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Short Communication

Breast Cancer: Current Knowledge and Future Perspective

Sandeep Kumar Singh[1] and Sachidanand Singh[2]*

[1]*Research Scientist, GenTox Research and Development, Lucknow, India*

[2]*Dean, Faculty of Biotechnology, Institute of Bio-Sciences and Technology, Shri Ramswaroop Memorial University, Lucknow, India*

***Corresponding Author:** Sachidanand Singh, Dean, Faculty of Biotechnology, Institute of Bio-Sciences and Technology, Shri Ramswaroop Memorial University, Lucknow, India.

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In coming years, breast cancer may become the leading cause of cancer worldwide, as it is also evident by global cancer statistics provided by GLOBOCAN [1]. In 2018, breast cancer along with lung cancer was the most commonly diagnosed cancer (11.6%). It is still one of the major causes of death in women [1-3]. Unrestrained progression of malignant cells in the mammary epithelial tissue is one of the main characteristics of breast cancer [3]. Though breast cancer affects different areas of breast such as lobules, ducts or tissues in between, type of breast cancer is defined by affected cell type. Further classification is based on invasiveness and pathological features of breast cancer, such as non-invasive, invasive and metastatic cancer [3].

Like most part of the world, breast cancer is a major cause of morbidity and mortality in India [2]. In comparison to developed world, mortality rate is much higher in India. In India, we have National Cancer Registry Program which provides comprehensive epidemiological data from 25 population-based cancer registries to shed light on current incidence rate, mortality rate, cancer type and some other important information. These reports suggest a variation in age adjusted incidence rate of breast cancer [2]. Breast cancer patient's demography suggests women living in urban area are more prone to breast cancer in comparison to women living in rural areas. This can be attributed to altering life style of urban population.

Nature and nurture both play important role in disease etiology of complex diseases such as breast cancer [4]. Epidemiological studies in India have identified several risk factors associated with increased breast cancer risk such as, no or less breast-feeding, obesity, lack of physical activity, higher waist to hip ratio, alcohol consumption, tobacco chewing, increasing age and low parity [2]. Marital status and literacy rate in women are also associated with breast cancer risk. It seems that there is a correlation between marital status and parity. Although breast cancer risk increases with age worldwide, but incidence rate is much higher in younger women, age 40 to 50, in India [2]. Why incidence of breast cancer is higher in younger women in India is still a major challenge to address. Majority of these studies are observational in approach, thus these studies only provide association with breast cancer risk, not causation. Hence, there is more research work to be done to establish causative factors in breast cancer risk in Indian women.

Some of these risk factors are causative and have been confirmed by applying experimental approaches in breast cancer studies [5]. For example, age is a well established risk factor for breast cancer morbidity and mortality. It has been suggested that it might be a cumulative effect of carcinogenic exposure, such as tobacco, certain chemicals, infections, hormonal changes and immunosenescence [5]. Evidence suggests a causal association between physical activity and breast cancer risk via lessening sex hormones production and immunoenhancing effect. Nulliparity is also a major risk factor as studies identified alterations in gene expression pattern in breast cancer tissues between nulliparous and multiparous women [5]. There are several other established risk factors of breast cancer risk such as, race and ethnicity, chest radiation therapy of previous cancer, exposure to diethylstilbestrol (DES), contraceptives for birth control, hormone replacement therapy (HRT) after menopause, excessive alcohol consumption, significantly overweight or obesity and less or no breastfeeding [3].

Family history is another major risk factor of breast cancer, as 5-10% of breast cancers are associated with genetic mutation [3]. *BRCA1* and *BRCA2* genetic mutation are the best example of heredi-

tary mutation in women. If a woman has inherited *BRCA1* or *BRCA2* mutation, she may have 70% chance of getting breast cancer by age 80 [3]. Risk of breast cancer of a woman harbouring these BRCA mutations also relies on diagnosis of breast cancer in other family members. Apart from *BRCA* mutations, *ATM, TP53, CHEK2, PTEN, CDH1, STK11* and *PALB2* mutations also increase the risk of breast cancer [3]. Nature and nurture together may have synergistic effects on the development of breast cancer.

Gene-environmental (G x E) interactions are an important research area of all diseases, including cancers [4]. It has been suggested that G x E interaction will be more productive to obtain estimate of population attributable risk, providing more comprehensive view of biological pathways through identification of novel genes and identification of more susceptible individuals to cancer [4]. For example, *NAT2, XRCC1* and lifestyle, *TGFB1* and exogenous hormones interactions have been implicated in breast cancer risk [4]. Nonetheless, all of these studies are candidate gene studies and suffer from inadequate sample size and multiple comparison issues [4]. Application of genome-wide interaction studies with increased sample size will be a better option to examine G x E interactions.

Although technological advancement has augmented our knowledge of breast cancer risk factors, breast cancer management and treatment, this malignancy is still a major public health concern worldwide [6]. It is now a well known fact that germline and somatic mutations not only increases the risk of a cancer, but also progression of a disease [6]. Utilization of these genetic risk factors for early detection, monitoring and cancer prognosis as biomarkers will be conducive. Genomics, transcriptomics, proteomics or next-generation sequencing are hallmark of current 'omics' approaches. Tons of -omics datasets are available and inclusion machine learning and artificial intelligence approaches will be beneficial to improve our knowledge, current research and treatment protocols.

It is important to identify individuals at higher risk of developing cancer [7]. Germline mutations such as *BRCA1* and *BRCA2* are pivotal for earlier diagnosis of breast cancer risk, however, somatic mutations may shed more light on tumour characteristics and address better selection of treatments, time and dose [7]. Hence, our current knowledge of breast cancer risk is moving towards cancer precision medicine where we will be able to target a proper treatment to an individual breast cancer patient. Public health approaches such as breast cancer awareness program, screening and preventive measures are required across India [2]. Due to paucity of these public health approaches, majority of Indian women reach hospital at advance and metastatic stage. Apart from awareness programs and medical treatment, psychological treatment of breast cancer patients is also imperative. Earlier diagnosis of breast cancer will definitely improve overall survival in India.

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