.	Denmark	105.0
3.	France	104.5
4.	The Netherland	99.0
5.	The Bahamas	98.9
6.	Iceland.	96.3
7.	U K.	95.0
8.	Barbados	94.7
9.	U S	92.9
10.	Ireland	92.3

SYMPTOMS OF BREAST CANCER :

The first sign of breast cancer is a new lump or mass in the breast that you can feel, the lump is painless , hard and has uneven edges is more likely to be cancer .but sometimes cancers can be tender , soft ,and rounded .so as soon as any unusual changes are seen the person goes to the physician. They are some of the main symptoms that may be seen during breast cancer are –

• swelling of all or part of the breast.

• skin irritation or dimpling.

• Breast pain.

• Nipple or the nipple turning inward

• Redness , thickening of the nipple or breast skin.

• A nipple discharge other than breast milk.

• A lump in the underarm area.[5]
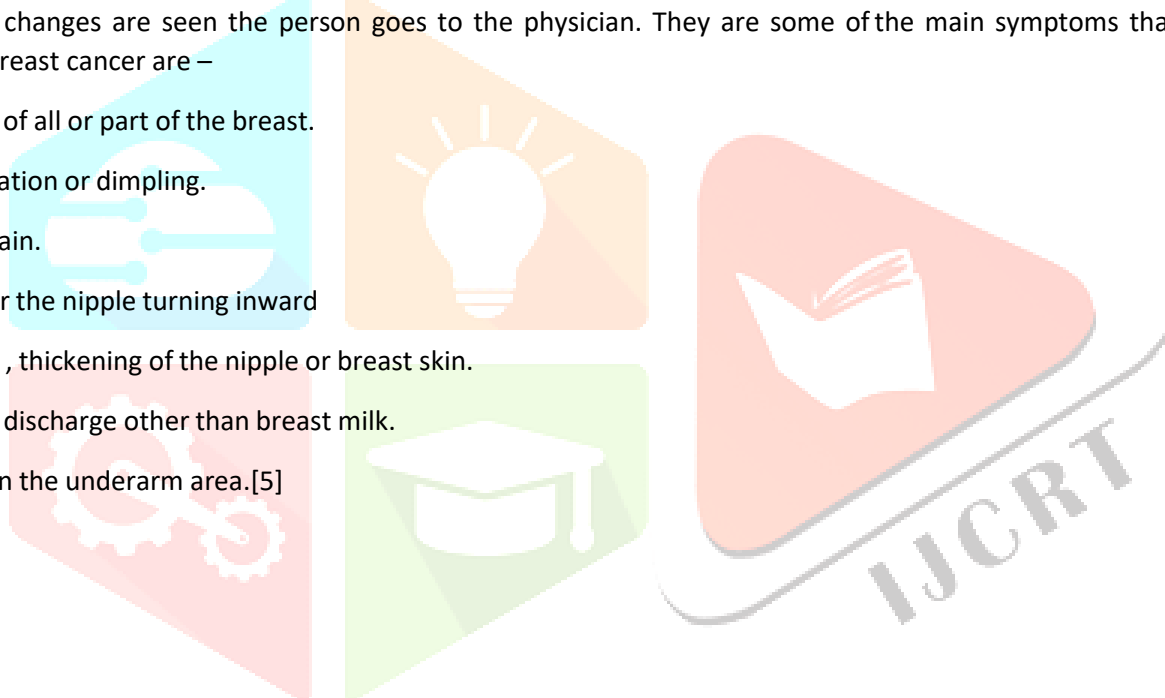
RISK FACTORS FOR BREAST CANCER : A schematic diagram of risk factors is depicted in a pyramid-style structure (figure.1).
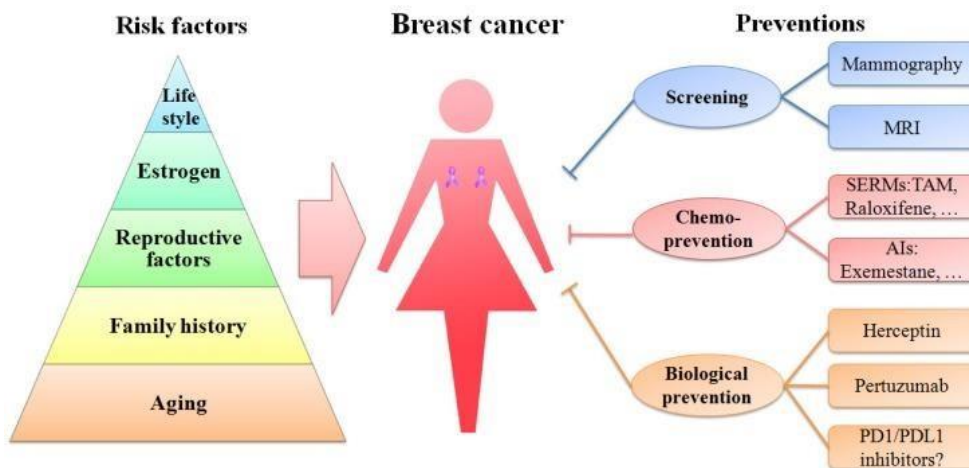
1. AGEING :
2. Currently, about 80% of patients with breast cancer are individuals aged >50 while at thesame time more than 40% are those more than 65 years old [6].The incidence rate of breast cancer increases significantly with age and reaches its peak in the age of
   menopause and then gradually decreases or remains constant[7]
3. FAMILY HISTORY:
4. A quarter of all breast cancer cases are related to family history. Women, whose motheror sister has a breast cancer, are prone to this disease. A cohort study of over 113,000 women UK demonstrated that women with one first-degree relative with breast cancerhave a 1.75-fold higher risk of developing this disease than women without any affectedrelatives. Moreover, the risk becomes 2.5-fold or higher in women with two or more first-degree relatives with breast cancer .[8]
5. REPRODUCTIVE FACTORS :
6. Reproductive milestones that increase a woman's lifetime estrogen exposure are
   thought to increase her breast cancer risk. These include the onset of menarche before12 years of age, first live childbirth after age 30 years, nulliparity, and menopause after age 55 years.[9]
7. ESTROGEN :
8. Both endogenous and exogenous estrogens are associated with the risk of breast cancer.The endogenous estrogen is usually produced by the ovary in premenopausal women and ovariectomy can reduce the risk of breast cancer [10]
9. LIFESTYLE :
10. Modern lifestyles such as excessive alcohol consumption and too much dietary fat intakecan increase the risk of breast cancer. Alcohol consumption can elevate the level of
    estrogen-related hormones in the blood and trigger the estrogen receptor pathways. Ameta-analysis based on 53 epidemiological studies indicated that an intake of 35-44 grams of alcohol per day can increase the risk of breast cancer by 32%, with a 7.1%increase in the RR for each additional 10 grams of alcohol per day [11]
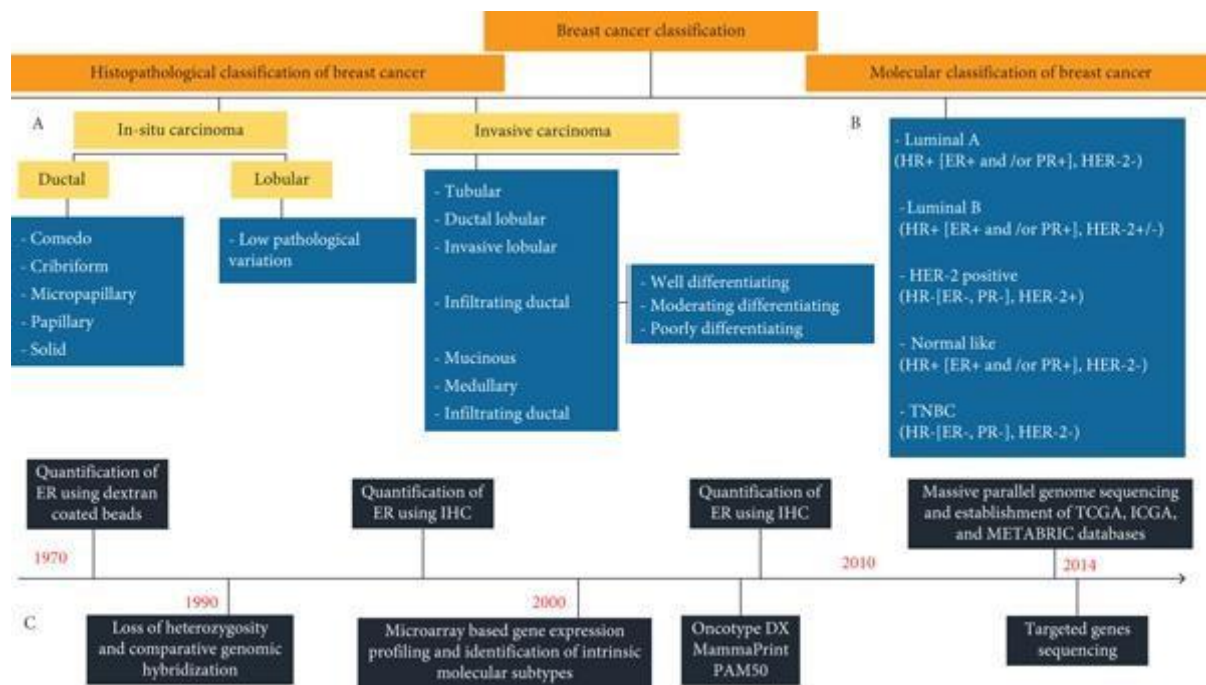
Schematic representation of (a) histopathological classification, (b) molecular classification, and (c) timeline showing important events during understanding of breast cancer biology. (Figure.2)

THERAPIES FOR BREAST CANCER

•1 ENDOCRINE THERAPY:

Endocrine therapy is the main strategy to treat HR positive invasive BC. The purpose of this therapy is to target the ER directly (selective estrogen receptors modulators and degraders) or the estrogen synthesis (aromatase inhibitors) [12]Estrogen and progesterone are the primary regulators of breast tissue growth and differentiation. Both steroid hormones are primarily produced in the ovaries. They exert their cellular effects through binding to and activating specific nuclear receptors, the estrogen receptors (ERs) and progesterone receptors (PRs). Once activated,the receptors exhibit transcriptional and membrane localized signaling activities. ERα and ERβ are the 2 major ERs. The majority of breast cancers express ERα (70%), while ERβ is less well characterized[13]
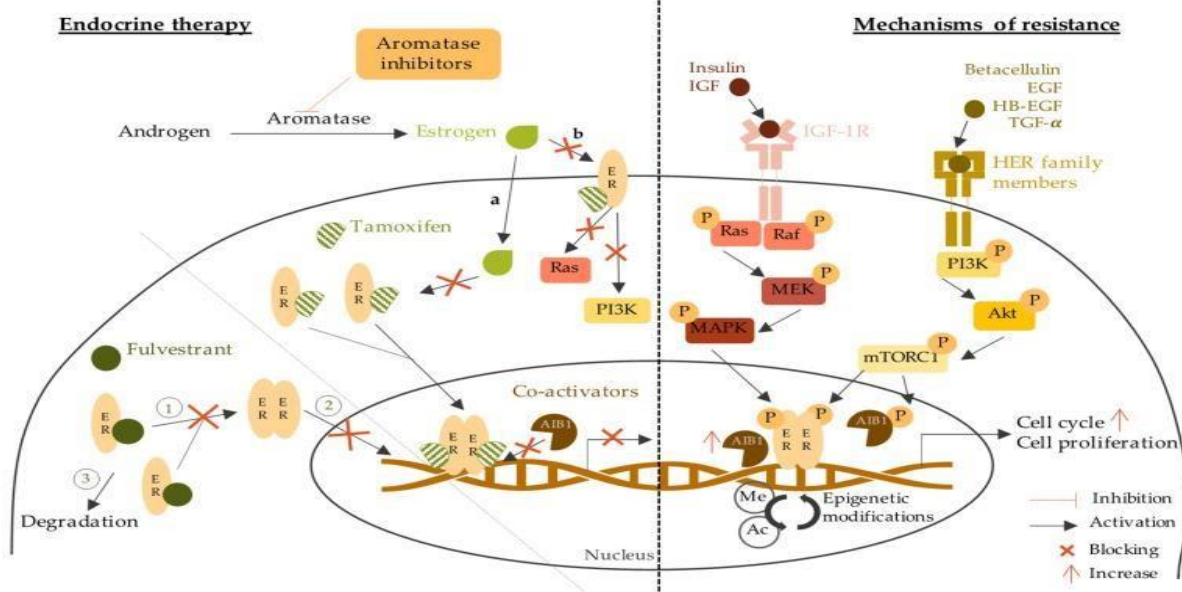
- Drug

  *Letrozole : Generic name : Femara Commercial name : Femara

  Average molecular weight : 285.31g/mol

  Mechanism of action : By effectively blocking estrogen synthesis, letrozole inhibits the growth or induces the regression of hormone-responsive breast tumors in vivo

  Route of administration : oral administration

  Terminal half life : 42 hr

  Toxicity : letrozole when administered for a long duration, results in severe liver damage.

  Contraindications: 1.Hypoestrogenism 2.Sweating

  3.Hot flushes

- 2 ANTI – HER2 THERAPY :
There are three monoclonal antibodies against HER2 that are currently approved: trastuzumab, pertuzumab, and margetuximab. Trastuzumab and pertuzumab bind to different extracellular domains of the HER2 receptor and thus have complementary mechanisms of action. Though pertuzumab alone has shown only modest clinical antitumor activity, it has a synergistic effect when combined with trastuzumab.[14]
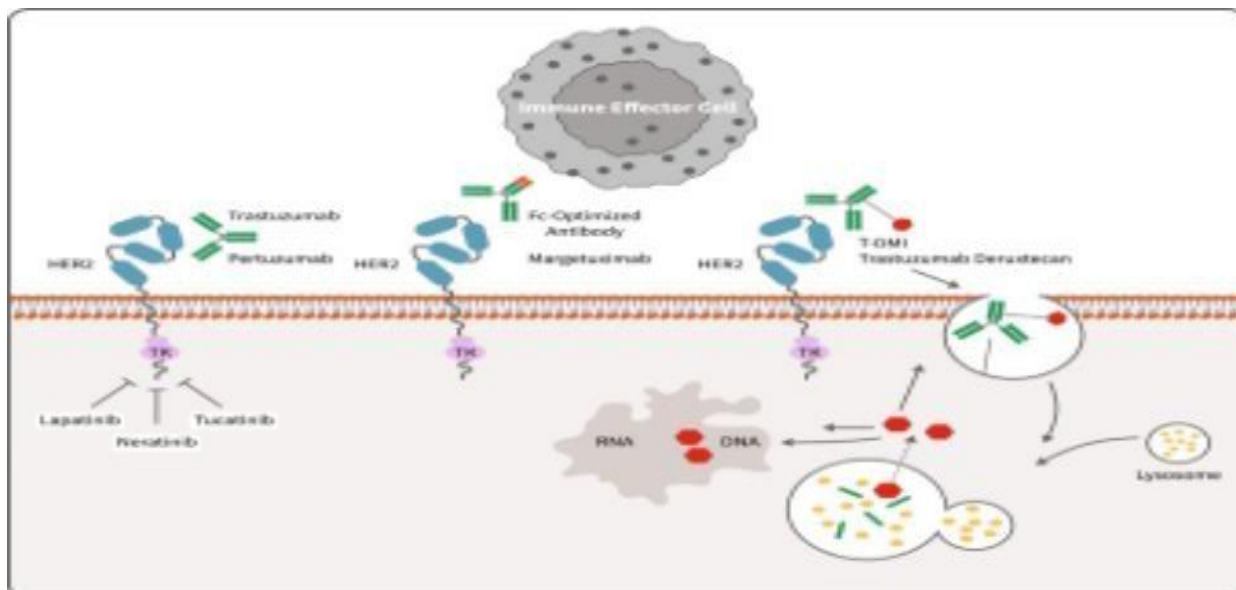
- <u>Drug</u> :

  *Trstuzumab: <u>generic name</u> : Trastuzumab<u>Commercial name</u>   : Herceptin

  <u>Synonyms.</u>   : Anti -HER 2

  <u>Avg molecular wt.</u>   : Approximately 150k dalton

  <u>Mechanism of action</u>   : Trastuzumab binds to an extracellular domain of this receptor and inhibits HER2 homodimerization, thereby preventing HER2-mediated signaling. It is also thought to facilitate antibody-dependent cellular cytotoxicity, leading to the death of cells that express HER2.

  <u>Route of administration.</u>   : I.V.

  <u>Terminal half life</u>   : 28 days

  <u>Toxicity</u>   : Cardiac toxicity was an unexpected side effect of trastuzumab treatment in the pivotal trials that led to its approval. Chills, dyspnea, hypotension, bronchospasm

1. <u>Contraindications</u> :
2. 1.Hypersensitivity
3. 2.Severe dyspnea
4. 3.Maligancy
5. 4.Arthralgia

REFERENCE:

1. Poorkiani M, Hazrati M, Abbaszadeh A, Jafari P, Sadeghi M, Dejbakhsh T, Mohammadian Panah M. Does arehabilitation program improve quality of life in breast cancer patients. Payesh. 2010;9(1):61–68. [Google Scholar] [1]

2. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36Cancers in 185 Countries. CA Cancer J Clin. 2021; 71(3): 209– 49.[2]

3. Smith H, Kameerer – Doak D , Barbo D , Sarto G , Hormone Replacement Therapy in the Menopause; A pro opinion. CA-A cancer Journal for clinicians 1996;46:343.[3]

4. DeSantis CE, Fedewa SA, Goding Sauer A. et al. Breast cancer statistics, 2015: Convergence of incidence rates between black and white women. CA Cancer J Clin. 2016;66:31–42. [PubMed] [Google Scholar] [4]

5. Breastcancer.org, Stages of breast cancer http://www.breastcancer.org/symptoms/diagnosis/staging.[5]

6. Benz C.C. Impact of aging on the biology of breast cancer. Crit. Rev. Oncol. 2008;66:65–74. Doi: 10.1016/j.critrevonc.2007.09.001. [PMC free article] [PubMed] [CrossRef] [Google Scholar] [6]

7. Kim Y, Yoo K-Y, Goodman MT. Differences in Incidence, Mortality and Survival of Breast Cancer by Regions and Countries in Asia and Contributing Factors. Asian Pac J Cancer Prev.2015;16(7):2857–2870.[7]

8. Brewer HR, Jones ME, Schoemaker MJ, et al. Family history and risk of breast cancer: an analysis accounting for family structure. Breast Cancer Res Treat. 2017; 165: 193-200.[8]

9. Doren A,Vecchiola A,Aguirre B,Villaseca P, Gynecological-endocrinological aspects in women carriers of BRCA1/2 gene mutations. Climacteric : the journal of the International Menopause Society. 2018 Oct 8 [PubMed PMID: 30295091] [9]

10. Endogenous H, Breast Cancer Collaborative G, Key TJ. Et al. Sex hormones and risk of breast cancer in premenopausal women: a collaborative reanalysis of individual participant data from seven prospective studies. Lancet Oncol. 2013;14:1009–1019. [PMCfree article] [PubMed] [Google Scholar] [10]

11. Hamajima N, Hirose K, Tajima K, et al. Alcohol, tobacco and breast cancer—collaborativereanalysis of individual data from 53 epidemiological studies, including 58,515 women with breast cancer and 95,067 women without the disease. Br J Cancer. 2002; 87: 1234- 1245 [11]

12. Howlader N., Altekruse S.F., Li C.I., Chen V.W., Clarke C.A., Ries L.A.G., Cronin K.A. US Incidence of Breast Cancer Subtypes Defined by Joint Hormone Receptor and HER2 Status.
J. Natl. Cancer Inst. 2014;106 doi: 10.1093/jnci/dju055. [PMC free article] [PubMed] [CrossRef] [Google Scholar][12]

13. Bland KI, Copeland EM. . The Breast E-Book: Comprehensive Management of Benign and Malignant Diseases. Elsevier; 2009. [Google Scholar] [13]

14. Von Minckwitz G, Procter M, de Azambuja E, Zardavas D, Benyunes M, Viale G, Suter T, Arahmani A, Rouchet N, Clark E, Knott A, Lang I, Levy C, Yardley DA, Bines J, Gelber RD, Piccart M, Baselga J. Adjuvant pertuzumab and trastuzumab in early HER2-positive breast cancer. New England Journal of Medicine. 2017;377:122–131. Doi: 10.1056/NEJMoa1703643. [PMC free article] [PubMed] [CrossRef] [Google Scholar[14]