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A REVIEW ON INCIDENCE OF TYPES OF BREAST CANCER AND ADVERSE REACTIONS OF CHEMOTHERAPY IN CANCER PATIENTS

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ABSTRACT
Cancer is also called as Neoplasm or Tumor, is a mass of tissue formed as a result of abnormally excessive, uncoordinated autonomous, purposeless proliferation of cells. Several types of cancers are there depending upon origin, type of tissue involved, grading system. "BREAST CANCER" is the type of cancer that starts in the breast (based on origin). It can start in one or both breasts. The breast is an organ that sits on top of the upper ribs and chest muscles. There is a left and right and each one has mainly gland, ducts, and fatty tissue. Most breast cancers are carcinomas (based on tissue type). Breast cancers are also classified by certain types of proteins or genes each cancer might make. These proteins are estrogen receptors and progesterone receptors and the HER-2 gene or protein. These proteins can help to decide the stage of the cancer and treatment option. Now a day, breast cancer is the most frequently diagnosed life threatening cancer in women leading to death among women. The aim of this article is to determine and describe the incidence of types of breast cancer and adverse reactions in Breast Cancer patients who were taking the chemotherapeutic drugs involved in their treatment options. These symptoms may vary in terms of occurrence, severity and distress and be effect the treatment or illness.

KEYWORDS: Cancer, Breast cancer, Chemotherapy, Radiation therapy, Mastectomy, Carcinoma, Biopsy.

INTRODUCTION

Cancer is also called as Neoplasm or tumor is a mass of tissue formed as a result of abnormally excessive, uncoordinated autonomous, purposeless proliferation of cells. The branch of science that deals with the study of cancers is called as "ONCOLOGY".

TYPES OF CANCERS

Pathologically, tumors are generally classified by four ways

BASED ON ORIGIN: It is based on the tumor is developed from which part or organ or region of the body.
EX: Breast cancer, Liver cancer, Prostate cancer etc…..

BASED ON TISSUE TYPE: It involves which type of tissue having Neoplasm or Tumor.
Carcinoma: Carcinoma refers to a malignant neoplasm of epithelial origin or cancer of the internal or external lining of the body.
Sarcoma: Sarcoma refers to cancer that originates in supportive and connective tissues.
Myeloma: Myeloma is cancer that originates in the plasma cells of bone marrow.
Leukemia: The disease is often associated with the over production of immature WBC.
Lymphoma: Lymphomas develop in the glands or nodes of the lymphatic system.
Mixed types: The type components may be within one category or from different categories.[1]

- **Benign Tumor:** A tumor that remains confined to its original location, neither invading surrounding normal tissue nor spreading to distant body sites is known as benign tumor.

Ex: Skin wart

- **Malignant Tumor:** A tumor which is capable of both invading surrounding normal tissue and spreading (metastasis) throughout the body via the circulatory or lymphatic systems is known as malignant tumor. Only malignant tumors are properly referred to as cancer.
- Pathologically, cancers are classified into three categories: carcinomas, sarcoma, and leukemia.[2]
  Cancers cells are formed from normal cells due to a mutation or modification or changes of DNA and/or RNA. Cancer develops if the immune system is not working properly and/or the amount of cells produced is too great for the immune system to

eliminate. The rate of DNA and RNA mutations can be too high under some conditions such as: unhealthy environment, chemical carcinogens, radiation energy, food products, infectious agents and genetic predispositions to mutations.

Worldwide, Breast cancer 10.4%of all cancers incidences among women, making it the second most common type of non skin cancer and the fifth most common cause of cancer death. Breast cancer is about times more common in women than in men, although males tend to have poorer outcomes due to delays in diagnosis.[3]

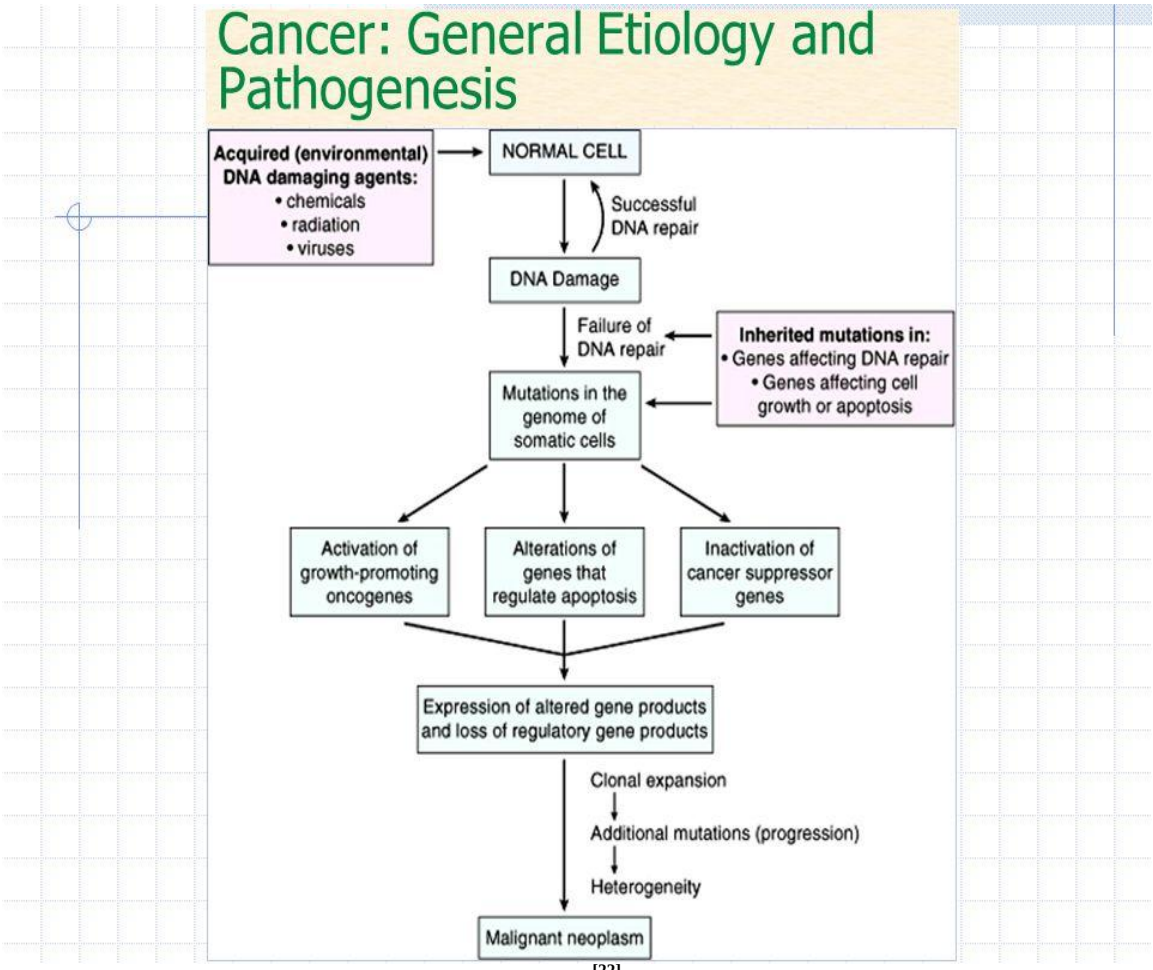

Fig: 1[22].

BREAST CANCER

Breast cancer usually refers to tumor starts from different parts of the breast tissue. The breast is an organ that sits on top of the upper ribs and chest muscles. There is a left and right breast and each one has mainly glands, ducts, and fatty tissues.[4]

ANATOMY AND PHYSIOLOGY OF BREAST

The breasts or mammary glands are accessory glands of the female reproductive system. They exist also in male, but in only a rudimentary form.[5]

STRUCTURE

Lobules: Lobules are the glands that make breast milk. Cancers that originates here are called LOBULAR CANCERS.

Ducts: Ducts are small canals that come from the lobules and carry the milk to the nipple. The most common place for occurrences of breast cancer. Cancers that originates here are known as DUCTAL CANCERS.

- The nipple is a small conical eminence at the centre of the breast surrounded by a pigmented area, the areola. A less common type of breast cancer Paget disease of the breast can start in the nipple.
- On the surface of the areola are numerous sebaceous glands (Montgomery's tubercles) which lubricate the nipple during lactation.[5]
- The fat and connective tissue (Stroma) surround the ducts and lobules and help keep them in place. A less common type of breast cancer called PHYLLODES TUMOR.[3][4]
- Blood vessels and lymph vessels are also found in each breast. Angiosarcoma is a less common type of breast cancer that can originates in the lining of these vessels[4]

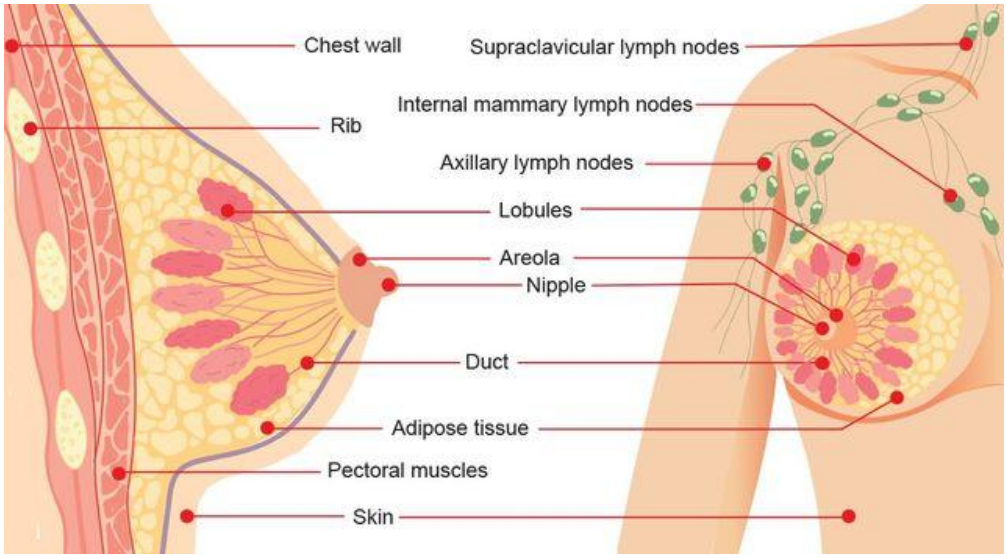

Fig:2 (23).

FUNCTION
The organs primary functions are to secrete Milk.

ETIOLOGY
We do not know what causes Breast cancer.

RISK FACTORS
Breast cancer is the primary cause of mortality among women aged 45-55years and is the second leading cause of cancer induced Death. The primary risk factors are age, high hormone level, race, economic status, and iodine deficiency in diet.

- Personal history of Breast cancer.
- The cigarette smoking; The emphasis of some articles has been on active cigarette smoke during childhood or married to a cigarette smoker are more prone to Breast cancer.[6]
- The onset of smoking in younger age increases the risk of cancer breast. Women who started smoking at 10-14years were more prone to breast cancer.
- The risk of breast cancer is higher in women with family history of breast cancer, ovarian cancer of both.[8]
- Epidemiological evidence highlights the presence of risk factors (such as Age, Obesity, Alcohol use, and exposure to Estrogen in lifetime).
- Mutations of BRCA1 raises the risk of breast cancer to 51%and 85% by the age 50and 70 years respectively[6][3][7]

INCIDENCE AND TYPES OF BREAST CANCER ACCORDING TO SITE
NON –INVASIVE BREAST CANCER: Cells that are not invade to surrounding fatty and connective tissue of the breast. Ductal carcinoma insitu (DCIS) is the most common form of non invasive breast cancer. Lobular carcinoma insitu (LCTS) is less common Breast cancer.[10,9,3]

- DCIS treated with biopsy alone, invasive cancer develops with in the same breast.[3][9]
- LCIS is generally agreed to be a marker of an increased risk of Breast cancer.
- The probability of Breast cancer in women in whom LCIS has been diagnosed is estimated to be 1% per year.
- If LCIS is detected on core needle biopsy, an excisional biopsy without lymph node sampling should be performed to the rule out DCIS or invasive cancer since these are found in 10-20% of patients.[8]

LOBULAR CARCINOMA INSITU: LCIS, lobular neoplasia. The term "insitu" refers to cancer that has not spread past the area where it initially develops.

DUCTAL INSITU CARCINOMA: DCIS is the most common of non-invasive breast cancer, is confined to the ducts of the Breast. For example ductal comedo carcinoma.[3][9][8]

INVASIVE BREAST CANCER: Cells that spread into surrounding fatty or connective tissue.

- The most common types are invasive ductal carcinoma and invasive lobular carcinoma.
- The invasive ductal carcinoma makes up about 70-80% of all Breast cancers.

Invasive lobular carcinoma: ILC is also known as Infiltrating Lobular Carcinoma. ILC originates in the milk glands (lobules) of the breast and start spreads to other regions of the body.

- ILC accounts for 10-15% of Breast cancers.

Invasive ductal carcinoma: IDS is also known as infiltrating ductal carcinoma. IDC originates in the milk ducts of the breast and invades the wall of the duct, the fatty tissue of breast and possibly regions of the body.

INFLAMMATORY BREAST CANCER: Inflammatory breast cancer is an aggressive type of

invasive breast cancer in which cancer cells block lymph vessels in the skin, causing the breast to look inflamed[12]

- It is extremely fast growing.
- It is rare and incidence about 1-5% of all breast cancers.[13]

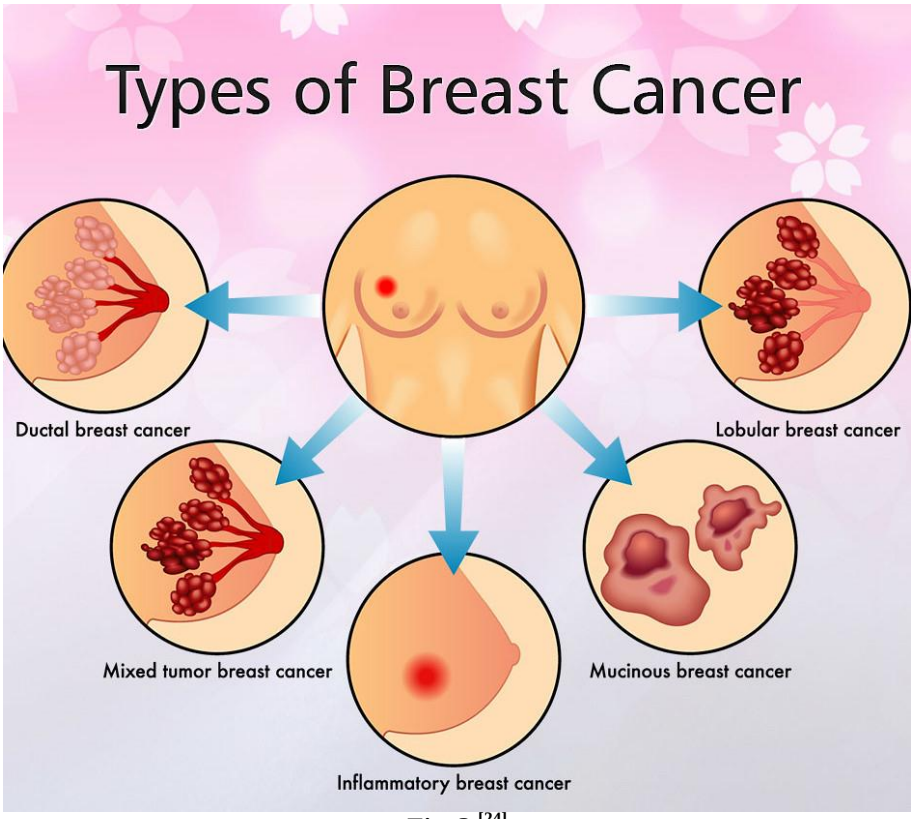

Fig. 3.[24]

LESS COMMONLY OCCURING BREAST CANCER

Medullary carcinoma: Medullary carcinoma is an invasive breast cancer that forms a distinct boundary between tumor tissue and normal tissue. Only 5% of breast cancers are medullary carcinoma.

Mutinous carcinoma: Also called colloid carcinoma, mutinous carcinoma is a rare breast cancer formed by the mucus –producing cancer cells. Women with mutinous carcinoma generally have a better prognosis than women with more common types of invasive carcinoma.

Tubular Carcinoma: Tubular carcinomas are a special type of infiltrating (invasive) breast carcinoma. Women with tubular carcinoma generally have a better prognosis than women with more common types of invasive carcinoma. Tubular carcinomas account for around 2% of breast cancer diagnoses.

PAGET DISEASE OF BREAST

- Paget carcinoma is rare i.e.1% of all breast cancer
- It involves the skin of the nipple and the areola (the dark circle around the nipple).
- It usually found along with either ductal carcinoma or invasive breast cancer.
- The signs and symptoms of Paget disease are; the skin of the nipple and areola often looks crusted, scaly, and red, there may be blood or yellow fluid coming out of nipple. Nipple looks flat or inverted sometimes. Itching or burning of breast.
- This can be diagnosed with mammogram, breast ultrasound, breast MRI and by Biopsy.[8]

ANGIO SARCOMA

- Sarcomas of the breast are rare making up less than 1% of all breast cancers.
- Originates in cells that line blood vessels or lymph vessels.[11]

PHYLLODES TUMOR

Phyllodes tumor are rare breast tumors. They develop in the connective tissue (Stroma) of the breast. Most are benign but there are others that are malignant.[9]

TRIPLE NEGATIVE BREAST CANCER (TNBC)

- TNBC accounts for about 10-15% of all breast cancers.
- The term TNBC refers to the fact that the cancer cells don't have estrogen or progesterone receptors (ER or PR) and also don't make any or too much of the proteins called HER-2. These cancers tend to be more common in women younger than age 40, who are black, or who have a BRCA1 mutation.
- TNBC differs from other types of invasive breast cancer in that they grow and spread faster, have

limited treatment options and have a worse prognosis (outcome).
- The TNBC diagnosed by checking for certain proteins such as estrogen, progesterone receptors and HER-2 proteins. If these proteins are not present indicates TNBC.[14]

STAGES OF BREAST CANCER[15]

Stage is based on primary tumor extent and size (T1-4), presence and extent of lymph node involvement (N1-3), presence or absence of distant metastases (M0-1). Simplistically stated these stages may be presented as:

EARLY BREAST CANCER

Stage 0: Carcinoma insitu or disease that has not involved the basement membrane.
Stage I : Small primary invasive tumor without lymph node involvement.
Stage II: Involvement of regional lymph nodes.

LOCALLY ADVANCED BREAST CANCER

Stage III: Usually a large tumor with extensive nodal involvement in which the node or tumor is fixed to the chest wall, also includes inflammatory breast cancer, which is rapidly progressive.

ADVANCED OR METASTATIC BREAST CANCER

Stage IV: metastases in organs distant from the primary tumor.

SIGNS AND SYMPTOMS

- A painless, palpable lump is the initial sign of breast cancer in most women.
- Armpit or breast pain.
- A rash around or on one nipple.
- Discharge from nipple, which may contain blood.
- Sunken or inverted nipple.
- Peeling, flaking or scaling of skin of the breast.

DIAGNOSIS

Laboratory findings

- Serum tumor markers such as carcinoembryonic antigen (CEA) and CA15-3 or CA27-29 are not recommended for diagnosis of early lesion or for routine surveillance for recurrence after a breast cancer diagnosis.

Imaging

- For lesions felt only by the patient: Ultrasound is often valuable and mammography essential when an area is felt by the patient to be abnormal but the clinician feels no mass.
- For metastatic lesion: For patients with suspicious symptoms or signs. Chest imaging with CT or radiographs may be done to evaluate for pulmonary metastases. PET scanning alone or combined with CT (PET-CT) may also be used for detecting soft tissue or visceral metastases in the patients with symptoms or signs of metastatic disease.

Diagnostic Tests

Biopsy: The diagnosis of breast cancer depends ultimately on examination of tissue or cells removed by Biopsy. The safest course is biopsy examination of all suspicious lesions found on physical examination or mammography or both.

Large needle(core) Biopsy: Removes a core of tissue with a large cutting needle (14- Guage) is the diagnostic procedure of choice for both palpable and image-detected abnormality core biopsy allows the tumor to be tested for the expression of biological markers such as estrogen receptor(ER),progesterone receptor (PR) and HER2

FNACytology: is a technique where by cells are aspirated with a small needle and examined cytologically.

Open biopsy: under local anesthesia as separate procedure prior to deciding upon definitive treatment has become less common with the increased use of core needle biopsy.

MANAGEMENT OF BREAST CANCER

Surgery, Radio therapy and Drug therapy are the three main treatment options considered when a treatment plan is formulated for patients undergoing active management of their cancer. Treatment options include

SURGERY

- Breast conserving surgery
- Modified Radical Mastectomy

RADIATION THERAPY

ADJUVANT SYSTEMIC THERAPY

- Chemo therapy
- Targeted therapy

‣Monoclonal antibodies Ex: Trastuzumab, Pertuzumab, Hyaluronidase
‣Antibody drug conjugates Ex: Ado Trastuzumab
‣Kinase Inhibitors Ex: Lapatinib, Neratinib

BIOPHOSPHOSPHANATES – Zolendronic acid
ADJUVANT CHEMOTHERAPY IN OLDER WOMEN – Oral chemo- Capecitabine
HORMONAL THERAPY- Tamoxifen, Fulvestrant

TREATMENT AIMS

The treatment aims are

- Eradicate the disease; cure the patient
- If eradication is not possible then control the disease, induce a remission and prolong survival.
- If neither cure nor remission is possible then control symptoms.

CHEMOTHERAPY

The drug used to treat cancer are cytotoxic drugs, i.e. drugs that kill the dividing cells commonly referred to as chemotherapy.[17]

Chemotherapeutic Drugs Used in Breast Cancer:[16]

1. ANTI METABOLITES
- 5-Fluorouracil ADRUCIL
- Capecitabine XELODA
- Gemcitabine GEMZAR

2. ANTIBIOTICS
- Doxorubicin ADRIAMYCIN
- Epirubicin ELLENCE

3. ALKYLATING AGENTS:
- Cyclophosphamide CYTOXAN

4. MICROTUBULE INHIBITORS
- Docetaxel TAXOTERE
- Paclitaxel TAXOL
- Vinblastine
- Vinorelbine NAVELBINE

A) Adjuvant chemotherapy: is given after more definitive therapy such as Surgery, to eliminate any remaining disease or undetected micro metastasis in Breast.

B) Neoadjuvant chemotherapy: is given to decrease the tumor burden before definitive therapy, such as Surgery or Radiation.

C) Palliative therapy: is usually given when complete eradication of the tumor is considered unlikely or the patient refuses aggressive therapy. Palliative chemotherapy may be given to decrease the tumor size, control, growth and reduce signs and symptoms.

D) Salvage chemotherapy: is given as an attempt to get a patients into remission, after previous therapies have failed.[18]

General Toxicity of Chemotherapeutic Agents[19][20]

Chemotherapeutic agents are most toxic to rapidly proliferating cells, including mucous membranes, skin, hair, gastroinstinal tract (GIT) and Bone marrow. The most important target of action are the nucleic acids and their precursors & rapid nucleic acid synthesis occurs during cell division.

Bone marrow: Suppression is the most common dose limiting side effects of cancer and may be one of the most life threatening. Infections, Bleeding, Anemia and fatigue are usual complications

Dermatological toxicity
- Alopecia is the loss of hair associated with chemotherapy chemo therapy agents that commonly cases alopecia include Cyclophosphamide, doxorubicin, Mechlorethamine, Paclitaxel,
- Skin changes such as dryness and photosensitivity are the complications.

GI Toxicities
- Nausea and vomiting are prominent with many cytotoxic drugs. This is due to direct stimulation of CTZ by the drug, as well as generation of emetic impulses/mediators from the upper GIT.
- Stomatitis is a generalized inflammation of oral mucosa or other areas of the GI Tract.
- Includes Erythema, pain, and dryness of the mouth, burning or tingling of the lips, ulceration, and bleeding.
- Diarrhea, constipation, anorexia, and taste changes may also occur.

Lymphoreticular Tissue

Lymphocytopenia and inhibition of lymphocyte function results in suppression of cells mediated as well as humoral immunity. Infections by fungi, viruses, pneumocystis jiroveci and toxoplasma are seen primarily in patients treated with anticancer drugs.

Chills and Fever

This Fever generally can be differentiated from fever owing to infection because of its temporal relationship to chemotherapy administration. This reaction is commonly associated with bleomycin, cytarabine, monoclonal antibodies and IL-2.

Hyper calcemia: May occur in patients with solid or hematologic malignancies and can often be the presenting sign of malignancy.

Pulmonary Toxicity: Shortness of breath, non productive cough, and low grade fever.

Cardiac Toxicity: Electrocardiograph abnormalities and left sided heart failure. Risk factors include chest irradiation and high cumulative doses of cardiotoxic chemotherapy.

Neurotoxicity: Peripheral neuropathy, ototoxicity, cerebellar toxicity, Arachnoiditis, Encephalopathy.

Gonads: Inhibition of gonadal cells causes oligozoospermia and impotence in males; inhibition of ovulation and amenorrhea are common in Females. Damage to the germinal cells may result in mutagenesis.

Infertility: Many cytotoxic agents cause sterility; this must be discussed prior to starting treatment and appropriate action undertaken. Conversely, treatment with chemotherapy is not a guarantee of birth control.

GENERAL ADVERSE REACTIONS OF CHEMOTHERAPEUTIC DRUGS USED IN BREAST CANCER

ALKYLATING AGENTS
- **Cyclophosphamide**: Nausea, vomiting, Myelosuppression, Hemorrhagic cystitis, Immunosuppression, Alopecia, Mouth sores, Stomatitis.

ANTIMETABOLITES

- **5-Fluorouracil**: Stomatitis, Myelosuppression, Diarrhea, Nausea, Vomiting, Cerebellar Ataxia.
- **Gemcitabine**: Myelosuppression, Fever, Flu-like syndrome, Rash, Mild nausea, Vomiting.
- **Capecitabine**: Diarrhea, Stomatitis, Nausea, Vomiting, Hand foot syndrome, Myelosuppression.

ANTIMETABOLITES

- **Doxorubicin**: Myelosuppression, Cardiotoxicity, Stomatitis, Alopecia, Nausea, Vomiting.
- **Epirubicin**: Myelosuppression, Nausea, Vomiting, Cardiotoxicity, Alopecia.

MICROTUBULE INHIBITORS

- **Docetaxel**: Myelosuppression, Fluid retention, Hypersensitivity, Paresthesias, Rash, Alopecia.
- **Paclitaxel**: Myelosuppression, Peripheral neuropathy, Alopecia, Mucositis, Anaphylaxis, Dyspnea.
- **Vinblastine:** Myelosuppression paralytic ileus, Alopecia, Stomatitis.
- **Vinorelbine:** Peripheral neuropathy, Myelosuppression, Nausea and Vomiting, Hepatic dysfunction.

CONCLUSION

Breast cancer is a disease that involves the patient, family, and community and wastes many financial and spiritual resources.[6] In this study, reveled the incidence of types of breast cancer and adverse reactions forced by Breast cancer patients who were taking chemotherapy. There are so many approaches in treatment of the cancer of breast such as Surgery, Radiation therapy, Chemotherapy, Hormonal therapy and recently Nanotechnology and Gene therapy. With advances in screening, diagnosis, and treatment, the death rate for breast cancer has declined.[3] Receiving chemotherapy treatment was not easy, and the side effects experienced had a negative impact on their bodies and moods. The chemotherapy related side effects commonly experienced by local cancer patients. Though these symptoms have been well characterized, their high prevalence and impact on patients, QOL and physiosocial aspects were of concern. Early detection of drug toxicity during treatment will help physician to modify the doses or drug regimen to minimize toxic effects. Pharmacovigilance helps in reducing the ADR's by changing the dosage.[21] In fact, findings of patient's perceptions and informational needs may serve as a valuable guide for clinical pharmacists to help in side effect management. The prophylactic treatment has to be encorporated to overcome the chemotherapy induced complications in cancer patients.[20]

REFERENCES

1. National cancer Institute SEER Training Modules https://training.seer.cancer.gov/disease/categories/classification.html
2. Cancer: etiology, pathophysiology, types, diagnosis and treatment by Gaurab Karki, December 20, 2019. Online biology notes.com http://www.onlinebiologynotes.com/cancer-etiology-pathophysiology-types-diagnosis-andtreatment
3. Ganesh N. Sharma, Rahu Dave, Sandhya J, Sharma P, Sharma KK. Various types and management of breast cancer: an overview. J Adv pharm Technol Res.2010 Apr: 1(2): 109-26. PMID: 22247839; PMCID: PMC3255438.
4. Henry NL, ShahPD, Hider I, Freer PE, Jagsi R, Sable MS. Chapter 88: cancer of the breast. In: Niederhuber JE, Armitage JO, Doro show JH, Kastan MB, Tepper JE, eds. Abeloff's clinical oncology. 6th ed. Philadelphia, Pa: Elsevier; 2020.
5. Ross and Wilson, Anne Waugh and Allison Grant: Anatomy and physiology in Health and Illness, 12th edition pg.No:458-459.
6. MR Ataollahi, J sharifi, MR Paknahad, A Paknahadi Breast cancer and associated factors: a review J Med life.2015; 8(spec Iss 4):6-11 2015 Dec 15. PMID 28316699; PMCID: PMC5319297.
7. Maximiliano Ribeiro Guerra, Julitte coignard, severine Eon- Marchais, Nadine Andrieu; Diagnostic chest x-rays and breast cancer risk among women with a hereditary predisposition to breast cancer unexplained by BRCA1 or BRCA2 mutation 2021.
8. Maxine A.Papadakis, MD, Stephen J.MCPhee, MD. 2019 current medical diagnosis & treatment, 58th edition, McGraw-Hill, Lange.pg.No: 753-775; 1611-1680.
9. Esteva FJ and Gutierrez C. chapter 64: Non epithelial malignancies of the breast. In : Harris JR, Lippmann ME, Morrow M, Osborne CK, eds.Diseases of the breast. 5th ed.Philadelphia, pa: Lippincott-William& Wilkins; 2014.
10. National cancer Institute. Inflammatory breast cancer.2016. accessed at http://www.cancer.gov/types/breast/ibc-fact-sheetonaugust30,2021.
11. Chugh R, sable MS, and Feng M.Breast sarcoma: Epidemiology, risk factors, clinical presentation, diagnosis, and staging. In shah S, ed.Upto date. Waltham, Mass: Up to date,2021. http://www.uptodate.com last updated March30. 2021. Accessed August 30, 2021.
12. Curigiliano G. Inflammatory breast cancer and chest wall disease: The oncologist perspective. Eur J surg oncol. 2018 Aug; 44(8): 1142-1147.
13. American joint committee on cancer. Breast In: AJCC Cancer staging Manual 8th ed. New York, NY: Springer; 2017: 589.
14. Anders CK and Carey LA. ER/PR negative, HER-2 negative (Triple Negative) breast cancer. In vora SR, ed.Upto Date. Waltham, Mass: Up to Date, 2021. http://www.uptodate.com. Last updated July 21, 2021. Accessed August 30, 2021.

15. Barbara G.wells, Terry L.Schwinghammer, Joseph T. Dipiro, Cecily V.Dipiro pharmacotherapy handbook, 10th edition, pg.no:834-848.
16. Karen whalen. Lippincott Illustrated Reviews: Pharmacology 6th edition, wotters kluwer Health/Lippincott William& Wilkins. Pg.No:587-618.
17. Gerard A. McKay, Mathew R.Walters. clinical pharmacology and therapeutics lecture notes. 9th edition, wiley-Black well, Pg.No:185-196.
18. https://www.cancer.org/cancer/breast-cancer/treatment/chemotherapy-for-breastcancer-html
19. Leon Shargel, Alan H.Mutnick, Paul F.Souney, Larry N. Swanson.comperehensive pharmacy review for NAPLEX, 8TH edition, Lippincott William& Wilkins, a wolters kluwer, Pg.No: 1001-1018.
20. A.Vijaya Madhavi et.al. World Journal of current Med and pharm Research.2019, vol-1, Iss-6, 216-222.
21. Rama subbu Sk, pasricha RK, Nath UK, Das B. Frequency, nature, severity and preventability of adverse drug reactions arising from cancer chemotherapy in a teaching hospital. J family Med Prim Care 2020; 9:3349-3355.
22. Cancer: Etiologic agents and general mechanisms by Salvador J. Diaz-Cano http://www.onlinebiologynotes.com/cancer-etiology-pathophysiology-types-diagnosis-and-treatment.
23. http://pathology.jhu.edu/breast/overview-stucture-functionsofbreast
24. http://www.cancer.org/cancer/breast-cancer/about/how-common-is-breast-cancer.html