IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals
ISSN 2349-7203
HUMAN

Human Journals
Review Article
January 2018 Vol.:11, Issue:2

A Review Article on Breast Cancer

IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals
ISSN 2349-7203
HUMAN

Biplob Dey*, Arun Kumar

Dev Bhoomi Institute of Pharmacy and Research
Dehradun, Uttarakhand, India

Submission: 30 December 2017
Accepted: 5 January 2018
Published: 30 January 2018

Keywords: Breast Cancer, Cancer, Oestrogen, Progesterone, Mammography

ABSTRACT

The aim of this study was to give a brief explanation about Breast Cancer, its causes, factors that cause breast cancer, diagnosis, treatment, etc. in India and in World. Also given a brief description of Cancer, and its types. Breast cancer is the most common female cancer in the world, Breast cancer incidence is rising all over the world, at different rates. Worldwide, breast cancer is ranked second in terms of incidence after lung cancer. It is estimated that worldwide 1.67 million new cancer cases diagnosed in 2012 survey by WHO and in India, it is approximately 25.8 per 100,000.It has now become the most common female cancer in urban as well as rural India. Breast Cancer not only grows in female but it can also grow in male, although it is very less. Less than 1% of all breast cancer cases develop in men, and only one in a thousand men will ever be diagnosed with breast cancer.

INTRODUCTION:[1,2,3,4,5,6,7]

Breast cancer is a very common type of cancer in women, breast cancer is characterized by the uncontrolled growth of abnormal cells in the milk production glands of the breast or in the passages (ducts) that deliver milk to the nipples. It is a malignant tumor that starts in the breast tissue of male and female. Like the female, the male also has breast tissue too, comprised of fat, fibrous tissues, fine ducts and glandular elements or lobules. The majority of breast cancers begin in the ducts (ductal cancer). A small number start in the sacs or lobules (lobular cancers). Within these two groups, there are different subtypes of breast cancer. Some grow very slowly, while others grow at a rapid speed. Breast cancer can spread to lymph glands and to other parts of the body, such as the bones and liver. Breast cancer is typically detected either during a screening examination, before symptoms have developed, or after a woman notices a lump. Cancer is a major cause of morbidity and mortality in developing and developed countries like Asian countries, America, Africa, Australia, etc. In many low-income and middle-income countries, including India, most of the population does not have access to a well organized and well-regulated cancer care system. Globally breast cancer incidence increased from 641,000 (95% confidence intervals 610,000-750,000) cases in 1980 to 1,643,000 (1,421,000-1,782,000) cases in 2010, an annual rate of increase of 3·1%. For women aged 15-49 years, twice as many breast cancer cases were recorded in developing countries than in developed countries. This variation in incidence may be due to multiple factors, including geographic variation, racial/ethnic background, genetic variation, lifestyle, environmental factors, the presence of known risk factors, utilization of screening Mammography, stage of disease at diagnosis and the availability of appropriate care.

Beginning in the 1980s, screening mammography led to sweeping improvements in early detection of breast cancer. Mammography is a specialized medical imaging that uses a low-dose x-ray system for scanning the breasts. A mammography exam, called mammogram, helps in the early detection and diagnosis of the breast diseases in women. Screening mammograms are administered to detect breast cancer in women who have no apparent symptoms.

What is Cancer?[5,6,7]

It is known to everyone since ancient that cancer is a very serious disease which destroys the complete organ or may affect the whole body. Now it became the very common disease in

both developed and developing countries. Our body is made up of billions of cells. These cells are so small that we cannot see it with our naked eyes, it needs microscope to make it visible. Cells comprise together to form the tissues and organs of our bodies. Now, when there is the uncontrolled growth of cells due to some physical factors or chemical factors inside the body, then that phase is known as cancer. Normal cells are constantly subject to signals that command whether the cell should divide, differentiate into another cell or die. But due to some changes, the cell becomes unable to divide and starts growing by making its own path which is known as cancer.

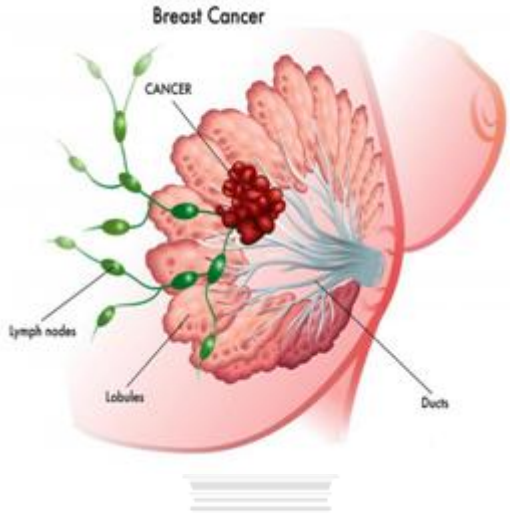

Figure: 1 Breast Cancer

Cancer may grow in any part of the body or cell. Cancer grouped according to the type of cell they start in. There are 5 main types. They are as follows-

- **Carcinoma** – Cancer that begins in the skin or in tissues that line or cover internal organs. There are different sub-types, including adenocarcinoma, basal cell carcinoma, squamous cell carcinoma and transitional cell carcinoma

- **Sarcoma** – cancer that begins in the connective or supportive tissues such as bone, cartilage, fat, muscle or blood vessels

- **Leukaemia** – cancer that starts in blood-forming tissue such as the bone marrow and causes abnormal blood cells to be produced and go into the blood

- **Lymphoma and myeloma** – cancers that begin in the cells of the immune system.

- **Brain and spinal cord cancers** – these are known as central nervous system cancers

Cancers are classified into two main types:

- **Benign:** Benign cancer is a type of cancer that does not spread its surroundings.
- **Malignant:** Malignant cancer is a type of cancer that may spread its surroundings.

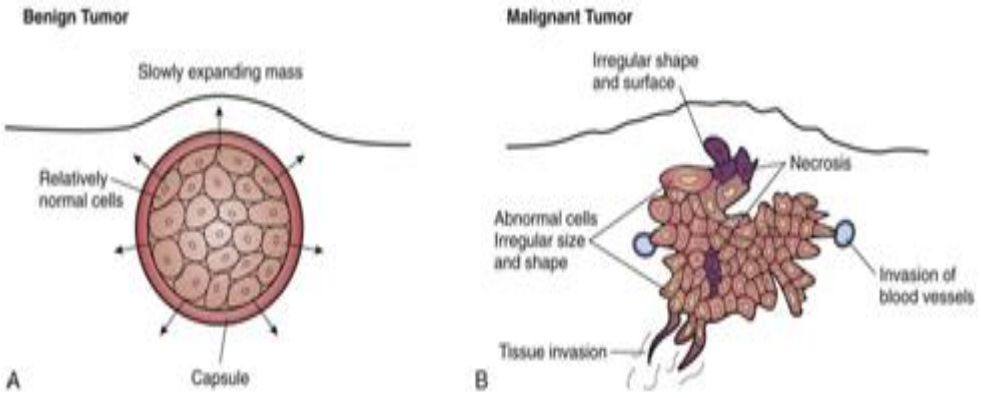

Figure: 2 Benign and malignant cancer

MATERIALS AND METHODS:[8,9,10,11,12,13,14,15,16,17,18,19,20,21,22,23]

The vast majority of breast cancers begin in the parts of the breast tissue that are made up of glands for milk production, called lobules, and ducts that connect the lobules to the nipple. Nowadays breast cancer became the fastest growing cancer in women both in developed and developing countries.Breast cancer may grow in two types:

1) **In Situ:** Ductal carcinoma in situ (DCIS) is a condition where abnormal cells replace the normal epithelial cells of the breast ducts and may greatly expand the ducts and lobules. DCIS is considered a noninvasive form of breast cancer because the abnormal cells have not grown beyond the layer of cells where they originated. It is the most common type of in situ breast cancer, accounting for about 83% of in situ cases diagnosed during 2008-2012. DCIS may or may not progress to invasive cancer; in fact, some of these tumors grow so slowly that even without treatment they would not affect a woman's health.

2) **Invasive:** This is very common, most breast cancers are invasive, or infiltrating. These cancers broke the walls of the glands or ducts where they originated and grow into surrounding breast tissue.

Breast cancer can begin in different areas of the breast -the ducts, the lobules, or in some cases, the tissue in between. Here, the different types of breast cancer, including non-

invasive, invasive, recurrent, and metastatic breast cancers, as well as the intrinsic or molecular subtypes of breast cancer in female as well as male.

- DCIS- Ductal Carcinoma In Situ.
- IVC- Invasive Ductal Carcinoma.
- IDC type-Tubular Carcinoma of Breast
- IDC Type: Medullary Carcinoma of the Breast
- IDC Type: Mucinous Carcinoma of the Breast
- IDC Type: Papillary Carcinoma of the Breast
- IDC Type: Cribriform Carcinoma of the Breast
- ILC — Invasive Lobular Carcinoma
- Inflammatory Breast Cancer
- LCIS — Lobular Carcinoma In Situ
- Male Breast Cancer
- Molecular Subtypes of Breast Cancer
- Paget's Disease of the Nipple
- Phyllodes Tumors of the Breast
- Recurrent & Metastatic Breast Cancer

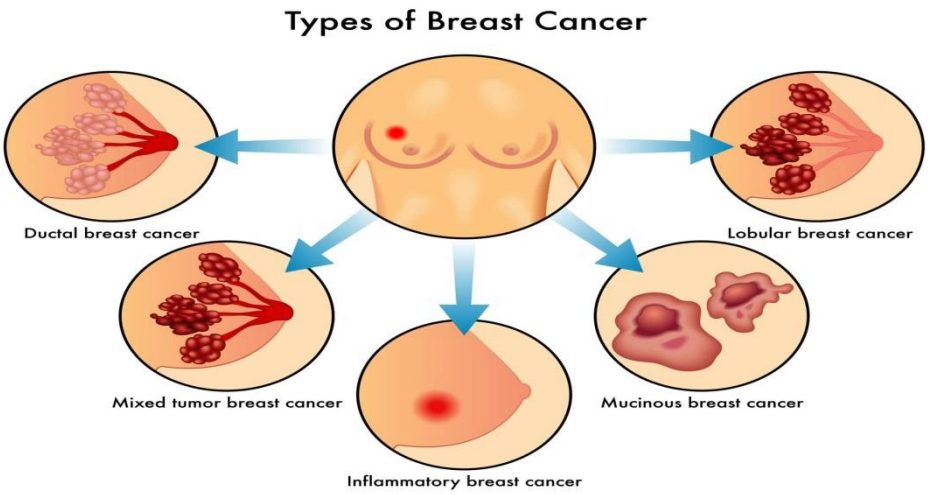

Figure 3: Types of Breast Cancer

History of Breast Cancer:[10,11,12]

Ancient Egyptians were the first came to know the disease more than 3,500 years ago.In 460 B.C., Hippocrates, the father of Medicine, described breast cancer as a humoral disease. He postulated that the human body is formed of four senses of humor - blood, phlegm, yellow bile, and black bile. He said that cancer was caused by the excess of black bile. Again, thereafter in A.D. 200, Galen described cancer as well. He also suggested excessive black bile.He suggested medications like opium, castor oil, liquorice, sulfur, salves etc. for medicinal therapy of the breast cancers.In 1680, French physician Francois de la Boe Sylvius, he hypothesized that cancer did not come from an excess of black bile. He suggested it came from a chemical process that transformed lymphatic fluids from acidic to acrid. In the 1730s, Paris physician Claude-DeshaisGendron also rejected the systemic theory of Galen and said that cancer developed when nerve and glandular tissue come together and get merge with lymph vessels. In 1713 Bernardino Ramazzini's developed a hypothesis that high frequency of breast cancer in women was due to lack of sex. Ramazzini said that without regular sexual activity, reproductive organs, including the breast may get deactivate or destroyed and develop cancers. Again, another researcher Friedrich Hoffman of Prussia postulated that women who had regular sex but still developed cancer were practicing “vigorous” sex. This could be leading to lymphatic blockage. Later, many research has been done by many scientists on breast cancer and its treatments. After many research scientists suggested that surgical removal of the tumor could help to treat breast cancer. By the mid-nineteenth century, surgery was the available treatment for breast cancer. The development of antiseptic,

anesthesia and blood transfusion during this time also made survival after a surgery more possible.

In1976, Fisher published results using simpler breast-conserving surgery followed by radiation or chemotherapy. He noted that these were just as effective as radical mastectomy. With the development of modern medicine, by 1995, less than 10 percent of breast cancer-inflicted women had a mastectomy. This time also saw the development of novel therapies for breast cancer including hormone treatments, surgeries, and biological therapies. Mammography was also developed for early detection of the cancers. Scientists then isolated the genes that cause breast cancer: **BRCA 1, BRCA2 and ATM**.

Stages of Breast Cancer:[13,14]

The stages of breast cancer ranges from 0-4

(0-IV).

- Stage 0
- Stage I
- Stage II
- Stage III
- Stage IV

Cancer stage is based on four characteristics:

- The size of the cancer
- Whether the cancer is invasive or non-invasive
- Whether cancer is in the lymph nodes
- Whether cancer has spread to other parts of the body beyond the breast.

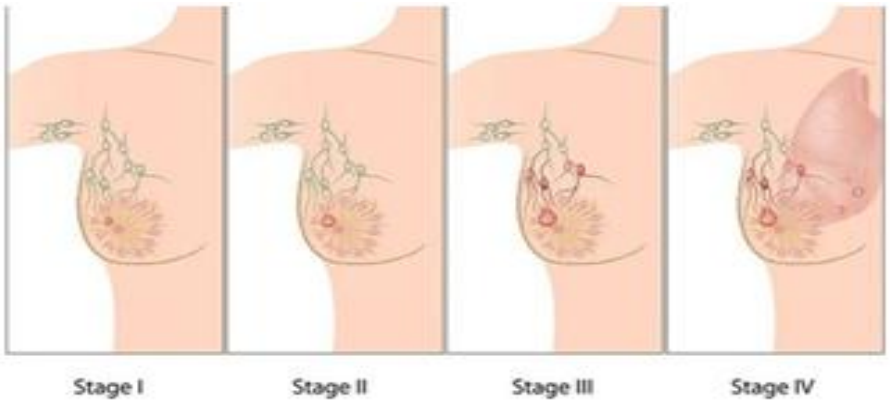

Figure 4: Stages of breast cancer

Cancer may also describe as-

- Local
- Regional
- Distant.

1) Stage 0: This breast cancer means that breast cancer cells have developed, but they cannot spread to any other surrounding tissues, or to the lymph nodes or other organs.

2) Stage I: The first stage of breast cancer means that tumor size is less than 2 cm. The I stage is divided into two Stage IA & Stage IB.

- **Stage IA**: The tumor measures up to 2 cm and cancer have not spread outside the breast; no lymph nodes are involved.
- **Stage IB**: There is a tumor in the breast that is no larger than 2 cm, and there are small groups of cancer cells larger than 0.2 mm but not larger than 2 mm in the lymph nodes.

On the 1st stage, the survival rate during 5 years is almost 100%.

3) Stage II: Stage II is divided into subcategories known as IIA and IIB**.**

- **Stages IIA:** It this tumor size is less than 2 cm.In this tumor spread to no more than 3 lymph nodes under the arm, forming metastases more than 2 mm in diameter.
- **Stages IIB**: The tumor is larger than 2 cm but not larger than 5 cm, small groups of breast cancer cells larger than 0.2 mm but not larger than 2 mm are found in the lymph nodes.

4) Stage III: Stage III is divided into subcategories known as IIIA, IIIB, and IIIC.

- **Stage IIIA:** Indicates that tumor is not more than 5 cm and has spread to not more than 9 lymph nodes in the axilla or formed metastases in the lymph nodes in the mammary gland, but not to internal organs.

- **Stage IIIB:** In this stage, the tumor starts growing in the chest and skin but did not form metastases in the internal organs**.**

- **Stages IIIC:** It describes invasive in which tumor start starts developing. In this cancer effect more than 10 axillary lymph nodes. The tumor may be any size and may have spread to the chest wall and the skin of the breast.

5) Stage IV: It is described as invasive breast cancer that has spread beyond the breast and nearby lymph nodes to other organs of the body, such as the lungs, distant lymph nodes, skin, bones, liver, or brain**.**

Symptoms of Breast Cancer:[13,15]

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 should go 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 pain 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.

Risk Factors for Breast Cancer:[15,16,17]

Many studies found that breast cancer caused due to the combination of many diseases in women. Most of the cancer cases are found in the women who are older than 50.the major risk factors that may cause Breast cancer is as follows-

- **Getting older**- The risk of breast cancer increases with age, most breast cancers are diagnosed after age 50.

- **Genetic mutations**- Inherited changes (mutations) to certain genes, such as BRCA1 and BRCA2. Women who have inherited these genetic changes are at higher risk of breast and ovarian cancer.

- **Early menstrual period**- Women who start their periods before age 12 are exposed to hormones longer, raising the risk for breast cancer by a small amount.

- **Late or no pregnancy**- Having the first pregnancy after age 30 and never having a full-term pregnancy can raise breast cancer risk.

- **Late Menopause** -If you have a late menopause (after the age of 55) this increases your breast cancer risk compared to women who have an earlier menopause.

- **Obesity** -Older women who are overweight or obese have a higher risk of getting breast cancer than those who have normal weight.

- **Having dense breasts**- Dense breasts have more connective tissue than fatty tissue, which can sometimes make it hard to see tumors on a mammogram. Women with dense breasts are more likely to get breast cancer.

- **Using combination hormone therapy**- Taking hormones to replace missing estrogen and progesterone in menopause for more than five years raises the risk for breast cancer. When hormones progesterone and estrogen are taken together it increases the risk of breast cancer.

- **Taking oral contraceptives (birth control pills)**- Certain forms of oral contraceptive pills have been found to raise breast cancer risk.

- **A family history of breast cancer**- A woman's risk for breast cancer is higher if she has a mother, sister, or daughter or multiple family members on either her mother's or father's side of the family who has had breast cancer. Having a first-degree male relative with breast cancer also raises a woman's risk.

- **Previous treatment using radiation therapy**- Women who had radiation therapy to the chest or breasts (like for treatment of Hodgkin's lymphoma) before age 30 have a higher risk of getting breast cancer later in life.

- **Drinking alcohol**-Studies show that a woman's risk for breast cancer increases with the more alcohol she drinks.

- **Smoking** – Smoking tobacco also causes the risk factor for breast cancer.

Death by Breast Cancer Globally:

It is estimated that worldwide **1.67million** new cancer cases diagnosed in 2012 survey by WHO and in India, it is approximately **25.8** per **100,000**.In the USA at present, there are about **3 million** women living with breast cancer. In 2018, an estimated **2,66,120** new cases of invasive breast cancer are expected to be diagnosed in women in the U.S., along with **63,960** new cases of non-invasive (in situ) breast cancer. About 40,920 women in the U.S. are expected to die in 2018 from breast cancer. In Australia, the number of deaths from breast cancer increased from **1,435** (19 males and 1,416 females) in 1968 to **2,844** in 2014.In 2017 approximately **17,730**(Female & Male) new cases have been diagnosed in Australia. In Africa, it is estimated that in 2012 94,000 women developed breast cancer and 48,000 died from it in sub-Saharan Africa.

The countries with the top 10 highest incidences of breast cancer-

Table-1: Top 10 countries with the highest number of Breast Cancer

Rank	Country	Age-Standardised rate per 10000 (world)
1	Belgium	111.9
2	Denmark	105.0
3	France	104.5
4	The Netherlands	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

Treatments for Breast Cancer:[3,22,23]

Breast cancer treatment options vary depending on the stage of cancer. There is various way to treat breast cancer. They are divided into two –

- **Local Treatment**: Local treatment is done for localized area meaning only the tumor is treated without involving the other organ of the body. Types of local treatments are-

1) **Surgery**: This is the best treatment option for patients whose breast cancer has not spread to other parts of the body. The types of breast cancer surgery differ in the amount of tissue that is removed with a tumor, this depends on the tumor's characteristics. Some of the most common types of surgery are-

a) Breast-conserving therapy or Lumpectomy: This involves the removal of the cancerous area, the surrounding tissue and in some cases the lymph node.

b) Partial Mastectomy or Quadrantectomy: This surgery is done where a larger portion of tissue is removed.

c) Total Mastectomy: This surgery involves the removal of the entire breast, without the removal of lymph nodes.

2) **Radiation Therapy**: It is a treatment in which high-energy rays (such as x-rays) are used to destroy cancer cells. They are divided into two main types –

a) External beam radiation: Radiation comes from a machine outside the body.

b) Internal radiation: In this method, a radioactive source is put inside the body for a short time.

- **Systemic Treatment:** Drugs used to treat breast cancer are considered systemic therapies. They are of three types-

1) **Chemotherapy:** Chemotherapy may be given before the surgery (neo-adjuvant) with the aim to reduce tumor size and the need for extensive surgery, or after surgery (adjuvant) to reduce the chances of cancer coming back.

2) Hormonal therapy: Medicines that block or inhibit the actions of the sex hormones estrogen and progesterone are often used in this treatment. It reaches to almost all part of the body not only in the breast.

3) **Targeted therapy:** Targeted therapies are a relatively new step for cancer treatment and target specific biological processes that are often essential to tumor growth. Targeted therapy can include the use of antibodies, vaccines and gene therapies. These targeted drugs are designed to block the growth and spread of cancer cells. These drugs attack all cells that are growing quickly in the body.

RESULTS AND DISCUSSION:

Nowadays breast cancer became the fastest growing cancer type especially in the women in both developed and developing countries, it is due to many factors it may be physical, chemical, genetic, it may be due to in taking of pills which contain high level of estrogen and progesterone, late pregnancy after 30 years also increase the risk of breast cancer. Although nowadays there are various new techniques are developed to treat breast cancer but they can only treat cancer from 0-II stages only and III & IV stages are very serious stages and they cannot be treated easily once they spread over the whole breast.

CONCLUSION:

In this article, we have briefly explained about the Breast Cancer, history, its risk factors, symptoms, death by breast cancer in India and in world & treatments which we have studied from many review and research article that have been published by many National and International journal. Breast cancer mainly causes due to the hypersecretion of sex hormones (estrogen & progesterone)&due to blockage of ducts in the breast. So, in a taking of pills

which contain the high amount of estrogen and progesterone must be avoided or should not take continuously because it increases the risk of developing cancer. And body weight must be maintained because overweight women have a higher risk of getting breast cancer than those who have normal weight.

REFERENCES:

1) WHO programmes BreastCancer: Prevention and Control.
http://www.who.int/cancer/detection/breastcancer/en/index1.html
2) National Breast Cancer Foundation, Inc., Male Breast Cancer.
http://www.nationalbreastcancer.org/male-breast-cancer
3) A guide for journalists on breast cancer and its treatment-Roche
https://www.roche.com/dam/jcr:5260dc48-ffc1-4991-9f3f-0bdae3e42128/en/med-breast-cancer.pdf
4) M.Badaway Samir, A. Hefnawy, E. Zidan, T. GadAllah, Breast Cancer Detection with Mammogram Segmentation: A Qualitative Study,*(IJACSA) International Journal of Advanced Computer Science and Applications, Vol. 8, No. 10, 2017*
5) Cancer treatment centers of America
http://www.cancercenter.com/what-is-cancer/
6) Instructor- ArtemCheprasov.
http://study.com/academy/lesson/benign-vs-malignant-definition-characteristics-differences.html
7) National Cancer Institute, What is Cancer
https://www.cancer.gov/about-cancer/understanding/what-is-cancer
8) DC Allerd, Ductal carcinoma in situ: terminology, classification, and natural history, Department of Pathology and Immunology, Washington University School of Medicine, 660 South Euclid Ave, Campus Box 8118, St Louis, MO 63110, USA, NCBI Review.
https://www.ncbi.nlm.nih.gov/pubmed/20956817
9) American Cancer Society, Breast Cancer fact, and figures 2015-16.
https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/breast-cancer-facts-and-figures/breast-cancer-facts-and-figures-2015-2016.pdf
10) Dr.MandalAnanya, History of Breast Cancer, News Medical Life Sciences.
https://www.news-medical.net/health/History-of-Breast-Cancer.aspx
11) Brechon Sarah, Maurer Foundation Breast Health Education, A Brief History of Breast Cancer.
https://www.maurerfoundation.org/a-brief-history-of-breast-cancer/
12) Random History, A History of Breast Cancer.
http://www.randomhistory.com/1-50/029cancer.html
13) Breastcancer.org, Stages of breast cancer.
http://www.breastcancer.org/symptoms/diagnosis/staging
14) MitsukAnzhelika, Breast cancer information for young women, Turku University of Applied Science.
https://www.theseus.fi/bitstream/handle/10024/123683/thesis%2020.12%20new.pdf?sequence=1
15) Chun Christina, What are the sign and symptoms of Breast Cancer, Healthline.
https://www.healthline.com/health/breast-cancer/warning-signs#causes
16) Cancer Research UK, Breast Cancer.
http://www.cancerresearchuk.org/about-cancer/breast-cancer/risks-causes/risk-factors#collapse-113901
17) Centre for Disease Control and Prevention(CDCP), Breast Cancer.
https://www.cdc.gov/cancer/breast/basic_info/risk_factors.htm
18) Canadian Cancer Society, CancerInformation, Risk Factors for Breast Cancer.
http://www.cancer.ca/en/cancer-information/cancer-type/breast/risks/?region=on
19) ASCO, Cancer statistics.
https://www.cancer.net/cancer-types/breast-cancer/statistics
20) Australian Government, Cancer Australia, Cancer Statistics.

https://breast-cancer.canceraustralia.gov.au/statistics
21) World Cancer Research Fund, Breast Cancer Statics.
http://www.wcrf.org/int/cancer-facts-figures/data-specific-cancers/breast-cancer-statistics
22) American Cancer Society, Treating Breast Cancer.
https://www.cancer.org/cancer/breast-cancer/treatment.html
23) Breastcancer.org, Treatments and side effects of breast cancer.
http://www.breastcancer.org/treatment