

Breast Cancer: Its Types And Available Therapies

Arnika Singh, and Jeena Gupta*

Department of Biochemistry, School of Bioengineering and Biosciences, Lovely Professional University (LPU), Jalandhar-Delhi G.T. Road, Phagwara, Punjab (India) – 144411

E-mail: jeena.20104@lpu.co.in

Abstract: Nowadays we are noticing that, breast cancer is recorded as broadly detected dangerous disease amongst women and the primary reason of death from disease among women. Work on breast cancer has resulted in significant enhancement in our understanding of the disease over the last two eras, which result in highly efficacious and harmless therapies. Improved public knowledge and screening methodology have resulted in identification at early stages likely to provide curative therapies and surgical resection. Accordingly, the rate of survival from breast cancer has improved significantly, predominantly in young women. This article is about the breast cancer and its types and different kind of therapies associated with it to treat the breast cancer.

Introduction

Breast cancer is something which is occurring mostly among women and it is second most occurring reason of death among women all over the world. Breast cancer is defined as the cancer which initiates from the tissues present in breast, mostly initiates at the innermost lining of ducts supplying milk or lobules which supply milk with ducts. Throughout the world, the occurrence of breast cancer accounts around 10.4 % among all cancers in women, and due to this it is one the second types of cancers (non skin) most common after lung cancer, also due to this it comes in 5th position in causing death due to cancer. If we see the report of breast cancer according to WHO statistics, in 2004 due to breast cancer 519,000 people died worldwide. If we compare women and men, it shows about 100 times more occurrences among women than men but due to late in diagnosis, males possess poor results. [1]

Similarly, during measuring the approximate number of age matched deaths from breast cancer between 2011 and 2015 by examining the proportional deaths for different age group to the total estimated deaths in year 2017. The approximate female deaths from breast cancer shows aversion due to decreased levels of death from breast cancer was determined by first calculating the death number from cancer that may resulted if the rate of deaths had remained at its 1989 point. The predicted death toll was calculated by applying the age- death rates in 1989 from cancer to the 1990 to 2015 corresponding age- populations. The discrepancy between the reported age matched cancer deaths to the predicted numbers shows the overall aversions breast cancer. The similar approach was used to impute missing data in status of progesterone receptor (PR) and estrogen receptor (ER) [9], while assuming the random absence of PR and ER and conditional on diagnosis year, race / ethnicity, sex, and ER / PR status. In particular, the joint distribution of ER and PR status (negative, positive and missing) was used for 2- stage imputation.

In the first phase, the missing PR or ER status cases (not both) were allocated to either negative and positive ER / PR groups based on the distribution of established ER / PR status in each year, race / ethnicity, age and ER / PR category. Second step includes, those cases

having missing status of both PR and ER which were allocated to HR-positive (either PR-positive or ER-positive) and HR-negative (both PR-negative and ER-negative) groups based on the updated HR status distribution obtained in step 1. [2]

Cancer cells look exactly like their originated normal cells of organisms and possess similar DNA and RNA but it is not identical. It is the main reason that the immune system of human being couldn't able to detect if weakened particularly. Cancerous cells generally composed from cells normal and it mainly occurs due to modification and mutation in DNA and RNA. The reason behind occurring such mutations is due to spontaneous increase in thermodynamics law entropy or may be other factors are also included in inducing them and such factors are electromagnetic radiation (ultraviolet rays, microwaves, gamma rays, x-rays etc.), nuclear radiation, bacteria, viruses and fungi are also one of the reasons to induce the cancerous cells, parasites (due to irritation, heat, tissue inflammation, chemicals present in the air).

Ageing of DNA and RNA also one of the reasons to cause cancer cells to mutate. All these factors mentioned above are the reasons to create mutation due to which cancer occurs or initiates. Therefore, cancer can be referred as 'entropic disease' as it is linked with the increase of entropy among organisms to a point where the organism is unable to correct this itself. External affairs are necessary to allow organism to be able to go back to an entropic stable state. Main reason behind developing of cancers is that our system is not working properly or may be cell counts is too much for the immune system unable them to eliminate. Under some conditions such as radiation, chemicals, which increase the rate of DNA and RNA mutation, poor diet is also one of the reason for mutations in RNA and DNA. People with age above 80 and genetic predisposition are also causing mutations in RNA and DNA.

Types of Breast Cancer

As we already discussed that breast cancer is the commonly diagnosed cancer among women in US and worldwide, it is generally referred as heterogeneous disease. It is generally divided into:

1. *INSITU* BREAST CANCER

Ductal carcinoma in situ: women who suffers from ductal carcinoma in situ or also referred as stage 0 breast cancer mostly face a second primary breast cancer (DCIS or invasive) and some of them also die due to the breast cancer [3].

Ductal carcinoma in situ (DCIS) is an occurrence of proliferation of neoplastic epithelial cells restricted to the mammary ducts with invasion, consist of mammographically detected breast neoplasms about 25% to 50%. Before anyone perform the mammography, DCIS is appearing as a palpable mass, discharge from the nipple or the formation of benign lesion [4]. Lobular carcinoma in situ patients are at higher risk for the cause of invasive cancer. In this kind of insitu cancer of female breast generally emerge at the end parts of the lobule to which it is called as lobular carcinoma in situ. It virtually is not possible to diagnose the lobular carcinoma in situ by examining clinically. [5]

2. *INVASIVE* BREAST CANCER

Invasive carcinoma ductal and invasive carcinoma lobular are the most common invasive breast cancer types. Invasive lobular breast cancer also contains various subtypes and those are low grade adenosquamous carcinoma, adenoid cystic carcinoma, medullary carcinoma, papillary carcinoma, mucinous carcinoma, and tubular carcinoma [6]. Adenoid cystic carcinoma is one of the rare form of histologic form of breast cancer consist in most series less than 1% of all mammary cancers. Tumour appeared in salivary glands, upper respiratory tract, and other sites are similar to adenoid cystic carcinoma if see the pattern microscopically

[7].

Low grade adenosquamous carcinoma is a type of metaplastic breast cancer which rarely occurs and shows both glandular and squamous differentiation. Due to their overlapping problem with benign lesions is difficulty in diagnosing. It is generally defined as formation of well developed glands mixed with solid mass of squamous cells in a spindle cell [8]. Medullary carcinoma is a type of cancer that enter the skin, ulcerates and result in the formation of large masses produce rapid axillary node involvement and generally develop during lactation [9]. Mucinous is also a rare type of carcinoma which occur only about 2% breast cancers. Its gene expression profile is different from invasive ductal carcinoma. It shows lot of product of extracellular or intracellular mucin [10]. Papillary carcinoma shows the prevalence of invasive as well as *in situ* papillary carcinoma occur in post-menopausal women and sometimes in males. It include cellular proliferation around fibrovascular cores and can be with or without invasion [11].

Tubular carcinoma is known to exhibit favorable prognosis, it is impossible to find out whether it shows a distinct type of breast cancer or it may show the behaviour like other low grade luminal A-type breast cancer [12]. There are also such cancers whose occurrence is rare and these are inflammatory breast cancer, Paget's disease of the nipple, phyllodes tumours of the breast, metastatic breast cancer, triple negative breast cancer, male breast cancer.

Different Therapies for treating breast cancer

As far we discussed different types of breast cancer and to treat such kind of breast cancer there is no particular type of therapies that's why for every type of breast cancer there is different types of therapies have been followed. For *in situ* cancer there are different kind of therapies like lumpectomy, radiation therapy, mastectomy and for invasive breast cancer therapies such as use of biomarkers, unopposed estrogen, adjuvant radiations, preoperative therapy, targeted therapies, and hormone therapy.

a. Lumpectomy: Lumpectomy is the *in situ* cancer therapy generally done after radiation therapy, but only selected patients who are at the early stages of breast cancer. [13]

b. Radiation therapy: With the help of radiation therapy there is an improvement in cancer specific survival with post mastectomy RT. It can limit or reduce the toxicities in the normal tissues and increase the survival rate. As it is safe and efficacious dose, 3D treatment and intensity modulated RT is exposed as possible mechanism for improving RT delivery. [14]

c. Mastectomy: Sometimes women suffering from breast cancer unable to tolerate breast conserving therapy and in some cases it doesn't work then mastectomy with nipple areolar complex will be the good and safer approach. [15]

d. Biomarkers: Biomarkers play an important role in treating breast cancer as due to this biomarker which is formed predictively there is lot of changes in the treatment of breast cancer. It allows the application of more individualized therapies to different molecular subgroups. Some biomarkers like estrogen receptor and progesterone play an important role in selective patient benefitted from endocrine therapy. [16]

e. Hormone therapy: Hormone therapy includes endocrine therapy which came into existence more than 100 years ago but still it's one of the most effective treatment for positive hormone receptor breast cancer patients and tamoxifen is the widely used selected estrogen receptor modulator and it is one of the best known therapy for this positive hormone receptor breast cancer [17].

f. Targeted therapies: According to (FDA) targeted therapies is considered as approved label drug which are having a specific reference to a previously or simultaneously approved test of diagnosis which must be performed in the patient before the considered eligibility to

receive the drug. Example of this definition for targeted therapy is the approval of drug trastuzumab and the eligibility of diagnostic tests for selecting patients featuring expression of HER-2/neu protein or its gene amplification [18].

Strategies can be adopted to activate the immune cells which can fight against the cancerous cells and kill them. The M2 macrophages seem to support the growth of tumor cells, but M1 macrophages fight against the cancer cells. The recruitment of M2 macrophages is guided by VEGF, and it is observed in decidua during pregnancy that VEGF promotes polarization of macrophages to M2 type which supports the embryo implantation and successful pregnancy [19]. However, intervention in polarization can yield more M1 type and that can fight against the breast cancer cells. Novel drug delivery approaches are adopted for treatment of different types of cancers as discussed by Sharma et al. (2019) for lung cancer therapy [20]. Similar strategies can be adopted in breast cancer therapy as well. It is found that lung cancer can be diagnosed by CT images through image processing as studied by Chaudhary et al. (2012) [21]. The drug docetaxel delivery to breast cancer cells has been studied by Raza et al. (2015) by using C60 fullerenes [22]. Colloidal nano drug delivery system has added advantage for therapy of various cancer diseases besides its other uses [23]. Many studies on breast cancer and other cancer types have been done with successful findings [24-28].

DISCUSSION AND CONCLUSIONS:

The breast cancer occurrence in female with cases like mucinous carcinoma can be observed only about 2% of breast cancers and adenoid cystic carcinoma consist about 1% of total breast cancer population. We also concluded that papillary carcinoma generally occurs in postmenopausal women. There are other symptoms like nipple discharges, lumps and skin changes shows the occurrence of breast cancer. Now-a-days there are many methods for treating the cancers of breast such as mastectomy, radiation therapy, lumpectomy, hormone therapy, targeted therapies and biomarkers therapy. The death rate can be reduced with the help of diagnosis and treatment. Facts also show that large number of diagnosed women having breast cancers survive for maximum years. Still research is in progress for developing more effective therapy with any side-effects because in most cases it is not completely diagnosed or treatable.

References:

1. Sharma, G. N., Dave, R., Sanadya, J., Sharma, P., & Sharma, K. K. (2010). Various types and management of breast cancer: an overview. *Journal of advanced pharmaceutical technology & research*, 1(2), 109.
2. DeSantis, C. E., Ma, J., Goding Sauer, A., Newman, L. A., & Jemal, A. (2017). Breast cancer statistics, 2017, racial disparity in mortality by state. *CA: a cancer journal for clinicians*, 67(6), 439-448.
3. Kinne, D. W., Petrek, J. A., Osborne, M. P., Fracchia, A. A., DePalo, A. A., & Rosen, P. P. (1989). Breast carcinoma in situ. *Archives of Surgery*, 124(1), 33-36.
4. Pendas, S., Dauway, E., Giuliano, R., Ku, N., Cox, C. E., & Reintgen, D. S. (2000). Sentinel node biopsy in ductal carcinoma in situ patients. *Annals of surgical oncology*, 7(1), 15-20.
5. Fisher, E. R., & Fisher, B. E. R. N. A. R. D. (1977). Lobular carcinoma of the breast: an overview. *Annals of surgery*, 185(4), 377.
6. Downs-Holmes, C., & Silverman, P. (2011). Breast cancer: overview & updates. *The Nurse Practitioner*, 36(12), 20-26.
7. Ro, J. Y., Silva, E. G., & Gallager, H. S. (1987). Adenoid cystic carcinoma of the breast. *Human pathology*, 18(12), 1276-1281.
8. Tan, Q. T., Chuwa, E. W. L., Chew, S. H., Lim-Tan, S. K., & Lim, S. H. (2015).

Low- grade adenosquamous carcinoma of the breast: a diagnostic and clinical challenge. *International journal of surgery*, 19, 22-26.

9. Moore Jr, O. S., & Foote Jr, F. W. (1949). The relatively favorable prognosis of medullary carcinoma of the breast. *Cancer*, 2(4), 635-642.

10. Lacroix-Triki, M., Suarez, P. H., MacKay, A., Lambros, M. B., Natrajan, R., Savage, K., ... & Reis-Filho, J. S. (2010). Mucinous carcinoma of the breast is genomically distinct from invasive ductal carcinomas of no special type. *The Journal of pathology*, 222(3), 282-298.

11. Pal, S. K., Lau, S. K., Kruper, L., Nwoye, U., Garberoglio, C., Gupta, R. K., ... & Somlo, G. (2010). Papillary carcinoma of the breast: an overview. *Breast cancer research and treatment*, 122(3), 637-645.

12. Rakha, E. A., Lee, A. H., Evans, A. J., Menon, S., Assad, N. Y., Hodi, Z., ... & Ellis, I. O. (2010). Tubular carcinoma of the breast: further evidence to support its excellent prognosis. *Journal of clinical oncology*, 28(1), 99-104.

13. Smitt, M. C., Nowels, K. W., Zdeblick, M. J., Jeffrey, S., Carlson, R. W., Stockdale, F. E., & Gfinet, D. R. (1995). The importance of the lumpectomy surgical margin status in long term results of breast conservation. *Cancer*, 76(2), 259-267.

14. Vicini, F. A., Sharpe, M., Kestin, L., Martinez, A., Mitchell, C. K., Wallace, M. F., ... & Wong, J. (2002). Optimizing breast cancer treatment efficacy with intensity- modulated radiotherapy. *International Journal of Radiation Oncology* Biology* Physics*, 54(5), 1336-1344.

15. Cense, H. A., Rutgers, E. T., Cardoso, M. L., & Van Lanschot, J. J. B. (2001). Nipple- sparing mastectomy in breast cancer: a viable option? *European Journal of Surgical Oncology*, 27(6), 521-526.

16. Weigel, M. T., & Dowsett, M. (2010). Current and emerging biomarkers in breast cancer: prognosis and prediction. *Endocrine-related cancer*, 17(4), R245-R262.

17. Tokunaga, E., Kataoka, A., Kimura, Y., Oki, E., Mashino, K., Nishida, K., ... & Ohno, S. (2006). The association between Akt activation and resistance to hormone therapy in metastatic breast cancer. *European Journal of Cancer*, 42(5), 629-635.

18. Ross, J. S., Schenkein, D. P., Pietrusko, R., Rolfe, M., Linette, G. P., Stec, J., ... & Hortobagyi, G. N. (2004). Targeted therapies for cancer 2004. *American journal of clinical pathology*, 122(4), 598-609.

19. Wheeler, K.C., Jena, M.K., Pradhan, B.S., Nayak, N., Das, S., Hsu, C.-D., Wheeler, D.S., Chen, K. & Nayak, N.R. (2018). VEGF may contribute to macrophage recruitment and M2 polarization in the decidua. *PLoS One*, 13(1), e0191040.

20. Sharma, P., Mehta, M., Dhanjal, D.S., Kaur, S., Gupta, G., Singh, H., Thangavelu, L., Rajeshkumar, S., Tambuwala, M., Bakshi, H.A., Chellappan, D.K., Dua, K. & Satija, S. (2019). Emerging trends in the novel drug delivery approaches for the treatment of lung cancer. *Chemico-Biological Interactions*, 309, 108720.

21. Chaudhary A., Singh S.S. (2012). Lung cancer detection on CT images by using image processing. *Proceedings: Turing 100 - International Conference on Computing Sciences, ICCS 2012*.

22. Raza K., Thotakura N., Kumar P., Joshi M., Bhushan S., Bhatia A., Kumar V., Malik R., Sharma G., Guru S.K., Katara O.P. (2015). C60-fullerenes for delivery of docetaxel to breast cancer cells: A promising approach for enhanced efficacy and better pharmacokinetic profile *International Journal of Pharmaceutics*, 495(1):551-559.

23. Mishra V., Bansal K.K., Verma A., Yadav N., Thakur S., Sudhakar K., Rosenholm J.M. Solid lipid nanoparticles: Emerging colloidal nano drug delivery systems. *Pharmaceutics*,

10(4), 191, 2018.

24. Grewal R.K., Pathania A.S., Chawla M. Human sialyltransferases and its interaction with anticancer phytochemicals. *International Journal of Pharma and Bio Sciences*,5(3),2014.

25. Duggal S.K., Saroya A.S., Chauhan J.S. Complementary and alternative medicine approaches in the treatment of cancer. *Alternative Medicine: Practices, Health Benefits and Controversies*, 2013.

26. Chaudhary A., Singh S.S. Lung cancer detection on CT images by using image processing. *Proceedings: Turing 100 - International Conference on Computing Sciences, ICCS 2012*.

27. Patel S. Cereal bran: The next super food with significant antioxidant and anticancer potential. *Mediterranean Journal of Nutrition and Metabolism*, 5(2), 2012.

28. Bhatia A., Singh B., Raza K., Shukla A., Amarji B., Katare O.P. Tamoxifen-loaded novel liposomal formulations: Evaluation of anticancer activity on DMBA-TPA induced mouse skin carcinogenesis. *Journal of Drug Targeting*, 20(6),2012.