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The Future of Breast Cancer in Pakistan in the Age of New Gene Mutation

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Abstract

Breast cancer is influenced by factors like advanced age, family history, early menstruation, lactation difficulties, and late menopause. Hereditary breast cancer often involves mutations in *BRCA1* and *BRCA2* genes. Recently, researchers identified a new gene mutation, ATRIP, associated with an increased risk of breast cancer, particularly in Pakistani women, leading to early-onset breast cancer. PARP inhibitors have shown promise in treating breast tumors with ATRIP mutations. However, Pakistan faces challenges in handling the escalating breast cancer cases due to limited resources and modifications in the future. Immediate action is crucial to address this serious issue effectively. Awareness campaigns, early detection programs, and genetic testing facilities should be prioritized to identify at-risk individuals and provide timely interventions. Collaborative efforts between the government, medical practitioners, and researchers are essential to tackle the growing breast cancer burden in the country.

Keywords: Breast cancer; Hereditary breast cancer; ATRIP gene mutation; Pakistani population

Introduction

Among women, breast cancer holds the highest occurrence rate of any cancer type, affecting approximately 2,261,419 individuals globally, making up 11.7% of all cancer cases. Moreover, it is the primary contributor to cancer-related deaths in women, claiming nearly 684,996 lives each year, accounting for nearly 6.9% of all cancer-related fatalities [1,2]. Breast cancer has several unchangeable factors, including advanced age, a family history of the disease, early menarche, the inability to lactate, and late menopause [3]. Various genetic and environmental variables increase the risk of morbidity and recurrence, particularly when they coexist. Ionizing radiation, hormone therapy, women's reproductive behaviors, alcohol, other dietary issues, obesity, and a lack of physical activity are examples of environmental and lifestyle factors [4]. In most cases, hereditary breast cancer arises from mutations in two specific genes known as *BRCA1* and *BRCA2*, which are associated with increased susceptibility to breast cancer. Other proven susceptibility mutations include CHEK2, RAD51D, ATM, PALB2, PTEN, RAD51C, BARD1, and TP53, along with BRCA1/2 [5]. Researchers recently discovered an uncommon gene mutation in March that may be attributed to an increased chance of breast cancer. For the first time in many years, a new susceptibility gene, ATRIP (Ataxia telangiectasia and Rad3-related interactive protein), has been identified to help medical professionals and researchers better comprehend the causes of hereditary breast cancer. They discovered the mutation in 42 Polish breast cancer patients and 13 British patients, which was sufficient for them to draw a connection between the gene mutation and breast cancer susceptibility. Although carriers with ATRIP mutations have a greatly increased chance of getting breast cancer, these mutations may be less common than other genetic variations [6]. The ATRIP is the primary activator of DNA damage signaling [7], making breast cancer's prognosis more lethal.

Breast cancer has a much higher incidence rate than other cancers in both developed (55.9 per 100,000) and underdeveloped (29.7 per 100,000) states [1]. It occurs less frequently in Asia than in the West overall. The primary cause of cancer among Southeast Asian women, however, is breast cancer, according to current figures [8]. According to GLOBACAN 2020 data, in the last five years, there have been 117,149 cancer deaths and 178,388 new cancer cases in Pakistan. Additionally, the total number of cancer cases identified during this period is 329,547 [1]. Some studies suggest that almost one in nine Pakistani women has breast cancer [9]. According to the Cancer Registry of Karachi, breast malignancy was the most common overall (27.7%). Certain high-penetrance genetic mutations, such as those found in *BRCA1*, *BRCA2*, p53, and PTEN genes, can elevate the lifetime risk of cancer by 50% to 85%, and 10% of breast tumors are caused by inherited genetic mutations

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[10]. Estimates suggest that approximately 5% of breast cancer cases in Pakistan are attributed to germline mutations in the *BRCA1* and *BRCA2* genes. The frequency of *BRCA1* or *BRCA2* mutations was recently shown to be 42.8% and 11.9%, respectively, in Pakistan, with numerous instances of breast cancer. As a result, Pakistani women with either of these harmful mutations are at increased risk for early-onset breast cancer [11].

The most common initial sign of breast cancer in women is a painless lump in the breast, which holds a significant predictive value for malignancy. Less frequent symptoms include evidence of bloody nappy discharge, heaviness, redness, swelling, breast deformity, or retractions [12]. The only screening technique that has been shown to lower breast cancer is mammography. Therefore, the American Cancer Society recommends commencing screening mammography at age 45 or earlier and breast MRI as a mammography augmentation for women with a risk of breast cancer of more than 20% [13]. Treatment choices for breast cancer can encompass surgery, radiation therapy, chemotherapy, and hormone therapy, depending on factors such as the histological subtypes, stage, and molecular subtypes of the cancer [14,15]. Patients who have the ATRIP mutation in their breast tissue exhibit certain traits known as Homologous Recombination Deficiency (HRD). Targeted treatment with PARP (poly(ADP)-ribose polymerase) inhibitors effectively treats tumors with HRD [6]. Patients' overall survival has increased as breast cancer treatments continue to evolve. 90% of deaths are caused by metastases, which can develop in 20% to 30% of breast cancer patients after diagnosis [15].

Unfortunately, with the existing mutations, breast cancer can develop suddenly and is the most common, often diagnosed, and fatal malignancy among Pakistani women. If ATRIP mutations arise in the Pakistani population, there is no guarantee that the incidence of cancer will rise; nonetheless, they may affect the behavior of cancer cells, including how quickly they grow and respond to therapy and if they can metastasize. As a result, researchers and medical practitioners may need to modify diagnosis, treatment, and prevention techniques due to new mutations' potential impact on the efficacy of already available treatments. A robust cancer referral system should be established for Pakistani women and increase patient awareness of the importance of obtaining medical treatment when suspecting breast cancer. With the increase in capacity at public-sector tertiary care institutions, shorter diagnostic intervals and improved patient outcomes, especially regarding cancer-related mortality, are expected to be achieved. Recognizing the significance of regular mammography is crucial for the early detection of breast cancer. Pakistan has to take action immediately to address the pressing issue of breast cancer. The reporting and recording of cases should be improved, community awareness should be increased, early identification of breast cancer should be encouraged, barriers to the construction of better medical facilities should be removed, and diagnostic procedures should be made more effective.

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