An Overview of Breast Carcinoma

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ABSTRACT

The overview of the literature on breast cancer presented in this article covers a wide range of subjects, including epidemiology, diagnosis, pathology, "benign" breast disease, breast carcinoma in situ syndromes, staging, and post-treatment monitoring. The most typical malignancy in women is still breast cancer. In both public health and medical practice, early identification, treatment, and prevention of breast cancer are important topics. The most common cancer among women globally, breast cancer is treatable in 70–80% of people with early-stage, non-metastatic illness. With the treatments that are now available, advanced breast cancer with distant organ metastases is regarded as incurable. Breast cancer is a diverse illness from a molecular perspective; molecular characteristics include activation of HER2 (human epidermal growth factor receptor 2, encoded by ERBB2), activation of hormone receptors (oestrogen and progesterone receptors), and/or BRCA mutations. Molecular subtype influences treatment approaches differently. Breast cancer treatment is multimodal and incorporates systemic (radiation therapy and surgery) as well as locoregional (surgery) methods. Endocrine treatment, chemotherapy, anti-HER2 therapy, bone stabilizing medicines, poly (ADP-ribose) polymerase inhibitors for BRCA mutation carriers, and immunotherapy are examples of systemic therapies. Endocrine therapy is used for diseases that are hormone receptor positive. The current article gives a summary of modern, cutting-edge treatment approaches and discusses how several disciplines contribute to providing patients with breast cancer with the best, most personalised care possible. One of the most significant health problems for doctors working in the field of women's health will be breast cancer, and everyone caring for female patients will need to have a basic awareness of current treatment goals.

INTRODUCTION:

The question "What causes cancer?" has occupied people for generations. In 1950, the World Health Organization sponsored an international symposium, and attendees were fascinated by the dramatic differences in the types of cancer found in different parts of the world. [1]

More than 277 distinct forms of cancer diseases are referred to as cancer when used broadly. Different cancer stages have been found by researchers, demonstrating the involvement of numerous gene alterations in the etiology of cancer. Atypical cell proliferation results from these gene mutations.[2]

The significant issue of cancer has an impact on the wellbeing of all human cultures. At the tissue level, there is a range of diseases, which makes it difficult to accurately diagnose the condition and then determine how effective therapy will be. [3,4]

WHAT IS CANCER?

The development of cancer is caused by a succession of gene changes that alter how cells operate. Evidently, chemical substances have a part in the development of cancerous cells and gene alterations. Smoking also contains a number of chemical substances known to cause cancer and lung cancer.[5]

It's interesting to note that environmental chemicals with carcinogenic effects have an impact on the cytoplasm and nucleus of cells, causing genetic abnormalities and gene mutations. [5-9]

When examining cell destiny and the epigenetic alterations that play significant roles in the development of cancer, such as DNA methylation, histone modifications, and nucleosome location, epigenetics presents a dynamic scenario. [5,10,11] Cancer is a collection of many diseases, not one single illness. Types of cancer, such as cancer of the blood, lungs, colon, and rectum, prostate, skin, breast, uterus, thyroid, lymphatic system, etc. [12]

A BRIEF ABOUT BREAST CANCER

Breast cancer, a form of tissue cancer, mostly affects the inner layer of milk glands, also known as lobules, and ducts (tiny tubes that carry the milk). [13]

In the entire world, breast cancer is both the most often diagnosed cancer and the leading cause of cancer-related deaths in women. Breast cancer caused 2.08 million of the 18.08

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million new instances of the disease (a rate of 11.6%) and 626,679 of the 9.55 million cancer-related deaths (a rate of 6.6% of all cancer-related fatalities) worldwide in 2018.[14]

ETIOLOGY:

The second-leading cause of mortality is breast cancer, which is the most prevalent type of cancer. For women between the ages of 45 and 55, this illness is the main cause of death. [15,16]Nearly one in eight women will get breast cancer, which is often treated with total tissue excision, chemotherapy, radiation, and hormone treatment. [15,17]

Genetic mutations and DNA damage are what lead to breast cancer development, and estrogen exposure can affect these processes. DNA flaws or cancer-causing genes like BRCA1 and BRCA2 can occasionally be passed down through families. The chance of developing breast cancer is therefore increased by a family history of ovarian or breast cancer.[14]

Breast cancer, a form of tissue cancer, mostly affects the inner layer of milk glands, also known as lobules, and ducts (tiny tubes that carry the milk).[18]

SIGNS AND SYMPTOMS:

While male and female patients who are susceptible to this disease can self-evaluate themselves before seeing a doctor, doctors still need to perform various tests to determine whether a breast cancer is malignant or benign. Research on the signs or symptoms of breast cancer has contributed to lowering the disease's mortality rate. Regular breast examinations can help identify these symptoms early on to stop the spread of the disease. Other symptoms of breast cancer include redness or scariness of the nipple or breast skin, or a discharge. Changes in the way the breast looks or feels nipple and nipple discharge are all common symptoms of breast cancer. [19,20]
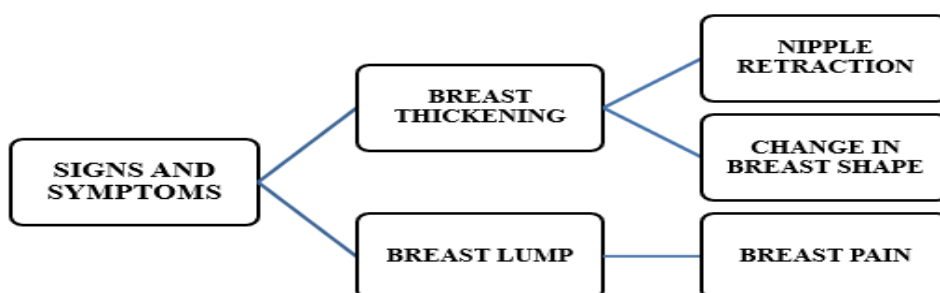

Fig No. 1 Signs & Symptoms of Breast Cancer

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Breast thickening: a region on your breast that is flat or pronounced. A tumor that you cannot see or feel could be the cause of this, swelling in the area around your collarbone or in your armpit. This may indicate that nearby lymph nodes have become infected with breast cancer.[21]

Breast lump: The most prevalent symptom, breast lump, was reported by 83% of women, or around 45% of all women. Nipple abnormalities (7%), breast soreness (6%), and abnormalities of the breast skin (2%) were the next most often reported presenting symptoms. A lump in the breast or armpit is the standard sign of breast cancer. [22,23]

Nipple Retraction: Breast self-examination (BSE) is an important method for learning about breast size, skin condition, cyclical variations, and breast texture.[24]

Breast cancer warning signs include inverted retracted nipple, persistent breast tenderness, discomfort or unusual breast pain, bloody or clear nipple discharge, scaly or pitted skin on nipple, lump mass or swelling of the breast, swelling in the armpit lymph nodes, and scaly or pitted skin on nipple.[25]

Change in breast shape: Natural alterations or any changes in body weight may have an impact on the size or form of the nipple.[26]

However, breast cancer may cause the nipple retract to go in and not return to its usual shape in some cases.[27] It is possible to diagnose issues with the milk ducts located beneath the nipple surface and areola using a mammography or ultrasound.[28]

After puberty, changes in the breast's size and shape may indicate swollen milk ducts or lobes deep inside the breast. These changes may also be brought on by the body's regular monthly hormonal cycles, fibrocystic breast cancer, or a more serious condition. [29,30]

Breast pain: If you are experiencing breast discomfort, take note of whether or not it changes with your monthly period and whether it affects just one breast or both. While it appears to be natural, it might nevertheless be painful and not necessarily alarming. [31]

It is advised to get checked out, though, if the pain just affects one breast, one armpit, or one cycle. Additionally, keeping a thorough record of your menstrual cycle may help you understand variations in your hormone levels in your breasts and aid medical professionals in determining what's wrong with you.[32]

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RISK FACTORS

Even though the precise causes of breast cancer are unclear, we are aware of the key aspects of chance. All things considered, few women who are believed to be at high risk for breast disease actually develop it, while many women who have no known risk factors do. Propelling age and a family history of breast cancer are two of the most important risk factors. Breast cancer is the most well-known illness, affecting 10% of women globally, and risk factors can assist determine when in one's life there is a chance of developing the disease.[33]
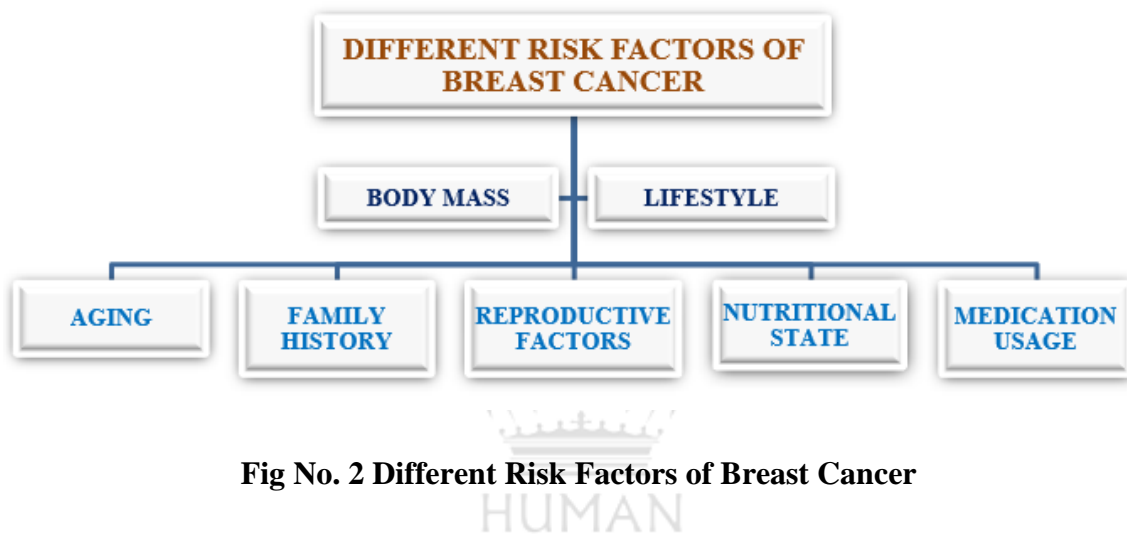

Fig No. 2 Different Risk Factors of Breast Cancer

BODY MASS: High body mass index (BMI), may also be associated with a worse outcome for people who have had breast cancer in the past and an increased risk of post-menopausal breast cancer. Breast density predicts the likelihood of developing breast cancer. According to an analysis, women whose breasts contain between 60 and 75 percent thick tissue have a 4–6 times higher chance of getting breast cancer than women without dense tissue. Despite the fact that an increase in BMI increases the risk of breast cancer, women with high BMI have low breast density. If the density of the breast is taken into account in analysis, BMI becomes a more reliable indicator of breast cancer risk.[34]

DIET/NUTRITIONAL STATE: There is mounting evidence that consumption of dairy protein and milk raises circulating IGF-I levels, which are associated with breast cancer. Through IGF-I, dairy consumption, particularly milk, may have a detrimental impact on breast cancer risk variables such a mother's and her children's birth weight, height, and number of menstrual cycles. [35]

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Egg consumption on occasion was linked to a lower risk when compared to twice to once a month, but a higher risk when compared to daily to once a week, among foods containing vitamin D. When compared to daily consumption, occasional mushroom eating was found to be substantially related with an increased risk of BC. Up until the age of 70, drinking alcohol raises the risk of developing breast cancer by 7%.[36]

DRUG/MEDICATION USAGE: Anti estrogens (tamoxifen, raloxifen) are used as part of pharmacotherapy to lower the risk. Due to side effects, the use should only be permitted in high-risk females having a strong family history of cancer or genetic mutations associated with breast cancer. A 4Gy radiation exposure dose administered to the breast was linked to a 3.2-fold increase in risk.[36]

Women who lived in a barrier-separated area of their primary childhood residential street or the cross street closest to it had a slight increase in their risk of developing breast cancer. A combined analysis revealed that a high exposure to traffic-related pollutants is linked to an overall increase in the risk of breast cancer, post-menopausal breast cancer, and invasive ER-breast cancer.[37]

AGING: Due to the strong correlation between the prevalence of breast cancer and advancing age, ageing is one of the most significant risk factors for breast cancer, second only to sex. Women over the ages of 40 and 60 were reported to have died from breast cancer in 2016, respectively, with 99.3% and 71.2% of all breast cancer-related fatalities in America.[38]

FAMILY HISTORY: Family history is a factor in close to 25% of all breast cancer incidences, according to 65. Women are more likely to contract this illness if their mother or sibling has the sickness. According to UK cohort research involving over 113,000 women, women who have one first-degree cousin who has breast cancer are 1.75 times more likely to get the disease than those who don't have any affected relatives. Additionally, the risk increases by 2.5 times or more for women who have two or more first-degree relatives who have breast cancer.[39]

The mutations in breast cancer-related genes like BRCA1 and BRCA2 are partly responsible for the inherited propensity for breast cancer.[40]

REPRODUCTIVE FACTORS: The risk of breast cancer can be increased by reproductive characteristics such early menarche, delayed menopause, late age at first pregnancy, and low

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parity. Breast cancer risk is increased by 3% for every year that menopause is postponed. Breast cancer risk is reduced by 5% or 10%, respectively, with every 1-year delay in menarche or for every additional birth. [41-43]

Reproductive variables greatly influence the ER status, with different odds ratios (OR) between ER+ and ER- breast cancer for parity (OR: 0.7 vs. 0.9 for 3 births vs. nulliparae) and age at the first birth (OR: 1.6 vs. 1.2 for age 30 vs. 25 years).[44]

LIFESTYLE: Breast cancer risk can be raised by contemporary lifestyle factors such excessive alcohol use and dietary fat consumption. Alcohol drinking can stimulate the estrogen receptor pathways and raise blood levels of hormones associated to estrogen. An intake of 35 to 44 grammes of alcohol per day can increase the risk of breast cancer by 32%, according to a meta-analysis based on 53 epidemiological studies, with a 7.1% rise in the RR for every additional 10 grammes of alcohol per day. [45,46]

The extra fat in the modern western diet, particularly saturated fat, is linked to mortality (RR=1.3) and a poor prognosis in breast cancer patients.[47]

GENETIC FACTORS:

Rare but responsible for severe and early-onset types of the disease are mutations in the BRCA1 and BRCA2 genes. Individual risks for this early-onset form of disease are determined by testing for mutations, typically linked to BRCA mutations, in women with a strong family history. However, the majority of patients (almost 95%) do not have obvious family history of either early- or later-onset disease. Less research has been done on how more prevalent breast cancer variations affect risk assessment.[48]

With a higher frequency of cancer risk at younger ages, the lifetime chances of breast cancer for women with BRCA1 mutations can reach 80%. Men who carry BRCA2 pathogenic variants also have a lifetime risk of breast cancer that is about 6% higher than that of BRCA1 carriers. BRCA2 pathogenic variants are associated with an increased risk of prostate cancer in male carriers.[1]

A total risk of breast cancer was linked to protein-truncating mutations in 5 genes (ATM, BRCA1, BRCA2, CHEK2, and PALB2) with a P value less than 0.0001. With a P value of less than 0.05 and a Bayesian false-discovery probability of less than 0.05, protein-truncating variations in 4 more genes (BARD1, RAD51C, RAD51D, and TP53) were linked to an

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overall risk of breast cancer. The upper limit of the 95% confidence interval of the odds ratio for breast cancer overall was less than 2.0 for protein-truncating mutations in 19 of the remaining 25 genes. For protein-truncating variations in ATM and CHEK2, odds ratios for ER-positive disease were higher than those for ER-negative disease; similarly, for variants in BARD1, BRCA1, BRCA2, PALB2, RAD51C, and RAD51D, odds ratios for ER-negative disease were higher than those for ER-positive disease. Rare missense mutations in TP53, CHEK2, and ATM together were linked to a reduced risk of breast cancer overall with a P value of less than 0.001. The risk of breast cancer was equivalent to that of protein-truncating variations for BRCA1, BRCA2, and TP53 missense variants (collectively), which would be regarded as pathogenic according to conventional standards.[49]
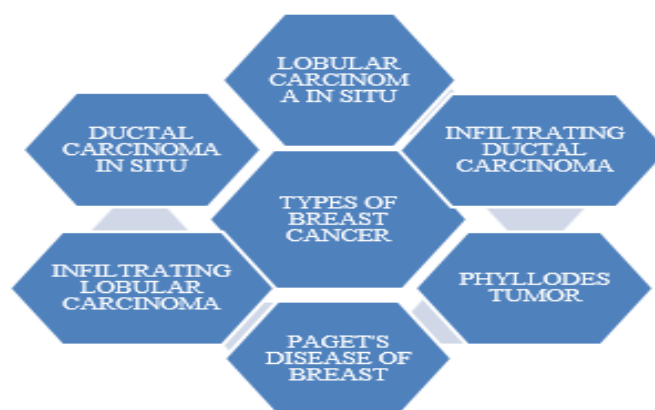
TYPES OF BREAST CANCER

Fig No. 3 Types of Breast Cancer

1. **Ductal carcinoma in situ:** Since it only affects the breast duct, it is the most prevalent type of non-invasive breast cancer. Ductal comedocarcinoma is a kind of in situ ductal carcinoma. [50,51]

2. **Lobular carcinoma in situ (LCIS):** Breast lobules form as the cancer of this kind spreads [52]. The lobules of the breast tissue are not outside of the breast cancer's original boundaries [53]. Commonly recognized as non-invasive breast cancer is lobular carcinoma in situ. [54]

3. **Infiltrating ductal carcinoma:** As this type of cancer progresses, breast lobules develop. The initial breast cancer limits do not extend to the lobules of the breast tissue. Lobular carcinoma in situ is often acknowledged as a kind of non-invasive breast cancer.[55]

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4. **Infiltrating Lobular carcinoma:** It is also known as invasive lobular carcinoma when it infiltrates the lobe. Although it often spreads to other parts of the body, ILC begins in the milk glands (lobules) of the breast.[56]

5. **Paget's disease of breast:** Red, itchy rashes around the nipple are some of its symptoms, and they occasionally extend to the rest of the skin as well. Although it mimics other skin illnesses like eczema and psoriasis, it may be distinguished because Paget's disease of the breast often affects only one breast and begins at the nipple rather than the areola. Other skin conditions, such as eczema and psoriasis, typically affect both breasts (breastcancercare.org.uk) Paget's disease is a kind of breast cancer that accounts for around 1-3% of all cases and can strike both men and women. There are a few ideas that support the etiology of Paget's disease of the breast, yet the real theory underlying its pathogenesis or development is still unclear. Their warning symptoms include breast lumps, nipple flattening or inversion, bleeding and leaking discharge, and others. A punch biopsy can be used to make the diagnosis. If it stays in the breast ducts or nipple, the prognosis is favorable.[57]

6. **Phyllodes tumor:** Malignant and benign phyllodes tumours are also possible.[58] Surgery is a possible treatment for phyllodes tumours, which form in the breast's connective tissues.[59] Less than 10 females each year in the United States pass away with phylloides tumours, which are highly rare.[60]

STAGES OF BREAST CANCER

According to a breast cancer.org report the size, kind, and depth to which the tumour cells have infiltrated the breast tissues determine the stage of the breast cancer.[61]

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STAGE	0	1	2	3	4
TUMAR SIZE	VERY SMALL	LESS THEN 2 CM	5-2 CM	5 CM & LARGER	ANY SIZE
LYMPH NODES	NO AFFECTED	NO AFFECTED	AFFECTED BY CANCER	AFFECTED BY CANCER & THE MUSCLES AND SKIN HAVE BEEN REACHED BY CANCER	AFFECTED BY CANCER
SPREADING	BASED ONLY IN THE BREAST AREA, NOT OUTSIDE	BASED ONLY IN THE BREAST AREA, NOT OUTSIDE	BASED ONLY IN THE BREAST AREA, NOT OUTSIDE	BASED ONLY IN THE BREAST AREA, NOT OUTSIDE	ANY PART OF THE BODY CONTAINS CANCER THAT HAS EXPANDED FROM THE BREAST AREA.
EXTRACELLULAR VESICLES (EVS)	-EV	-EV	-EV	-EV	+++EV
5 YEAR SURVIVAL RATE	100%	100%	87%	61%	20%

Fig No. 4 Different Stages of Breast Cancer

Stage 0 refers to non-invasive tumors, whereas stage 4 refers to invasive tumors. These are the details of those tumor stages. [50]

STAGE 0: The ductal cell carcinoma in situ tumour stage is an example of a non-invasive tumour stage in which both cancerous and non-cancerous cells are contained within the boundaries of the area of the breast where the tumour first appears and there is no evidence of their invasion of the tissues around that area (DCIS). [62]

STAGE 1: This stage is characterized as an invasive form of breast cancer, and microscopic invasion is still conceivable. It falls into two categories: stage 1A and stage 1B. Category 1A refers to tumors up to 2 cm in size with no lymph nodes implicated, whereas stage 1B refers to a tiny cluster of cancer cells larger than 0.2 mm discovered in a lymph node. [63]

STAGE 2: There are also two categories in Stage 2: 2A and 2B. Stage 2A depicts a tumour that is identified in the sentinel or axillary lymph nodes but not in the breast. The tumour can range in size from less than 2 cm to more than 5 cm. Stage 2B, however, states that the tumour may exceed 5 cm in size but cannot reach the axillary lymph nodes. [64]

STAGE 3: Three subcategories—3A, 3B, and 3C—have been established within it. There are two stages of breast cancer: stage 3A and stage 3B. Stage 3A describes that no tumour is found in the breast, but it may be found in 4–9 axillary lymph nodes or in sentinel lymph nodes. Stage 3B describes that the tumour may be of any size, but it may have caused

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swelling or an ulcer on the breast skin, and it may have spread to up to 9 axillary lymph nodes or to sentinel lymph nodes. Having red, heated, and swollen breast skin is indicative of stage 3B, which is an inflammatory form of breast cancer. Stage 3C, on the other hand, refers to the spread of a tumour to 10 or more axillary lymph nodes, as well as the lymph nodes themselves. [65]

STAGE 4: This stage of cancer is advanced and metastatic, and it depicts how the disease has progressed to several body organs, including the lungs, bones, liver, brain, and others. [66]

ROLE OF FAMILY AND SOCIETY

THE IMPACT THEY HAD:

The risk to women's physical, emotional, and social health posed by breast cancer is one of the most significant. The patient's self-awareness, self-confidence, sense of self-worthlessness, and ability to accept themselves are some therapeutic problems that can have an impact on them. The mental health of breast cancer patients is affected by a variety of reasons, including sickness, worry about one's family's future, dread of death, therapeutic problems, decreased performance, and mental imagery disorder.[67]

Losing a breast for a woman equates to losing her femininity. Additionally, although being a crucial component of cancer treatment, chemotherapy has a significant negative impact on patients' quality of life and their ability to maintain healthy bodies, minds, social lives, and spiritual lives.[68]

The entire family is affected by the condition of cancer. Numerous research has documented interference with family careers' daily lives. Two key themes emerged from qualitative research of partners' experiences: focusing on the partner's illness and caring for her, and focusing on the family to keep it together. The study's ancillary ideas were presence, reliance on the medical staff, decision-making, and managing finances.[69] The family as a whole is significantly affected by a family member's chronic illness. Family crisis comes from a number of variables in such situations, such as role change, uncertainty, losing control, entering an unfamiliar setting, economic concerns, etc. [70]

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THE WAY THEY ASSIST:

Breast cancer will affect one out of every nine women at some point in their lives. Although studies reveal that breast cancer is the second most common type of cancer in Iran, there are no reliable statistics on the prevalence of the disease there. [71,72]

One illness that has a significant psychological impact is breast cancer, when patients experience dread and anxiety due to thoughts of dying and getting a mastectomy. As they deal with and receive their diagnosis of the disease, cancer patients go through a number of psychological stages. A cancer patient's entire world abruptly and brutally comes crashing down. The patient becomes perplexed, and her modest expectations turn into significant disappointments. Nobody can truly comprehend her emotions, despite the fact that she desperately needs help. [73,74]

Researchers in the field have looked at the anguish that the affected ladies have been keeping secret and examined how they describe their illness and suffering. They gathered many accounts of changes in lifestyles and life cycles, in which terms like "transition," "transformation," "overcoming," and "discovery of meaning" were defined. The patient was given access to the accuracy, truth, balance, and integrity through the use of the found meanings. [75]

CURRENT SCENARIO

IN INDIA:

In the majority of Indian communities, early marriage, many pregnancies, and prolonged breastfeeding of all children are the norm. Due to shifting social attitudes and the pressures of working women's occupations, the urban educated class is bucking this pattern, with late-age delivery and little to no breastfeeding. The rising incidence of breast cancer may be partially attributed to these developments. The consistently found reproductive risk factors are nulliparity and a late age at the first delivery. According to case control research conducted in Mumbai, single women had a 4-5 times higher chance of having breast cancer than married women in the age range of 40-54 and above. [76,77]
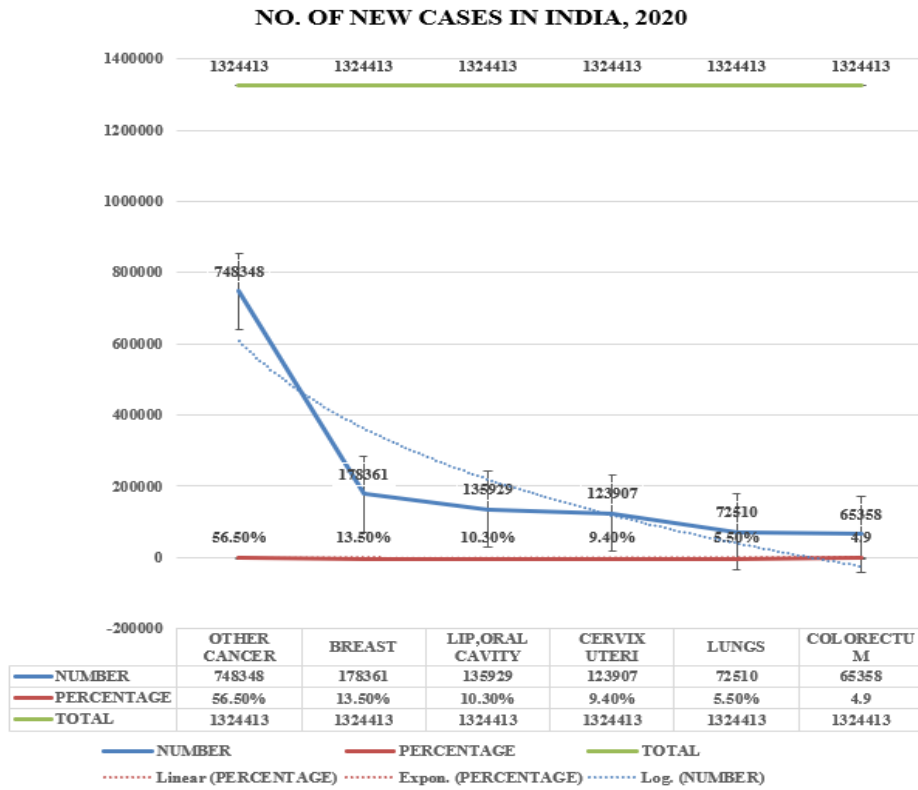
Approximately 5% of breast cancer cases are thought to be hereditary, with the BRCA1 and BRCA2 gene mutations being the two most common genetic causes. Nearly one-third of all

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breast cancer cases are thought to have a familial disease pattern. In research conducted in India on 226 breast cancer patients, 20.7% had a favorable family history.[78]

On the other hand, several other studies have noted a low prevalence of breast cancer with a family trend in Indian patients. Given that Indian breast cancer patients tend to be very young, this is particularly intriguing. Similar to data from other Indian institutes, only about 5% of all patients managed at SGPGIMS Lucknow had a confirmed family history of breast and/or ovarian cancer among first degree relatives. The majority of Indian centers do not routinely do genetic screening or testing due to a lack of resources and infrastructure. As a result, there is little information available about the genetic makeup and BRCA1/2 mutations in Indian patients. The existing research suggests that BRCA mutations occur only occasionally. Regardless of their family history, 6–10% of breast cancer patients in the majority of populations have a mutation in the BRCA gene. Numerous Indian studies have found BRCA mutations in 9–25% of cases of familial breast cancer, yet there are no reliable statistics to support this. [79-83]

Due to the secular mix of various races and religions in Indian society, people of various religious beliefs follow a wide range of lifestyle patterns and practices. Incidence rates for breast cancer are highest among Parsis and Christians in Mumbai, while Jains and Buddhists have the lowest rates. The westernized lifestyle, consanguineous marriages, and late marriage and childbearing ages of the Parsi community are potential causes of the high breast cancer prevalence.[84]

Nearly all Indian breast cancer patients identify their condition on their own, often when it has already caused secondary changes such localized skin or chest wall abnormalities or distant metastases.[85]

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NO. OF NEW CASES IN INDIA, 2020

	OTHER CANCER	BREAST	LIP, ORAL CAVITY	CERVIX UTERI	LUNGS	COLORECTUM
NUMBER	748348	178361	135929	123907	72510	65358
PERCENTAGE	56.50%	13.50%	10.30%	9.40%	5.50%	4.9
TOTAL	1324413	1324413	1324413	1324413	1324413	1324413

—— NUMBER ——— PERCENTAGE ——— TOTAL

········ Linear (PERCENTAGE) ········ Expon. (PERCENTAGE) ········ Log. (NUMBER)

Source : International Agency for Research on Cancer, WHO

Fig No. 5 Chart of No. of Cancer cases in India

Spread of Breast Cancer Across States

[†]PBCRs (Population Based Cancer Registry of India)

Source: Lok Sabha response on July 22, 2022
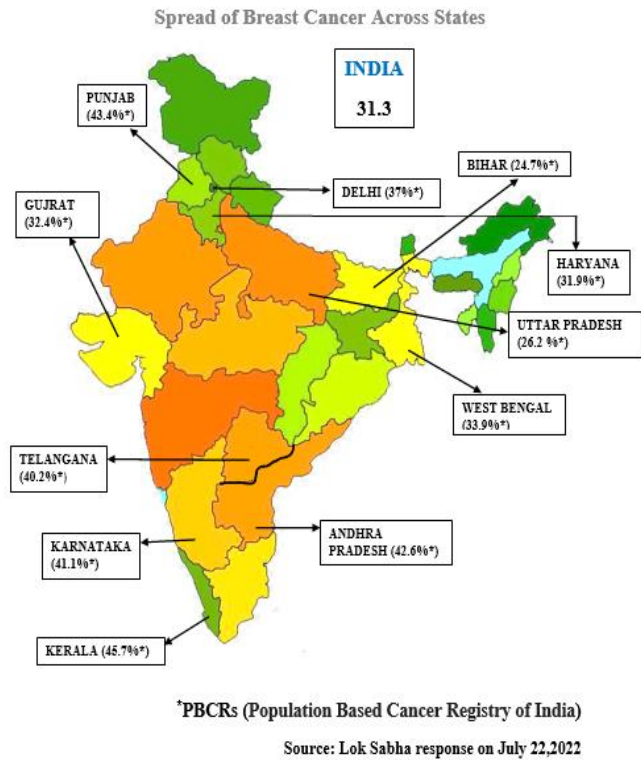
Fig No. 6 Spread of Breast Cancer Across State's

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IN WORLD:

Due to the high mortality and morbidity rates associated with breast cancer, it is a primary cause of worry for women. Even with adjuvant treatment, less than 30% of patients with metastatic breast cancer survive for five years.[86] 2.3 million new cases of breast cancer (11.7%) and a death rate of 6.9% were recorded in the most recent GLOBOCAN 2018 statistics from 185 countries, according to the IARC (International Agency for Research on Cancer).[87] The incidence of breast cancer is higher in high-income nations (571/100 000) than in low-income countries (95/10 000), which reflects the link to globalisation. Because there are several biological subtypes of breast cancer that each have a unique molecular profile and clinicopathological character, breast cancer is typically referred to as a collection of diseases (>100). [87,88]

Cancer is a serious and expanding global health issue that accounts for one in six deaths globally today and is a primary cause of morbidity and mortality [89,90]. 9.6 million people died in 2018 and there were 18.1 million new cases, with those numbers anticipated to rise in the next decades [91].The disease accounts for more than 2 million new cases each year, 11.6% of all cancer cases in 2018, and 24.2% of cases in women, making it the most common cancer worldwide and the top cause of death (6.6%) in women.[92]
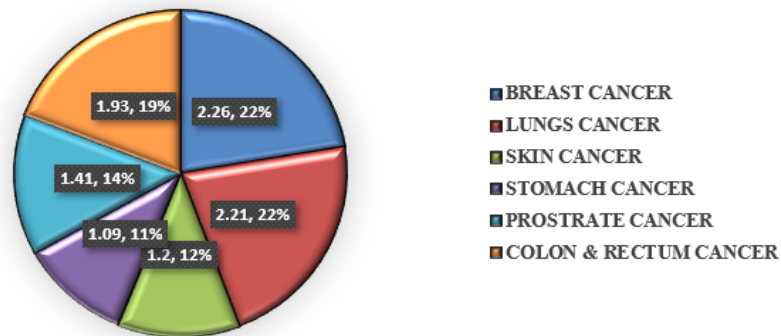
Breast cancer treatment faces significant obstacles on a global scale, demonstrating serious discrepancies. The World Health Organization (WHO) has released data showing that, despite the fact that 70% of nations have created cancer guidelines and 62% record screening programmes, 40% report significant management and treatment access limits and less than half have palliative care strategies. [93,94]

However, and this is crucial, we must acknowledge that not all new medications have a definite impact on outcomes and might not be the top priority for all nations. We recently proposed a paradigm to address the challenging problem of technology integration that can be applicable in various healthcare system settings.[95]

For instance, even though trastuzumab, which is on the WHO list of essential medications, has been linked to enhanced cure rates in patients with HER2 positive early breast cancer, we sometimes forget that chemotherapy alone, in the same situation, heals more than 60% of patients. [96-99]

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Finally, while acknowledging injustices is critical, taking action to address them is even more crucial. In that regard, we recently updated the state of cancer control in Latin America and the Caribbean and discussed ongoing challenges, especially in light of the COVID pandemic, which undoubtedly had a negative impact on diagnosis efforts and complicated patient access to healthcare systems not only in LMIC but across the globe.[100]

CASES OF DIFFERENT CANCER ACROSS ALL OVER THE WORLD (IN MILLIONS)

- ■ BREAST CANCER
- ■ LUNGS CANCER
- ■ SKIN CANCER
- ■ STOMACH CANCER
- ■ PROSTRATE CANCER
- ■ COLON & RECTUM CANCER

2.26, 22%
2.21, 22%
1.2, 12%
1.09, 11%
1.41, 14%
1.93, 19%

Source: WHO Report (Survey among 10 million's people all across the world), 3 February 2022

Fig No. 7 Cases of Different Cancer across the World

NUMBER OF DEATHS OUT OF TOTAL CASES

27%
20%
16%
16%
11%
10%

■ AFRICA   ■ ASIA   ■ SOUTH AMERICA   ■ EUROPE   ■ OCEANIA   ■ NORTH AMERICA
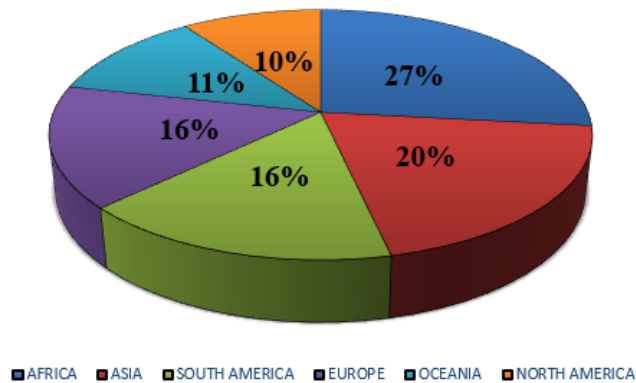
Source : International Agency for Research on Cancer, WHO, above data for year 2020

Fig No. 8 No. of Deaths out of Total Cases

TREATMENT:

Collaboration among several subspecialties is necessary for the accurate diagnosis and management of invasive breast cancer. In order to make surgical decisions on the management of the main tumour, staging of the axilla, and the order of therapy, a diagnosis

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must be made based on diagnostic imaging work-up and biopsy results. The extent of the disease is evaluated following confirmation of the diagnosis of breast cancer, which, in most cases, establishes whether or not preoperative (neoadjuvant) systemic therapy is recommended. Stage IV breast cancer that has been confirmed is thought to be incurable; unless there is a reason to remove the primary tumour for palliative purposes, systemic therapy is the only course of treatment for this condition.[101]

AYURVEDA:

According to Ayurvedic thought, each person has an innate mind-body constitution (known as prakruti), which is characterized by three physiologic principles (called doshas). The disease state known as vikruti is caused by an imbalance of these three doshas. Through diet, lifestyle changes, and other forms of therapy, the aim of vikruti is to return the doshas' equilibrium to the prakruti state (i.e., physiologic homeostasis). Key ideas in Ayurvedic nutrition include digestion, absorption, and metabolism, or agni. An Ayurvedic nutrition and lifestyle approach may be helpful for post-treatment cancer survivors who are vikruti (imbalanced) and have issues with agni (digestion and metabolism). But no research has been done on this before.[102]. Currently, the mainstays of management include chemotherapy and radiation therapy. However, because they can have negative side effects, their widespread usage has been constrained. The anti-cancer activity of Ayurvedic medicines that are sold around the world has been thoroughly investigated. Ayurveda has also produced a large number of such medications that can be used as adjuvant therapy or as a good anti-cancer alternative to standard treatment. Studies on numerous Ayurvedic plants, including Azadirachta indica, Carica papaya, Plumbago zeylanica, Ocimum sanctum, Tinospora cordifolia, and Catharanthus roseus, that are available in India are reviewed. These studies show that these plants are effective as adjuvant therapy in addition to chemotherapy and radiotherapy for many types of cancer.[103]

Since ancient times, Ayurveda has employed Azadirachta indica (Neem tree) to successfully treat malignancies. As revealed by a dose-dependent rise in DNA fragmentation and a decline in cell viability, recent research found that an ethanolic extract of neem can kill prostate cancer cells (PC-3) by causing apoptosis [104].Neem extracts have been demonstrated to have powerful anti-cancer effects against oral squamous cell carcinoma and to cause apoptosis in BALB/c mice models of 4T1 breast cancer. [105-107]

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ALLOPATHY:

Two well-known local treatments for invasive breast cancer are mastectomy and breast-conserving therapy (BCT). BCT has been shown to be safe and to provide survival outcomes comparable to mastectomy in stage I and stage II breast cancer in numerous randomized clinical trials with follow-up of up to 20 years [108-112]. Although a few earlier studies indicated locoregional recurrence (LRR) rates following BCT that were greater (10–22%) than those seen after mastectomy. [108, 110, 113]

The majority of patients who need a mastectomy have the option of a total mastectomy (simple mastectomy), a skin-sparing mastectomy, or a nipple areolar-sparing mastectomy. The chest wall's extra skin, nipple areolar complex, and breast parenchyma are all removed during a total mastectomy, leaving just enough skin to cover the incision. When the patient won't have an immediate reconstruction, it is typically employed. The skin-sparing mastectomy, which eliminates the breast parenchyma and nipple areolar complex to provide room for a tissue expander/implant or an autologous flap, was created to allow for rapid reconstruction. The skin-sparing mastectomy has been shown to be oncologic safe, with local recurrence rates of about 6%, comparable to those seen with the conventional simple mastectomy. [114-117]

Systemic chemotherapy is typically advised for high-risk patients. There are a number of standard chemotherapy regimens available, which commonly include both an anthracycline and a taxeme. Doxorubicin and cyclophosphamide for 4 cycles, followed by paclitaxel for 4 cycles (AC-T) is a popular chemotherapy treatment in the United States. After each chemotherapy cycle, dose-dense (dd) AC-T administered every two weeks with growth factor support is preferable to an earlier schedule of every three weeks.[118]

Adjuvant chemotherapy has been shown to reduce breast cancer mortality and recurrence, with a greater degree of effect in patients with HR negative disease.[119]

In addition to a chemotherapy foundation, HER2 targeted therapy is administered to patients with HER2 positive breast cancer. Patients with breast tumors who are HER2 positive now have a significantly improved prognosis thanks to theavailability of HER2 targeted treatments. Initial studies randomizing patients to chemotherapy alone or chemotherapy with trastuzumab, a monoclonal antibody aimed against the HER2 receptor, showed a reduction in the recurrence rate of about 50%. [120-125]

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ARTIFICAL INTELLIGENCE:

A "reservoir" of clinically insignificant disease, including incidental in situ carcinoma, which might be discovered by AI, exists because autopsy studies estimate that approximately 4% of women die from breast cancer rather than as a result of it. [126,127]

Mammographic characteristics are related to the illness spectrum (for example, ductal carcinoma in situ is often associated with microcalcifications). As a result, the structures inside the AI system as well as the instances on which it was trained may have a significant impact on the range of diseases that can be recognized. Interpretation may be problematic because these structures and processes in an AI system are not always apparent or understandable. Contrary to human interpretation, it may be challenging to comprehend how or why an algorithm came to a conclusion (a situation known as the "black box" problem.[128]

Since its debut in the late 1990s, computer-aided detection (CAD) has been plagued by high expectations that haven't been fully met. CAD was the first software announced for clinical application in the diagnosis of breast cancer. [129,130]Today, there are a number of commercial AI apps for breast cancer diagnosis that have received FDA approval, and early results on how well these systems work at the case level are encouraging. [131,132]

Other AI applications in breast imaging interpretation are being tested. These algorithms can be used as a "second opinion" to support the radiologist's judgement during the evaluation of a questionable breast mammogram. For instance, digital breast tomosynthesis (DBT) has been found to have a greater cancer detection rate than digital mammography alone, but its application in breast screening is currently constrained by issues including higher prices and longer evaluation times.[133]

By speeding up lesion detection in DBT pictures and enabling the use of both approaches during screening, AI can help radiologists who are using this technique for screening. Furthermore, given that the prevalence of breast cancer in the screening population is typically less than 1%, AI could set a threshold for the likelihood of malignancy and search through images to find mammograms with a high likelihood of being free of abnormalities, greatly reducing the burden on the radiologist and allowing clinicians to focus only on suspicious cases and DBT evaluation.[134]

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Another important area of application for artificial intelligence is predicting the tumor's reaction to treatment administration, and computational tools that integrate huge data to find effective drug-response patterns are now being developed.[135]

The field of radio genomics, which studies the relationship between diseases's radiographic and molecular or genetic traits, is another "omics" topic that is receiving particular attention in breast oncology. On the premise that cancers with specific genotypes cause phenotypical changes that can be inferred from radiological data, this area of research was founded. Despite being undetectable to the human eye, certain radiological traits correlate with particular tumour subtypes, and good findings have been reported in studies examining various imaging modalities. [136,137]

PREVENTION:

Primary prevention measures, such as refraining from using tobacco, exogenous hormones, and excessive exposure to ionizing radiation, as well as maintaining a healthy weight, exercising, breastfeeding, eating a balanced diet, and consuming alcohol in moderation, are currently the best ways to reduce a woman's risk of developing breast cancer.[138]

The prevention strategies used now, like as screening, chemotherapy, and biological prevention, are more direct and successful than those used in the past. Breast cancer mortality has declined. However, among women aged 20 to 59, breast cancer continues to be the main cause of cancer death.[139]

CONCLUSION:

In summary, the BC load is increasing considerably more quickly now than it was a decade ago. Making people aware of BC would start with acknowledging that it is currently one of the most common malignancies in India. It is quickly turning into a public health emergency, and society's uneasiness with discussing women's bodies has only made things worse. More readiness is required if the nation is to combat the effects. The urgent need is for a comprehensive awareness campaign and the successful implementation of a national cancer screening programme. On the healthcare front, we must likewise be proactive and achieve results.[140]

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