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Visualization of Genomic Sequence in BRCA1 and BRCA2

Mandeep Kaur[1], Amit Chawla[2,*], Bharti[3], Payal Rani[4], Mangilal[5], Vikramjit singh[3], Sachin Poonia[5], Mohit[5], Lovepreet[3]

Abstract

Heredity is the main reason of breast cancer in women and mutation or genetic variations also another reason for the spread of breast cancer. Heredity and genetic variations are responsible 5%–10%, 30%–50% respectively. There are 90% chances of developing neoplasm by the mutations. The effect of BRCA1 and BRCA2 may leads to the variations in DNA therefore it should be in limited amounts so that there will be minimum changes in DNA. The BRCA1 and BRCA2 helps to repair or heal the DNA sequences but it grows rapidly and causes cancer. BRCA1 and BRCA2 can carry out for the patients who have the past occurrence (family history) of the carcinoma. The history is done by the clinical evidence or diagnosis of the patient. For the diagnosis, we can use the various methods blood test, mammogram, breast ultrasound, biopsy etc. The ayurvedic and allopathic treatment is useful for the cure of various kinds of cancers, the ayurvedic medicines, such as herbal drugs are helpful because they have the anti-cancer properties as well as the allopathic treatment is also required because the tumour is suppressed by these and the examples of pharmacological treatment like alkylating agents, plant producers, etc. BRCA1 and BRCA2 are cancer suppressor genes, the sequence of these coding regions shows no similarity to the proteins with each other. If one copy in the gene is mutated, the result becomes hereditary and transfer breast and ovarian cancer from one generation to other generation.

Keywords: BRCA1, BRCA2, DNA, gene mutations, alkylating agents

INTRODUCTION

Near About 2 in 20 women in the world develop cancer of the breast and at least 6% of these cases are thought to result from a hereditary tendency to the disease (Rehman N. et al., 1998). These two genes have capability of causing breast cancer epitomized, more than 5 cases of breast cancer are diagnosed below the 60 years of their age in most families. If women who have loss of inherit loss of function of mutation in one allele, then there will be risk of up to 85% of breast cancer. Mutation is a major reason for the high risk of breast cancer and ovarian cancer. Most of the mutations of these genes come by the insertion or deletion of some bases or single base substitution that result in the stopping of premature codon. (Perrin–Vidoz et al., 2002; Narod and Foulkes, 2004) [1, 2]. The observed prevalence or frequency of BRCA1 mutations are lesser than predicted by linkage analysis, malignant and pathogenic variations in the coding region of the gene being arise is approximately two-thirds of BRCA1-linked families. There are number of cases of the breast cancer, some of them due to heredity and some due to genetic variations, like 5%–10% and 30%–50%, respectively. Examine the entire sequence of both the genes is necessary because in both cases the variants are spread uniformly along the entire coding region and complete sequences be situated along each axon. Since most of the mutations

***Author for Correspondence**
Amit Chawla
E-mail: amitchawla84@gmail.com

[1]Associate Professor, Maa Saraswati Institute of Pharmaceutical Sciences, Sitto Road, Abohar, Punjab, India.
[2]Professor-Principal, Maa Saraswati Institute of Pharmaceutical Sciences, Sitto Road, Abohar, Punjab, India.
[3]Research Scholar, Maa Saraswati Institute of Pharmaceutical Sciences, Sitto Road, Abohar, Punjab, India.
[4]Associate Professor, Seth GL Bihani SD College of Tech. Edu. Sriganganagar, Rajasthan, India.
[5]Assistant Professor, Maa Saraswati Institute of Pharmaceutical Sciences, Sitto Road, Abohar, Punjab, India.

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involved high penetration, have 80%–90% lifetime risk of developing these neoplasm (Neuhausen S. et al., 1996, Struewing JP. et al., 1995) [3, 4].

EVOLUTION AND CLINICAL IMPORTANCE OF SEQUENCE VARIANT IN BRCA1 AND BRCA2

Over a prolonged period, there is a use of gene changing matrix, which increased to such a great extent or offered the option of vaccinated surgery to prevent development of (further) carcinomas . They lead to the increased therapy of the BRCA1 and BRCA2 which acts upon the specific cells. Based on the therapeutic applications, some experts have demonstrated such genetic testing related to newly diagnosed breast cancer cases occurring before menopause as per the latest reports. Acc. to WHO and the recent data, mutations are more responsible irrespective of family history of cancer (Trainer et al., 2010) [5].

The patients having both pathogenic mutations as *BRCA1* and *BRCA2* are reported earlier (Tesoriero A. et al.,1999, Tsongalis GJ. et al., 1998) [6 , 7]. Hence, it does not show the neutrality of the *BRCA2* unclassified variants. However, testing has become considerably more widespread in the USA where it has been directly marketed to consumers, and physician practices and other health care workers, such as community oncologists and gynecologists, Despite current recommendations of the American Society of Clinical Oncology that all genetic testing, identification and genomic risk of BRCA1 and BRCA2 assessment is conducted in the setting of pre and post-test counselling (Robson et al., 2010) [8]. Chromosomal integrity maintenance is vital for every creature or living organism [9-12]. DNA healing or repair protein would be evolutionary defended, so it maintains the value of this process. The change must be minimal in the sequences of DNA over time. No doubt the BRCA1 gene is necessary for DNA repairing but there is also reported or evaluated that the gene has been increased rapidly and may cause breast and ovarian cancer in females, if the number of genes will increase day by day, the women with pathogenic variant found i.e. BRCA1 and BRCA2 can be advised to undergo for regular screening or detection by mammography and also advised for risk reducing surgery (Chang J. et al., 2001 and Eeles RA. et al., 2001) [11, 13]. Mutations of BRCA1 may cause the 30% to 40% chances of ovarian cancer whereas BRCA2 mutations carrier may cause the male chest cancer prostate and increase the risk of ovarian cancer (O'Donovan PJ. et al., 2010) [14].

Effect of BRCA1 and BRCA2 on the Breast Cancer

If carrier mutation occurs in BRCA1 or BRCA2 then risk of breast cancer is approximately 80% (Antoniou A et al., 2003 and Ford D et al., 1998), the chances which enhance the risk of breast cancer may decreases because of some modification factors [10, 15]. Now a days, the breast and ovarian cancer also depends on the reproductive factor in most of the population (Pike MC. et al., 1983), and from an observation, it is found that the risk of breast cancer is mainly in age of 40 in both BRCA1 and BRCA2 carrier (Jernstrom H. et al.,1999) [16 -20]. The size of study has not wide, but the limit of confidence level is wide according to the publication of original report. This information is evaluated with the help of much larger sample of subject. In women, who carrying mutation in either BRCA1 or BRCA2 having probability less than or equal to less than 1%, these genes are known as a non-carrier. In young girls, at the age of 20–29 years the chances are 10.5% by mutations, and at the age of 50–55 the number decreases to 10.5% to 7.5% (Clause B. Elizabeth et al., 1998) [12].

Recent studies of BRCA1 help to enhance and approve the understanding about the role of BRCA1genomic changes in ovarian and mammary carcinoma, which in turn will provide more accurate and reliable information and it can improve the better clinical decision making with respect to layout or design of cancer therapy. The major significance of this meta-analysis study was prognosticative results [21-28].

Diagnosis

- *Blood Test:* Blood tests are performed to diagnose breast cancer and the result may or may not be accurate. A complete blood count is performing while patients are taking medicines because some of the medicines can elevate the ranges of cells. It can help to detect liver by increasing the levels of alanine aminotransferase and aspartate aminotransferase, kidney and bones while the cancer cells spread to these organs, which may increase the levels of alkaline phosphate and calcium [8].
- *Examination of Breast:* During examination, check the armpit of patients and other abnormalities of any lumps, then proceed further to carry out the procedure.
- *Mammogram:* x-ray of breast and doctor will go for further evaluation or any abnormities. X-rays are used in screening mammograms to produce images of the breast. It can detect breast cancer early, even before a lump appears. It's currently the greatest screening test available to detect cancer in female patients [12].
- *Breast Ultrasound:* It is an important imaging technique for the detection of lesions in the breast. If the therapists identify any new lump, then ultrasound is carried out to find whether it is solid mass or liquid mass [9].
- *Biopsy:* It is used to remove cells and tissues from the body. There are 2 main types of biopsies, needle and surgical. It requires a hollow needle to collect samples from the tissues of the breast after following anesthesia. Needle biopsy is again subdivided into two categories, core needle biopsy and fine needle biopsy. Surgical biopsy can also be used to detect the complete sores in breast. During this, breast sample is taken and examined under a microscope to check division of cells and to identify the tumor [23].
- *CT Scan and MRI:* During MRI, an internal picture of breast is taken and before MRI dye is given to identify the cell.

Factors Affecting the Genetic Changes in BRCA1 and BRCA2 on Breast Cancer

Inheritance (hereditary) and Environmental Conditions

The incidence of mammary carcinoma in the non-hispanic white women is 65%, which is higher than the hispanic women living in the San Francisco Bay area. In Mexico, due to boundless environment exposures possibility to increase the risk of breast cancer. According to previous research study that the out of 1000 women, approximately 200 are suffering from breast cancer. Some of them were unaffected while some were categorized as carrier for breast cancer. There are chances of spread of the breast cancer is near about 95% according to the research of Mexico and WHO as well. During the research, it was found that the variation is must in the reproduction because chances of risk is high by the reproduction. The non-genetic mutation is necessary to prevent the spread of the disease [7].

Mounting

According to the research of WHO, the risk of breast cancer and ovarian cancer is more comparatively the weight will be less; hence it will be chances of breast cancer. During the therapy, the chances of reoccurrence of disease was shown when the patient makes sure to the recovery of the breast cancer by therapy and result shows negative impact rather than positive [21].

Relevance of Information

Varying information with varying number of physicians is a matter of great concern for the patients regarding complications and benefits of treatment. The hypothesis revealed that patient must accept physician's treatment and must be more specific [21].

Patient's Trust in the Therapy

One of the mythological beliefs of the people is that the trust play significant role as treatment would be more effective and will be accepted more frequently and were assured the chances of reoccurrence if no further treatments are taken [21].

Power of Therapy Suggested by Therapist

We aware the patient to take proper treatment from physician as prescribed and other services like value added services [21].

Disorder Regarding Changes

Number of lymph nodes, area of tumor and medical care examination [21].

CAUSES OF BREAST CARCINOMA

Early onset and offset of menses, irregular menses, other signs including malfunctioning of ovaries, uterus. Along with, morphology and age of women also matters. This data becomes more reliable and quite important when observed at international level along with frequency and duration of lactation.

- Some women who have children, but they don't breastfeed to their children due to formation of nodes.
- Duration of lactation of women for each child (in case of more than 1).
- It mainly scene in developed country and chances to decrease by proper breast feeding by young women to their children's.
- In young girls early and late menarche or early and late menopause.

Ionization Radiations

Mammary tissue is quite prone to malignant developed by ionization radiation. Excess mammary carcinoma has been observed in patients given multiple radiotherapy, fluoroscopes, and blow up of the thymus gland, survival of atomic bombings etc.

Alcohol

As per the reviewed data, Women who consume excess drinks a day, develop a breast cancer by 50% as well as those who don't consume alcohol develop a risk less than 50%. Association to the radiation is a major cause to the breast cancer and is serving as a major source of clinical research.

- *Early Life:* Early life may also be major cause for developing breast cancer due to early puberty in females and development of secondary sexual characters. Women who start to copulate with men at an early age without attaining the maturity. Irregular menstrual cycle somewhat leads to the development of breast cancer,
- *Exogenous Hormones:* Ovarian hormones are commonly taken exogenously, either for contraception, or as replacement therapy for symptoms believed to be due to low levels of the natural products, usually during or after menopause. Other hormones, such as progesterone, steroids, oestrogen play an important role in the transmission of the disease.
- *Age:* At an early age, it may lead to the development of breast cancer. Mainly, it occurs at an age of 40–45, because at that menopause is about to start and pregnancy most probably occurs at this age, similarly the development of breast cancer is mainly reported during this time [13].

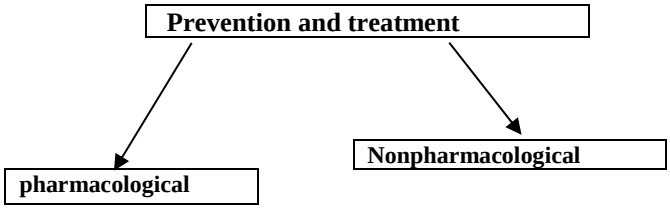

Figure 1. Prevention and treatment of breast cancer that occur by the gene BRCA1 and BRCA2.

Medication of Breast Cancer

- *Non-Pharmacological:* By physical activity like work out and control in weight, maintain diet, regular exercise, eat green vegetable, avoid fatty food, fast food, avoid smoking, excessive intake of alcohol and avoid the excessive intake of drugs in case of cancer (Figure 1).
- *Pharmacological*

- *Chemotherapy:* Used strong drugs to destroy the cancer cells.

Example of Drugs That Are Used in Chemotherapy

- *Alkylating Agents:* It is used in compound which alkylate the substance by joining through a covalent bond. They directly damage the DNA and prevent tumour cell by dividing. They produce cross linking of and mainly attack guanine residues of DNA. They are used in various disorder, such as breast carcinoma, sarcoma, ovarian syndrome examples mechlorethamine, thiotepa, busulfan [19].
- *Antibiotics:* They are not normal antibiotics used to treat infection but damage DNA inside cancer cells, for example, dactinomycin , daunorubicin, doxorubicin.
- *Plant Products:* Vincristine, Vinblastine from *Catharanthus roseus* is used in the treatment of breast cancer.

ADR of Chemotherapy

Hair loss, dizziness, drowsiness, hallucinations, etc. [27].

BREAST CANCER INCISION IN INDIA

Mostly incisions are done by the specialists in the early stage or initial days. According to the studies from hospitals and research centres the near about 80% patients who had abscission, so the biopsy is not possible which are referred for surgery whereas50% patients have seen early breast cancer or advanced breast cancer; this is only the reason behind any surgery or incision. In which some residues of infected cells remain in the area because the treatment was inadequate or insufficient. It may be due to poor quality of models, inefficient knowledge about patient, lack of diagnosis or analysis, circulatory system (lymphoid tissue). Incomplete biopsy report etc. Patient recommended for the evolution and re-surgery or repeat modification in the surgery and adjuvant treatment may require. According to studies and data of WHO, there is need to improve the surgical method from bad to good. Therefore, the poor quality of surgery replaced by the good quality to prevent the misleading to peoples or prevent from the re-surgery and complications [1].

Treatment by the Herbal Extracts

The herbal product shows many properties of anticancer. It also prevents from apoptosis, prohibition of proliferation. The herbal extracts stop the cell growth and suppress the tumor formation in the body. Near about the 3500 species of plants are used as the ant-cancer drugs. Some of the plants show the anti-cancer activities at laboratory scale [11].

CONCLUSIONS

The breast cancer and ovarian cancer is occurring by the genetic changes. It is observed that the 5 cases of breast cancer developing at the age below 60. So, the risk will be the 85%. If the loss of function and loss of inherit, mutation in one allele. For prevention, from the cancer there must be controls, like weight control, diet control and pollution control, etc., and the diagnose is done as soon as possible to reduce the excess growth of genes i.e. BRCA1 and BRCA2. We use the mammogram, blood test, breast ultrasound CT scan and MRI. Treatment is done by the chemotherapy by various routes i.e. oral, intravenous, intramuscular, etc. there are pharmacological and non-pharmacological action is there. The non-pharmacological treatment includes the intake of green vegetables, as well as exercise also includes. Avoid the alcohol consumption, pharmacological action includes some medications which is provided by the physician after proper diagnose.

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